CHAPTER 1

OXIDATIVE CLEAVAGE OF FURANS

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CONTENTS

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INTRODUCTION

The furan ring plays important roles in many areas of chemistry and biology.[1−6] This oxygen-containing heterocyclic ring system is a component of a variety of natural product structures, such as those found in pheromone **1** from the beetle *Galerucella clamariensis*,[7] epothilone macrolides exemplified by **2**,[8,9] and marine products like bipinnatin J (**3**).[10−12] The furan ring is also embedded within the backbones of substances that have a broad range of biological activities, including insecticides (resmethrin[13] (**4**)), therapeutic drugs (ranitidine[14] (**5**), a histamine H_2-receptor antagonist), antibiotics (cefuroxime[15](**6**) from the cephalosporin family), and antihypertensives (prazosin[16] (**7**)).

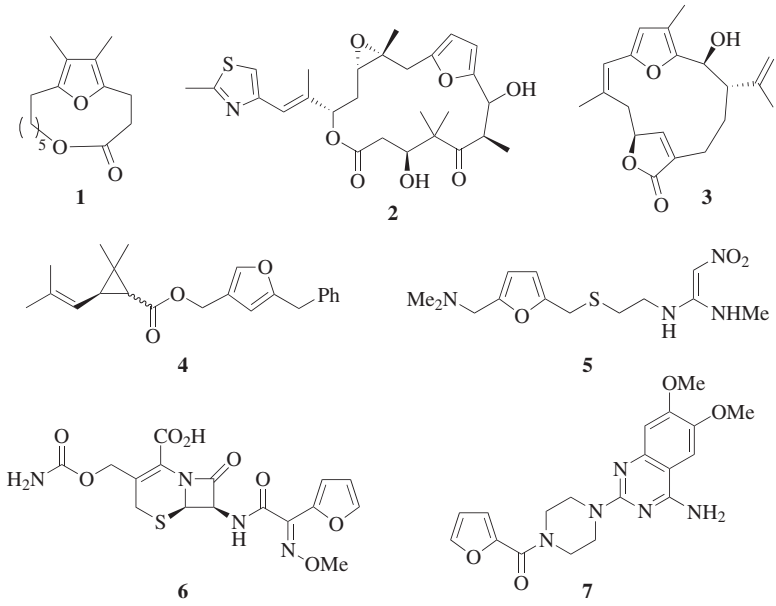
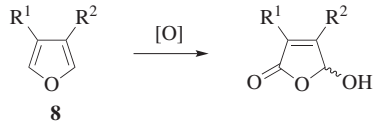


Figure 1. The furan ring system as a component of natural products and therapeutically active substances.

No discussion of furan chemistry would be complete without mentioning the intense efforts that have been directed at employing this heterocycle as a synthetic equivalent of a variety of four-carbon synthons. Owing to the presence of unsaturated carbons and an oxygen atom, furans have been used as starting materials for the production of polyhydroxylated compounds[17–19] and a number of natural products.[20,21] In the presence of different oxidizing agents[22] including bromine, chromium(VI) reagents, hydrogen peroxide, dioxiranes, and metal oxides, the furan ring is transformed to a variety of four-carbon, carbonyl-containing substances such as 1,4-dicarbonyl compounds.[23,24] One of the earliest examples of a process of this type involves oxidation of furan with vanadium pentoxide in the presence of air to generate maleic acid.[25] Several reviews have appeared describing photooxidation reactions of furans[26] and benzofurans,[27] as well as applications of furans in the synthesis of natural products[28] and multifunctional compounds.[29] Furan oxidation using peracids has also been reviewed.[30]

In many instances, oxidative cleavage reactions of furans produce molecular frameworks that contain functionality suitable for accessing a diverse range of organic compounds. Whereas 3,4-disubstituted furans **8** react to form butenolides under oxidative conditions (Scheme 1), their 2,5-disubstituted analogs **9** undergo oxidation reactions that afford corresponding 1,4-diketoalkenes (Scheme 2). In addition, depending on the nature of the oxidizing conditions used, C2 unsubstituted furans are transformed to 4-oxoalkenals ($R^2 = H$) or 4-oxoalkenoic acids ($R^2 = OH$).



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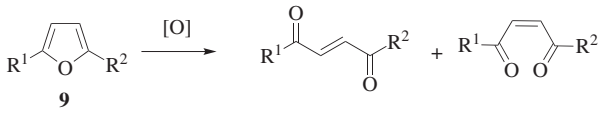
Scheme 1



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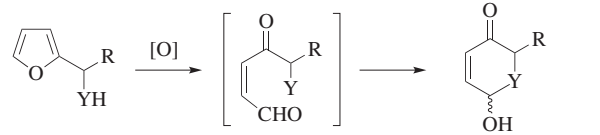
Scheme 2

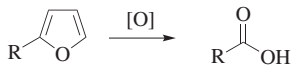
Furylcarbinols **10a** (Y = O) constitute a special case as the intermediate α,β-unsaturated aldehydes generated by oxidation undergo in situ cyclization to produce pyranones (Achmatowicz reaction) (Scheme 3), which have been employed as key intermediates in the synthesis of higher sugars.[31,32] A similar reaction, taking place upon oxidation of furfurylamines **10b** (Y = NH), has been used in the preparation of iminosugars.[33,34] Finally, because complete oxidation of furans generates the corresponding carboxylic acids, this oxygen heterocycle can be viewed as a protected form of a carboxylic acid moiety (Scheme 4).



10a Y = O furylcarbinols
10b Y = NH furfurylamines

pyranones
dihydropyridones

Scheme 3

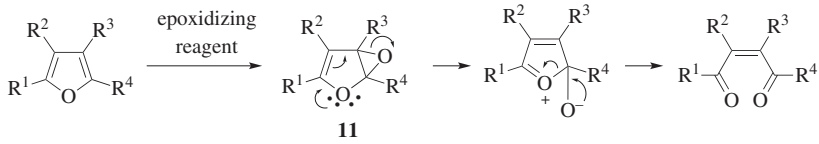


Scheme 4

MECHANISM AND STEREOCHEMISTRY

Some of the common oxidants employed for transforming furans into 1,4-dicarbonyl derivatives[24] are characterized by the presence of an electrophilic oxygen atom that is capable of acting as an epoxidizing agent. These oxidants include *m*-CPBA[35] and other peracids,[36] magnesium monoperoxyphthalate,[37] dimethyldioxirane,[38] oxaziridines,[39] and *tert*-butyl hydroperoxide (TBHP) in the presence of catalysts like $VO(acac)_2$,[40] $Mo(CO)_6$,[41] or Ti(IV) complexes.[42] It is

reasonable to assume that the first step in the oxidation reactions promoted by these reagents involves epoxidation of one of the double bonds of the furan ring system or related isobenzofurans[38] to form intermediate **11** (Scheme 5).[43] Importantly, initial formation of an intermediate epoxide in these processes has been demonstrated by using ^{18}O-labeled substrates.[44] Ring opening of intermediate **11**, which can be catalyzed by acids,[45] produces the 1,4-dicarbonyl product.[46] This mechanism is consistent with the observation that the corresponding *cis* isomers of the unsaturated 1,4-dicarbonyl products are generated in all cases. Moreover, the results of ^{18}O labeling studies demonstrate that the initial epoxidation process occurs preferentially on the more substituted double bond in the furan ring.[44]

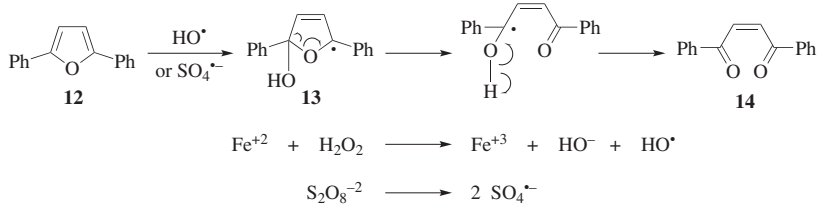


Scheme 5

Oxidations with Hydrogen Peroxide

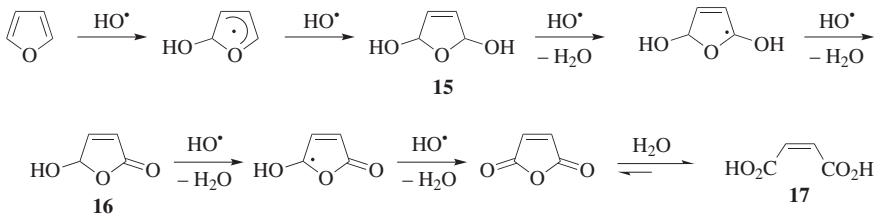
Additives. Oxidation reactions of furan derivatives with hydrogen peroxide have been carried out in the presence of a variety of promoters including sulfuric acid,[47] titanium(IV) silicalite,[48] methyltrioxorhenium,[49] sodium molybdate,[50] vanadyl sulfate,[51] and those described in the following sub-sections.

Iron(II) (Fenton's Reagent). Oxidation of 2,5-diphenylfuran (**12**) with hydrogen peroxide in the presence of Fe(II) (Fenton's reagent) to produce 1,4-diketone **14** takes place by a pathway involving addition of the in situ formed hydroxyl radical to the furan C2 position (Scheme 6).[52] The intermediate **13** generated in this manner can also be formed by treating furans with peroxydisulfate, which decomposes spontaneously in solution to form sulfate radical anions. Addition of a hydroxyl radical to furans has been studied using density functional theory (DFT) calculations. The results of these studies suggest that a pre-reactive hydrogen-bonded complex of furan and the hydroxyl radical is formed prior to addition yielding **13**.[53]



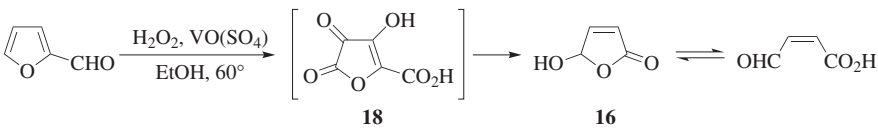
Scheme 6

Vanadium(IV) and (V) Salts. Oxidation of furans promoted by hydrogen peroxide in the presence of vanadium(IV) compounds also proceeds through a mechanism involving initial radical hydroxylation of the furan ring. This process, which yields 5-hydroxy-2(5*H*)furanone (**16**) and maleic acid (**17**), occurs through the intermediacy of 2,5-dihydroxy-2,5-dihydrofuran (**15**), which is usually not isolated (Scheme 7).[54] The reaction can be carried out either in a homogeneous aqueous alcohol solution or in a heterogeneous system in the presence of tridecylmethylammonium chloride. In both cases, the major product of the reaction is 5-hydroxy-2(5*H*)furanone (**16**), which exists in equilibrium with its tautomeric 1,4-dicarbonyl form, β-formylpropionic acid.[55] In the presence of ethanol, 5-ethoxy-2(5*H*)furanone is also generated.[56] Sodium acetate in the medium favors formation of the β-formylpropionic acid tautomeric form, a phenomenon that results in over-oxidation to succinic acid.[57]



Scheme 7

Oxidation of furfural with aqueous hydrogen peroxide in the presence of vanadyl sulfate and ethanol yields (*Z*)-4-oxobut-2-enoic acid (Scheme 8). Vanadyl sulfate exists in aqueous hydrogen peroxide as vanadium(V) peroxy complexes, which are the species responsible for the oxidation process. The proposal that this reaction proceeds through the intermediacy of keto lactone **18** is supported by isolation and full spectroscopic characterization of an ester derivative of **18**.[58] Although a mechanism for formation of **18** from furfural and for its transformation to malic acid has not been offered, the pathway to **18** does not involve the intermediacy of furoic acid.

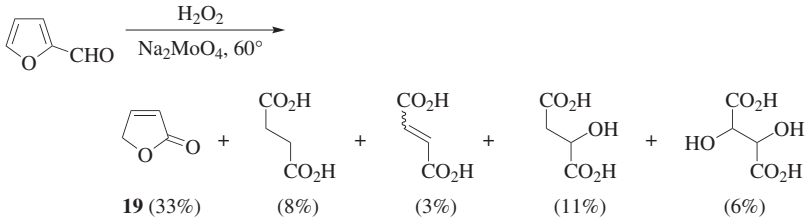


Scheme 8

Oxidation of furan in the gas phase at 300° in air, and in the presence of a vanadium–molybdenum–phosphorus catalyst on low-porosity corundum, to form maleic anhydride is proposed to take place through the generation of furyl radicals

on the surface of the catalyst.[59] This process is presumed to involve an initial electrophilic attack of the catalyst at C2 of the furan ring,[60] based on the results of infrared spectroscopic studies on the interaction between furan and the catalyst support.[61] Both the gas-phase oxidation of furans on vanadium catalysts and their liquid-phase oxidation on heterogeneous oxides, such as Ag_2O and Ag_2O/CuO, have been reviewed.[62]

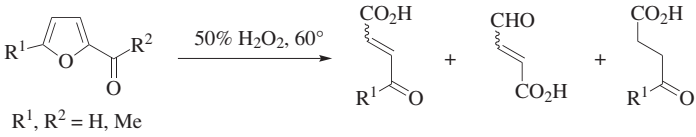
Molybdenum(VI), Chromium(VI), and Niobium Salts. The oxidation reaction of furfural with hydrogen peroxide in the presence of a catalytic amount of sodium molybdate, a source of Mo(VI), yields 2(5*H*)furanone (**19**) via a pathway that is thought to involve a molybdenum peroxide. Tartaric, malic, fumaric, and succinic acids are also formed as minor products in this process (Scheme 9).[63] Similar results are observed when this oxidation is conducted in the presence of potassium bichromate as a source of Cr(VI),[64] and $Nb(OAc)_2$ and Nb_2O_5 as sources of Nb(II) and Nb(V), respectively.[65] The conversion of 2(5*H*)furanone (**19**) into succinic acid under the reaction conditions has been demonstrated to take place in reactions performed at different pH values.[66]



Scheme 9

Spectroscopic studies, carried out on a Mo/Ti/O catalyst, have demonstrated that furan exhibits two adsorption modes on the surface of the catalyst,[67] and that the Mo=O bond in the catalyst does not play a role in the formation of maleic anhydride.

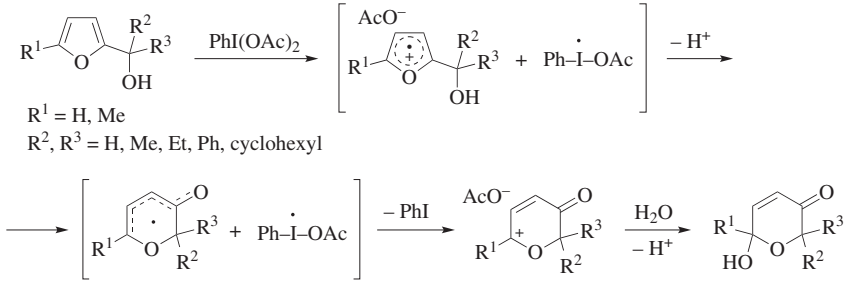
No Additives. Oxidations of furylketones and furfurals with hydrogen peroxide in the absence of additives have been studied.[68] Both furylketones and aldehydes undergo the same type reaction to give 1,4-dicarbonyl compounds (Scheme 10).



Scheme 10

Oxidations with Hypervalent Iodine Reagents

Cation radicals, similar to those produced in electrolysis and strong acid promoted reactions,[69] have been proposed to serve as intermediates in oxidation reactions of furan derivatives with $PhI(OAc)_2$ (Scheme 11),[70] and radical intermediates have been detected by using EPR spectroscopy. The addition of salts such as $Mg(ClO_4)_2$ or KBF_4 enhance the efficiency of the oxidation process.

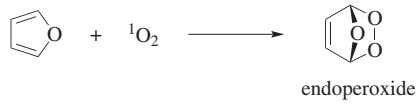


Scheme 11

Similar observations have come from studies of oxidation reactions of 9-furyl naphtho[2,3-*b*]furans with magnesium monoperoxyphthalate (MMPP) and pyridinium chlorochromate (PCC). The results of cyclic voltammometric studies suggest that these processes proceed through the intermediacy of 9-furyl naphtho[2,3-*b*]furan radical cations.[71]

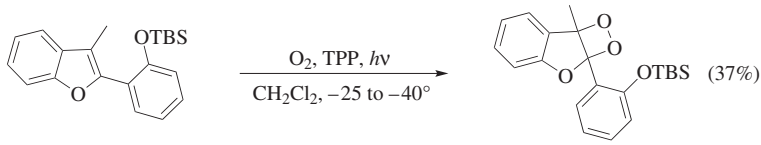
Photooxygenations with Singlet Oxygen

Furan derivatives react with singlet dioxygen through a formal [4 + 2] cycloaddition pathway to form ozonides (also called endoperoxides) that decompose in different ways depending on the reaction and work-up conditions.[72] Although several mechanistic pathways are possible for the formation of ozonides in these reactions, the results of kinetic experiments confirm that a concerted cycloaddition route is followed (Scheme 12).[26]



Scheme 12

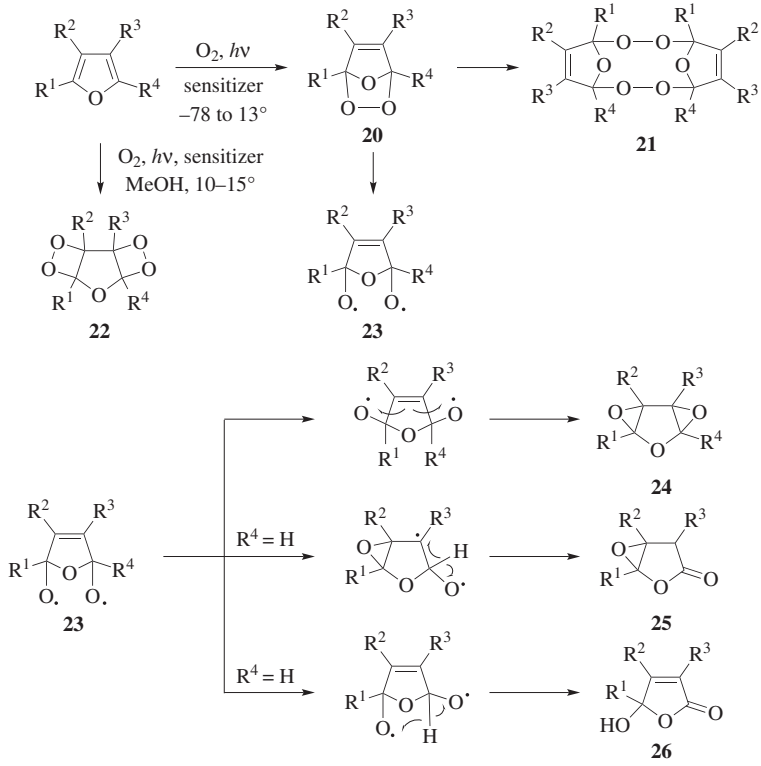
Singlet oxygen is usually formed through triplet energy transfer from a photosensitizer such as rose bengal, methylene blue, or tetraphenylporphyrin (TPP). When benzofuran derivatives are used as substrates for the photooxidation reactions, the corresponding dioxetanes are formed through [2 + 2] cycloaddition of molecular oxygen with the furan double bond (Scheme 13).[73]



Scheme 13

The use of pyrene as photosensitizer and solar or ultraviolet light irradiation for photooxidation of 1,3-diphenylisobenzofuran in aqueous dodecyltrimethylammonium chloride has been investigated.[74,75] In these reactions, chemical methods have been used to form singlet oxygen, such as those involving hydrogen peroxide with several reagents including PIFA ($PhI(OCOCF_3)_2$)[76] and heterogeneous catalysts containing MoO_4^-.[77] Other methods include generation of singlet dioxygen from fragmentation of monoactivated 1,1-dihydroperoxides.[78]

Ozonides **20** are typically produced in photooxidations of furans when irradiation is carried out in the presence of typical sensitizers, in solvents such as CCl_4, $CFCl_3$, CH_2Cl_2, benzene, acetone, or acetonitrile,[79] and at temperatures of −78 to 13° (Scheme 14). In some instances, these reactions occur even in the absence of

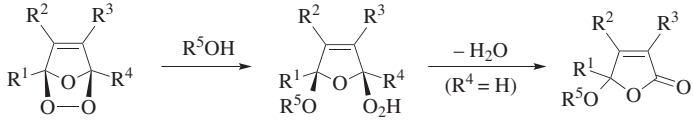


Scheme 14

sensitizers.[80] Photolysis of oxygen-saturated solutions of furan rings in the presence of the imidazolium-bound sensitizers provides the corresponding butenolides.[81] In addition, the use of rose bengal, either polymer-supported or immobilized on wool,[82] produces identical results. Under these conditions the ozonides **20** can be isolated at −15° and can be stored for several days. Bis-dioxetanes **22** have also been observed as products.[83] Ozonides **20** are observed to dimerize slowly to form bis-peroxide **21** in CCl_4 and $CFCl_3$ and more rapidly in 2:1 benzene/petroleum ether, and spontaneously and quantitatively at 55–60° in CCl_4.[79] Homolytic cleavage of the O–O bond in ozonides **20** produces biradical intermediates **23**,[84] which can form mono- and bis-epoxy derivatives **24** and **25** through epoxycyclization, followed by 1,2-hydrogen atom shifts when $R^4 = H$. In addition, biradical intermediates **23** can form 4-hydroxybutenolides **26** as a result of 1,4-hydrogen migration.

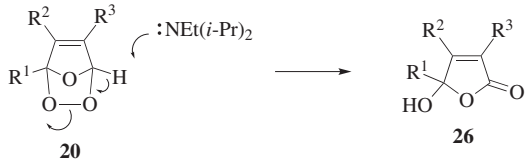
The distribution of products formed in photooxidation reactions is highly dependent on the substitution pattern of the furan derivatives and the reaction conditions. For example, whereas epoxylactones **25** and 4-hydroxybutenolides **26** are generated in the oxidation reactions of furans in benzene,[80] diepoxy derivatives **24** are also produced in reactions run in dichloromethane.[85] In some cases, mixtures of **24** and the corresponding 1,4-dioxoalkenes are also observed,[86] and when substituents are present that can exert neighboring-group effects other products are formed.[87]

Addition of primary and secondary alcohols to ozonides results in the formation of the corresponding alkoxyhydroperoxides **27**,[88] via a nucleophilic addition reaction that takes place stereoselectively to give *cis* OR^5 and OOH stereoisomers as a consequence of H-bonding between the incoming alcohol and displaced peroxy group (Scheme 15).[79] When a hydrogen is present at the hydroperoxide substituted carbon, **27** undergoes dehydration to form 4-alkoxybutenolides **28**.[80] As a result of these processes, hydroperoxides are formed when the singlet oxygen oxidation reactions of furans are carried out in alcohol solvents.[79] Moreover, depending on the work-up conditions employed, 4-alkoxy or 4-hydroxybutenolides are obtained as products of these reactions.



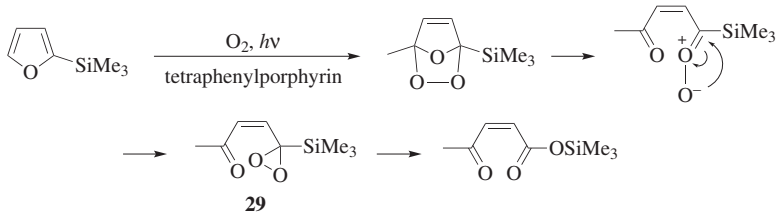
Scheme 15

Ozonides also participate in other non-radical processes. For example, the formation of 4-hydroxybutenolides from ozonides **20** ($R^4 = H$) can also be promoted by the action of bases such as diisopropylethylamine, which facilitates abstraction of the proton at C2 (Scheme 16).[89] This type of reaction can also be carried out in ionic liquids, the best results being obtained when chloride serves as the counter anion. Lower yields (11–16%) are obtained when the ionic liquids are associated with tetrafluoroborate, methyl sulfate, and lactate anions.[90]



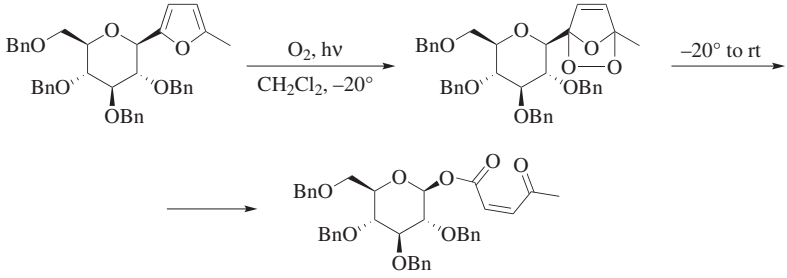
Scheme 16

Photooxygenation reactions of furan can generate 1,4-dioxoalkenes, which are believed to form through a pathway involving a sila-Baeyer–Villiger rearrangement of dioxirane intermediate **29** (Scheme 17).[91]



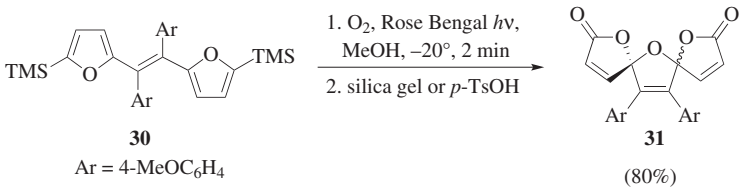
Scheme 17

Formation of 1,4-dioxoalkenes has also been rationalized by invoking a concerted mechanism involving 1,2-migration of the C2 substituent to the peroxide.[92] This type of process is often observed in photooxidation reactions of glycosylfurans,[86,93] indicating that the nature of the C2 furan substituent strongly influences the nature of the pathway followed in reactions of intermediate ozonides (Scheme 18).[94]



Scheme 18

In dimeric furans such as **30**, ozonide ring opening results in the formation of spirobutenolides **31** (Scheme 19).[95,96]



30

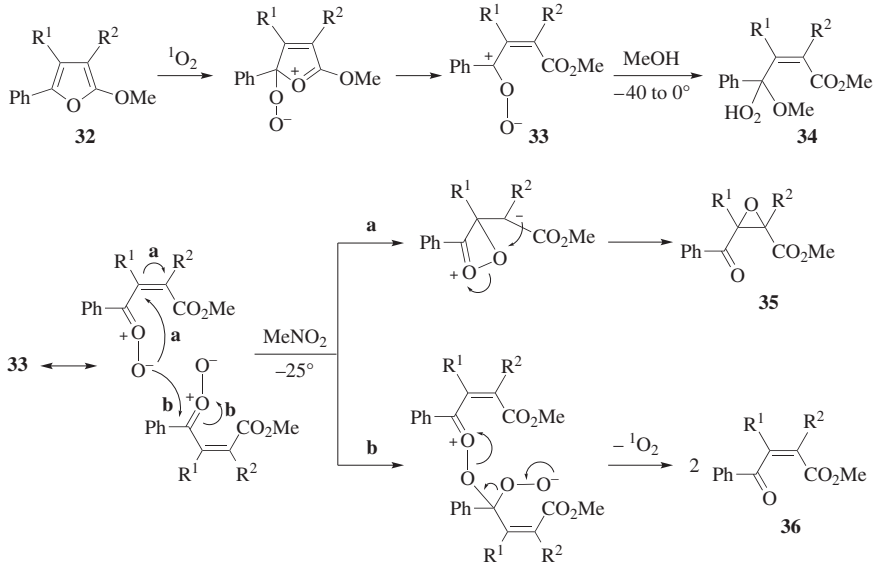
Ar = 4-MeOC$_6$H$_4$

31

(80%)

Scheme 19

Direct photooxygenation of 2-methoxy-5-phenyl furans **32** at −40 to 0° in MeOH yields α-methoxyhydroperoxides **34**, whose formation is proposed to take place through a carbonyl oxide intermediate **33** rather than via an ozonide followed by trapping with methanol (Scheme 20).[88,97] When these reactions are conducted in nitromethane, mixtures of epoxides **35** and 1,4-dioxoalkenes **36** are produced.[88] The formation of epoxides **35** can be rationalized by invoking a mechanistic route involving intramolecular Michael addition of the ylide oxygen atom to the double bond. In contrast, formation of dicarbonyl products **36** are believed to occur by dimerization of intermediate **33**. These processes serve as evidence for carbonyl oxide participation in sensitized photooxygenation reactions of furan derivatives.

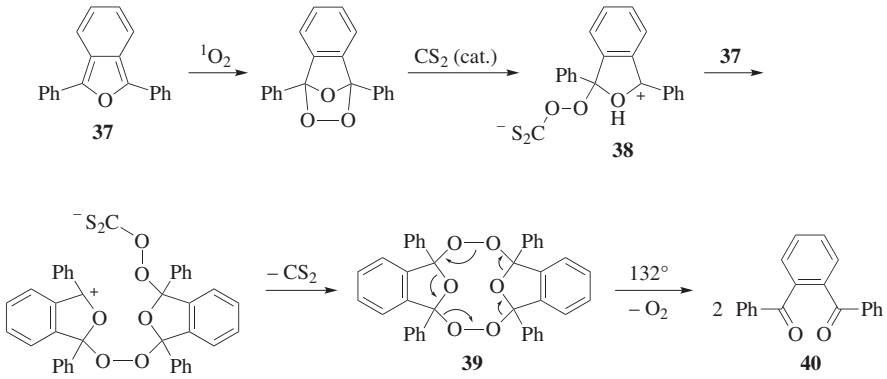


32 **33** **34** **35** **36**

Scheme 20

Photooxidations of furan and its 2- and 3-methyl derivatives in the presence of nitrous acid has been investigated using proton transfer reaction mass spectrometry. 1,4-Dicarbonyl compounds, the main products produced in the reaction, are formed by a radical process beginning with attack by a hydroxyl radical.[98] Carbon disulfide catalyzes dimerization of the ozonide derived from photooxygenation

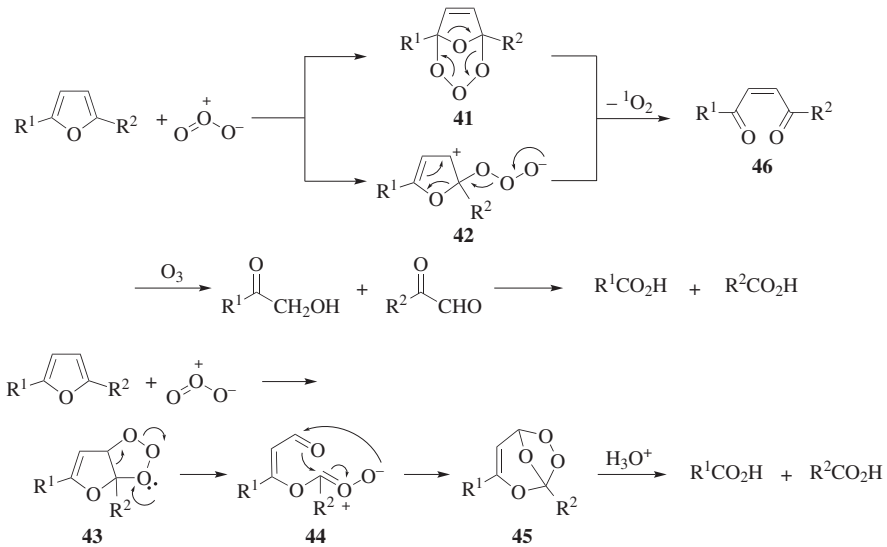
of 2,5-diphenylbenzoisofuran (**37**), a process that takes place via carbocationic intermediate **38**. The dimer **39** is then transformed to diketone **40** upon prolonged heating in chlorobenzene at 132° (Scheme 21).[99]



Scheme 21

Oxidations with Ozone

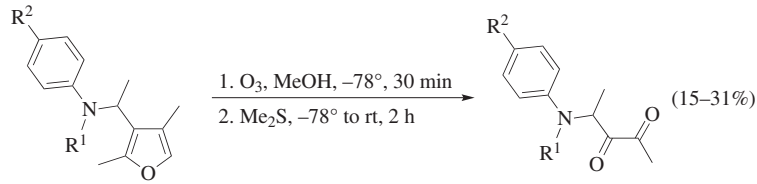
Reactions of furans with ozone may proceed by the formation of bicyclic intermediates **41** that are similar to the ozonide formed by cycloadditions with singlet oxygen.[100] Fragmentation of **41** may lead to the corresponding 1,4-dicarbonyl derivatives **46** (Scheme 22). An alternative mechanism involves electrophilic addition of ozone to the reactive α-position of the furan ring, leading to generation of zwiterionic



Scheme 22

intermediates **42**, which also can rearrange to generate the dicarbonyl compounds with loss of singlet oxygen.[101]

Ozone can also add to the double bond of the furan ring to give unstable primary ozonides **43**, which decompose through a cycloreversion process to give carbonyl ylide intermediates **44**. Intramolecular cycloaddition yields the more stable secondary ozonides **45**, which upon hydrolysis provide the corresponding carboxylic acids. The formation of intermediates **43–45** is in agreement with the Criegee mechanism suggested for ozonolysis of alkenes,[102] which has been further explored using ^{17}O spectroscopy[103] and confirmed experimentally.[104−106] Although hydrolysis of **45** can produce carboxylic acids, this reaction pathway is not the exclusive mechanism for carboxylic acid production.[107] It has also been proposed that the ozonization reaction first forms 1,4-dienones that undergo a second ozonization in which the double bond is cleaved, generating α-keto aldehydes,[108] which undergo further oxidation to form carboxylic acids. Indeed, glyoxal and methylglyoxal are observed products in ozonolysis reactions of furan and 2,5-dimethylfuran, respectively,[109] and 1,2-diketones are generated in ozonolysis reactions of tri- and tetrasubstituted furans (Scheme 23).[110] In some instances the two-step process involving 1,4-diketone formation and further oxidation can be accomplished in a sequential manner.[107] Finally, oxidations of furans to form carboxylic acids can be performed using ozone followed by dimethyl sulfide work-up,[111] a reaction that takes place through the same rearrangement process described above for endoperoxides.

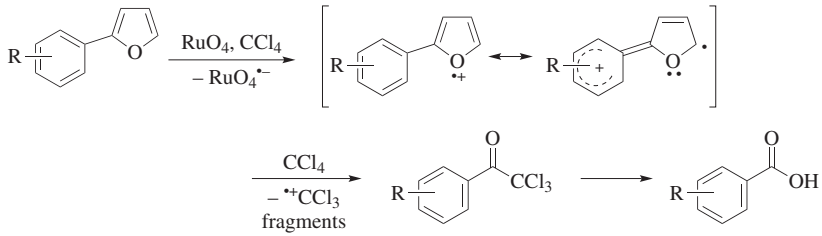


R^1 = Ac, CO_2Bn
R^2 = H, Cl, MeO

Scheme 23

Oxidations with Ruthenium Tetroxide

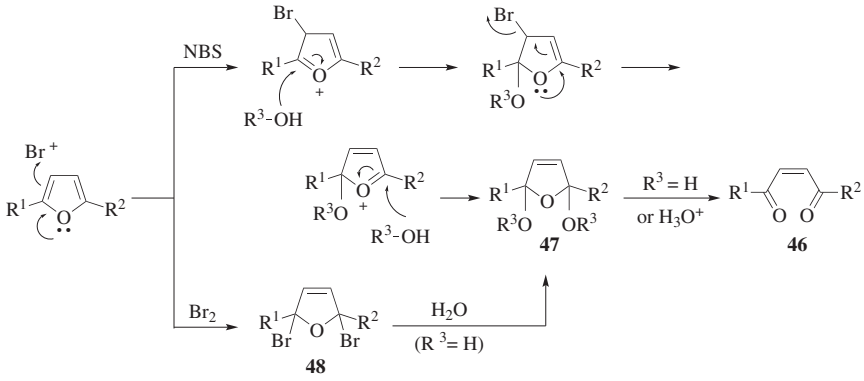
Ruthenium tetroxide is a strong oxidant that can be formed in situ by oxidation of a ruthenium(III) or (IV) compound such as $RuCl_3$ or RuO_2,[112] usually using $NaIO_4$[113] or other oxidants including KIO_4, NaClO, $NaBrO_3$, $Ce(SO_4)_2$, Oxone®, or H_5IO_6.[114] The participation of free-radical intermediates in oxidations of arylfurans with ruthenium tetroxide has been demonstrated using EPR spectroscopy (Scheme 24).[115] The results of a study based on furan adsorption on ruthenium at 80 K indicates that abstraction of oxygen by the furan ring takes place through the formation of a metallocycle-like intermediate.[116] The use of CCl_4 as the solvent is crucial for the success of this process owing to its promotion of the formation of intermediates that are precursors of the carboxylic acids. Moreover, due to the high reactivity of ruthenium tetroxide it must be used in halogenated organic solvents.[117]



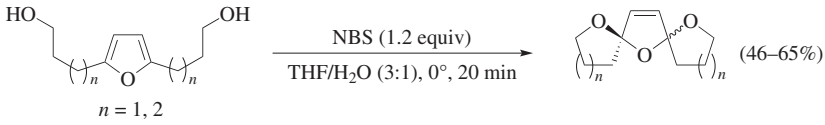
Scheme 24

Oxidations with *N*-Bromosuccinimide and Related Reagents

N-Bromosuccinimide serves as a source of bromonium ions, which undergo electrophilic addition to the furan ring. 2,5-Dialkoxydihydrofurans **47** ($R^3 \neq H$) or 1,4-dioxoalkenes **46** are generated when either alcohols or water, respectively, are used as solvents for the reaction. A similar mechanism is possible for transformations of furan derivatives to 1,4-dicarbonyl compounds by the action of bromine in water or methanol, although the formation of 2,5-dibromo-2,5-dihydrofurans **48** as intermediates has also been postulated.[118] In the latter mechanism, **48** is converted into the 2,5-dihydroxy derivative **47** ($R^3 = H$), which upon dehydration forms the 1,4-dicarbonyl compound **46** (Scheme 25).[119] Reactions of compounds containing hydroxy groups provide spiro derivatives through intramolecular addition (Scheme 26).[120]

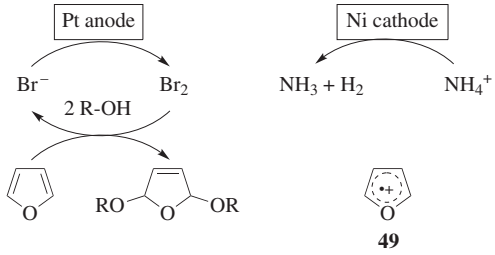


Scheme 25



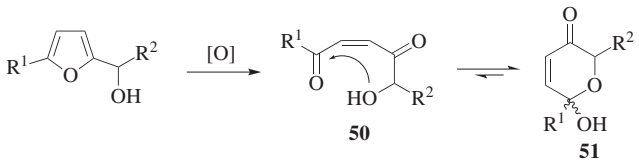
Scheme 26

Bromine can be generated in situ by electrochemical oxidation of salts such as NH_4Br.[121] Under these conditions, the reactions are cleaner and may involve the formation of tribromide anion (Br_3^-) (Scheme 27), an anion that has a similar redox potential to bromine. The radical cation **49** usually reacts with methanol.



Scheme 27

In the special case of furfuryl alcohols, initial oxidation leads to the production of 1,4-dicarbonyl derivatives **50**, which then undergo intramolecular addition of the hydroxy group to furnish the corresponding 6-hydroxy-2*H*-pyran-3(6*H*)-ones **51** through the well-known Achmatowicz reaction (Scheme 28).[31] A similar mechanistic pathway operates in reactions of furfurylamines, which yield 6-hydroxy-2*H*-pyrimidin-3(6*H*)-ones by the aza-Achmatowicz reaction.[33,34] It should be noted that isomers **50** and **51** exist in an equilibrium in which the cyclic isomer **51** is usually favored.



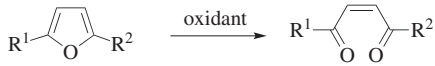
Scheme 28

SCOPE AND LIMITATIONS

Synthesis of 1,4-Dicarbonyl Compounds

1,4-Dioxoalkenes. 2,5-Disubstituted furans can be transformed to *cis* 1,4-dioxoalkenes utilizing a wide variety of reagents (Scheme 29).[24] In the first half of the 19th century, the first examples of oxidation reactions of di-, tri-[122] and tetrasubstituted[123] furan derivatives with nitric acid were described.[124] The procedure was also applied to oxidations of furans containing hydroxy functions in their side chains.[125] More recently, oxidation of triphenylfurans has been promoted by using milder conditions consisting of a stoichiometric amount of ammonium

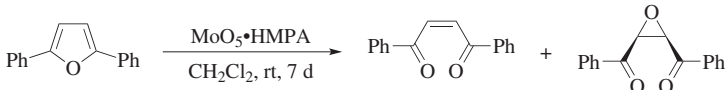
nitrate in refluxing 80% aqueous acetic acid.[126] These conditions have also been applied to the synthesis of 3-(2*H*)-furanones that have antitumor activities.[127] During the same period, oxidations of furan with air in the presence of various catalysts, including vanadium pentoxide, were developed[25] as were oxidations of 1,3-diphenylisobenzofurans with chromic acid.[128]



9 **46**

Scheme 29

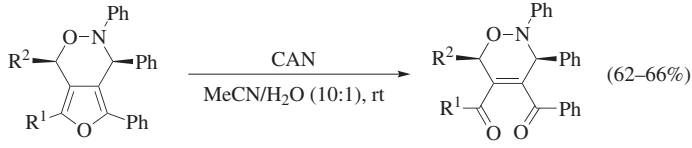
Metal Oxidants. The oxidation of 2,5-diarylfurans to *cis* unsaturated 1,4-diketones by the action of lead tetraacetate in chloroform was first studied in detail in 1957.[129] Low to moderate product yields attend these processes and some degree of substituent dependence is observed. 2,5-Diphenylfuran (**12**) is oxidized using MoO_5•HMPA to afford a mixture of *cis*-1,4-diphenyl-2-butene-1,4-dione (**14**) and *cis*-2,3-epoxy-1,4-diphenylbutane-1,4-dione (**52**) in 18% and 21% yields, respectively (Scheme 30).[130] Under the same conditions, benzo[*b*]furan reacts to yield a mixture of 2-hydroxy-3(2*H*)-benzofuranone (18%), 2(3*H*)-benzofuranone (7%), and salicylaldehyde (12%) with 15% of recovered starting material, rendering the process of limited synthetic utility.



12 **14** (18%) **52** (21%)

Scheme 30

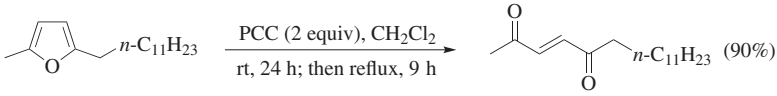
Metal-promoted oxidations are also possible using ceric ammonium nitrate (CAN),[131] but even though these reactions can be carried out in the presence of benzyl ethers they occur in low yields.[132] On the other hand, the compatibility of this method with the presence of N–O bonds leads to its application to the synthesis of 1,4-dienones in 62–66% yields (Scheme 31).[133]



R^1 = Me, R^2 = Ph
R^1, R^2 = $(CH_2)_3$

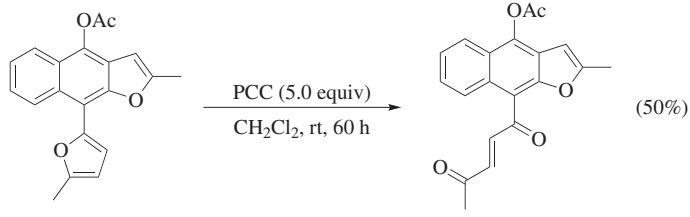
Scheme 31

2-Methyl-5-(2-pyrrolyl)furans react with CAN at low temperatures to afford *trans* 1,4-dicarbonyl derivatives. However, application of the same conditions to reactions of various 3-(2-pyrrolyl)furans leads to formation of products containing coupled furan rings.[134] In contrast, the use of pyridinium chlorochromate (PCC) for oxidations of alkyl furans produces *trans* 1,4-dienones (Scheme 32).[135]

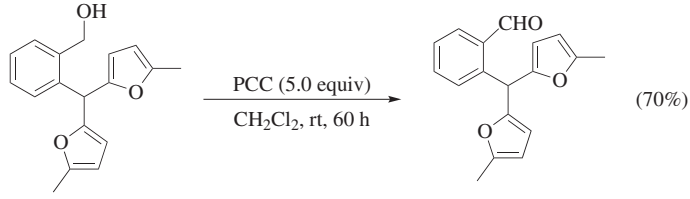


Scheme 32

By using PCC, it is possible to carry out selective oxidation of a furan ring in the presence of a benzofuran moiety (Scheme 33).[136] However, when a primary hydroxyl group is present, an aldehyde is selectively formed without oxidative cleavage of the heterocyle (Scheme 34). The reactivity of furans with Cr(VI) oxidants depends to a great extent on the reaction conditions. In some cases, it is possible to oxidize the side chain of furyl derivatives without altering the furan ring by carrying out the reaction using pyridinium dichromate (PDC) in organic solvents such as dichloromethane at 55° for 2 hours.[137]



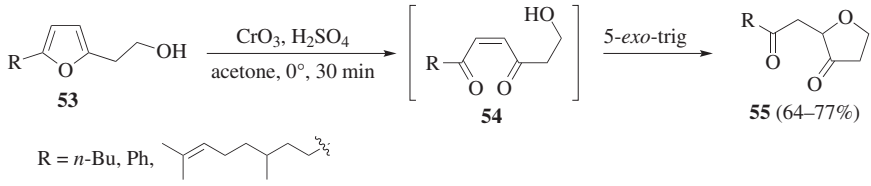
Scheme 33



Scheme 34

In contrast, oxidation of furanyl alcohols **53** with Jones reagent in acetone at 0° affords keto tetrahydrofurans **55**, through the intermediacy of 1,4-dicarbonyl compounds **54** (Scheme 35).[138] The formation of **55** takes place by 5-*exo*-trig cyclization

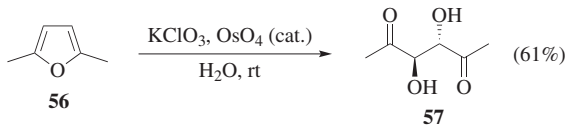
involving the hydroxy group in the side chain. However, 1,4-dicarbonyl compounds **54** are the isolated product when oxidation is carried out using magnesium monoperoxyphthalate
(MMPP).



Scheme 35

Indeed, the use of MMPP in oxidation of 2,5-dialkylfurans leads to high yields of *cis* enediones. These reactions take place in less than 1 hour at room temperature, with isomerization to form the *trans* enediones occurring after 2 hours at reflux.[139] This process cannot be used to oxidize substrates that contain electron-withdrawing groups directly attached to the furan ring.

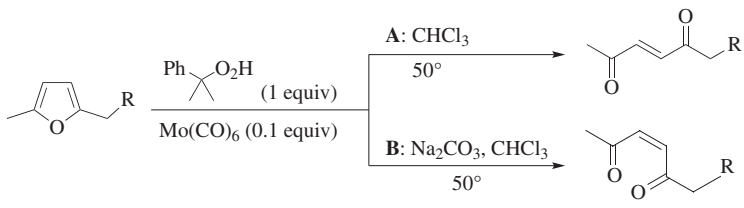
The potassium chlorate/osmium tetroxide oxidizing system is capable of transforming 2,5-dimethylfuran (**56**) into *erytho*-3,4-dihydroxyhexane-2,5-dione (**57**) in 61% yield (Scheme 36).[140] Similarly, this method can be applied to enantiomerically pure compounds and it tolerates amine protecting groups such as Cbz.[141]



Scheme 36

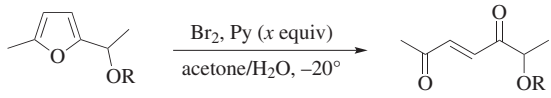
The use of peroxides in combination with metal catalysts is an effective oxidation strategy to ensure high degrees of conversions of furans to their oxidation products. Hydrogen peroxide in the presence of methyltrioxorhenium can be used to convert substituted furans to *cis* 1,4-dioxoalkenes in high yields.[49] Moreover, the reaction can be carried out using the safer urea/hydrogen peroxide complex (UHP). Cumyl hydroperoxide in the presence of $Mo(CO)_6$ also promotes oxidation reactions that generate *trans* 1,4-dioxoalkenes. Notably, if the reaction is carried out in the presence of sodium carbonate, *cis* isomers are obtained (Scheme 37).[41] Presumably, the presence of the base neutralizes the acid formed during the reaction, thus, preventing acid-catalyzed isomerization of the *cis* isomers to the more stable *trans* isomers.

Bromine. Oxidation of furans with bromine in aqueous medium under either acidic or basic conditions produces *trans* 1,4-dioxoalkenes in good yields.[118,142] The method is compatible with furans containing acetals[143] as well as protecting groups like benzoyl esters, and benzyl and silyl ethers (Scheme 38).[21]



R	Method	Time (h)	Yield (%)
n-C_4H_9	**A**	20	65
n-C_7H_{15}	**A**	16	67
n-C_9H_{19}	**A**	20	63
H	**A**	24	93
n-C_4H_9	**B**	20	64
n-C_7H_{15}	**B**	20	61
n-C_9H_{19}	**B**	24	63
H	**B**	12	53

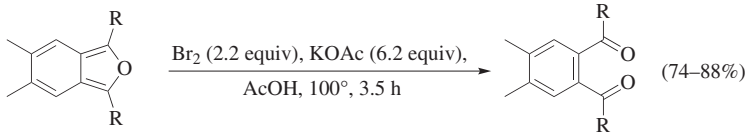
Scheme 37



	Yield (%)	
R	*x* = 4	*x* = 0
$PhCH_2$	89	87
PhCO	88	80
$MeOCH_2$	75	82
t-$BuMe_2Si$	73	83
t-$BuPh_2Si$	91	88

Scheme 38

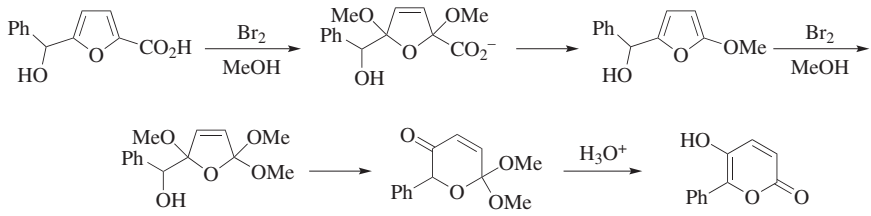
It is also possible to carry out the bromine-promoted oxidation reactions in the presence of acetic acid. When methanol is used as a solvent the formation of *trans* 1,4-dioxoalkenes takes place through intermediate 2,5-dimethoxyfurans, which are hydrolyzed in situ.[144] The same conditions can be applied to dihydrobenzo[*c*]furan derivatives to produce substituted diacylbenzenes (Scheme 39).[145]



R = Ph, 4-MeC_6H_4, 2,5-$Me_2C_6H_3$, 2,4,6-$Me_3C_6H_2$, 4-*t*-BuC_6H_4, 4-$MeOC_6H_4$, 4-ClC_6H_4, 3-O_2N-4-$MeOC_6H_3$, 3-Br-4-$MeOC_6H_3$, 2-thienyl

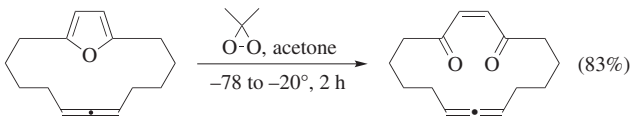
Scheme 39

In the oxidation of 2-furoic acids with bromine, however, 5-hydroxy-2*H*-pyran-2-ones are generated by an oxidative decarboxylation–ring expansion sequence (Scheme 40).[146]



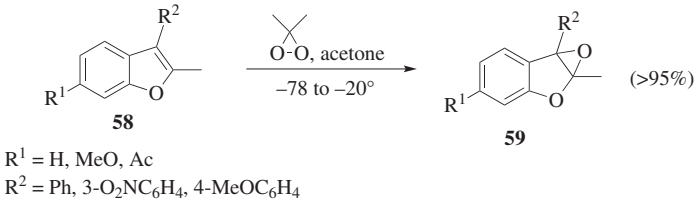
Scheme 40

Dimethyldioxirane. Dimethyldioxirane (DMDO) reacts with substituted furans to form *cis* 1,4-dioxoalkenes in excellent yields.[43] This process can be carried out on furans containing allene moieties[147] and deactivated double bonds (Scheme 41).[148]



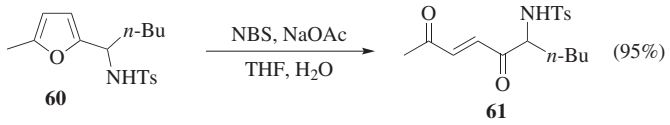
Scheme 41

In DMDO-promoted reactions of 4-oxo-2-amidotetrahydrobenzofurans, 4-oxo-2-oxazolines are formed as a consequence of the participation of the amide group in ring opening of the intermediate epoxide.[149] Similar reactions, occurring through intermediate epoxyfurans, have been described for 2,5-dimethylfuran containing an oxaziridine moiety.[39] By carrying out reactions of benzofuran derivatives **58** at low temperature, it is possible to isolate labile intermediate epoxides **59** (Scheme 42).[46] Depending on the substituents, either furan epoxides or quinone methides can be observed by ^{1}H NMR spectroscopy.[38]



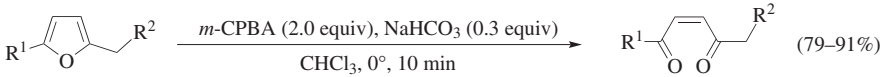
Scheme 42

N-Bromosuccinimide. Oxidation of 2,5-disubstituted furans with *N*-bromosuccinimide in basic medium affords *trans* 1,4-dioxoalkenes in good yields.[150] This process is compatible with various functional groups,[151] including MOM and TBS protecting groups,[152] and enables the generation of libraries of small molecules.[153] In some cases *trans* 1,4-dioxoalkenes such as **61** are formed even when furfurylamines, such as **60** (Scheme 43)[154] that are known to furnish the corresponding piperidones through the aza-Achmatowicz reaction, are used as substrates (see below).



Scheme 43

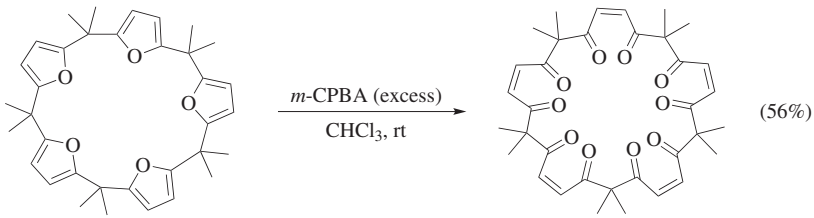
m-Chloroperoxybenzoic Acid. Peracids, such as *m*-CPBA, react with substituted furans[30] to produce *cis* 1,4-dialkenes in good yields and without simultaneous production of *trans* isomers,[45] although in some instances minor amounts of the *trans* isomers are observed even when the reaction is carried out at 0°.[155] The reaction can be performed at ambient temperature in dichloromethane with furans bearing both alkyl and aryl substituents (Scheme 44).[156] The use of an excess of the peracid, however, can lead to formation of over-oxidized byproducts.[44]



R^1 = Me, Et
R^2 = Ph, 3-$MeOC_6H_4$, 4-FC_6H_4, 3-ClC_6H_4

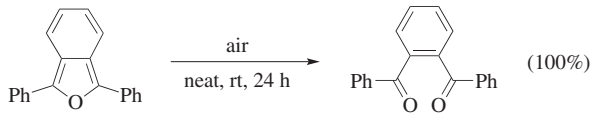
Scheme 44

Oxidation reactions of furans with *m*-CPBA are compatible with the presence of double bonds[157] including dienes, as well as protecting groups such as cyclic[158,159] and acyclic[160] acetals, esters,[161] and benzyl ethers.[162] The reactions of 1,3-diarylbenzo[*c*]furans with *m*-CPBA at room temperature lead to the formation of 1,2-diaroylbenzenes in good to excellent yields.[163] When two furan units are present in the same molecule, it is possible to oxidize only one ring by using one equivalent of the peracid.[164] On the other hand, when an excess of *m*-CPBA is employed, oxidations of all heterocyclic nuclei in the molecule take place (Scheme 45).[165] Sequential oxidation of different furan rings is also possible.[166] Finally, oxidation of the furan ring with *m*-CPBA followed by catalytic hydrogenation can be used as an alternative method to hydrolyze the heterocycle.[167]



Scheme 45

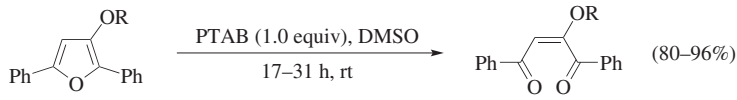
Other Oxidants. Exposure to air or oxygen for several hours[168–170] is suitable for transforming isobenzofurans to *o*-dibenzoylbenzenes (Scheme 46). The reaction also takes place in the presence of Lewis acids and on silica gel.[171] This method has been utilized in the synthesis of steroids[172] and terpenes.[173] The laccase-catalyzed ring opening of 2,5-dialkylfurans using air as an oxidant provides (*Z*)- or (*E*)-3-hexene-2,5-diones depending on the mediator employed: with TEMPO the (*Z*)-isomer is formed, while a combination of TEMPO and violuric acid gives the (*E*)-isomer.[174]



37

Scheme 46

3-Alkoxy-2,5-diphenylfurans **62** are converted to *cis* 1,4-dienones **63** upon treatment with phenyltrimethylammonium bromide (PTAB) in DMSO at room temperature (Scheme 47).[175] These oxidations can also be carried out using DDQ instead of PTAB as the oxidant but competitive formation of 3-(2*H*)-furanones is observed.[176] The latter compounds are also formed in reactions promoted by PTAB when an additional substituent is present at C4 of the furan ring, a consequence of steric effects that favor cleavage of the ether functional group.

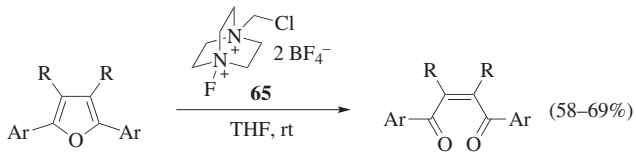


62 **63**

R = Me, *n*-Pr, *n*-Bu, *i*-Pr, *i*-Bu

Scheme 47

Oxidations of 2,5-diarylfurans **64** also occur using the N–F reagent Selectfluor® (**65**) to generate the corresponding *cis* enediones **66** along with trace quantities of the *trans* isomer in good yields (Scheme 48).[177]



64

Ar = Ph, 4-BrC_6H_4

R = H, Me

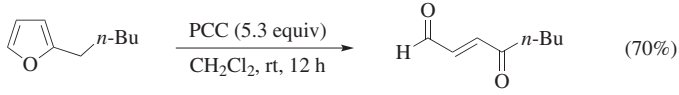
66

Scheme 48

Electrochemical oxidation of bis(2-furyl)benzene via a two-electron transfer mechanism gives a diketone, which upon further two-electron oxidation furnishes the corresponding tetraketone.[69]

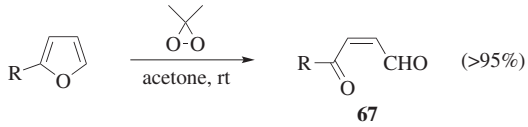
4-Oxoalkenals. In principle, the same reactions of 2,5-disubstituted furans leading to 1,4-dioxoalkenes might be applicable to transforming furans that do not contain substituents at C5 to 4-oxoalkenals. However, the formation of an aldehyde under oxidizing conditions makes it necessary to carefully select the oxidant to avoid overoxidations. Nevertheless, several examples of reactions of this type, occurring on some simple substrates, have been described.

Pyridinium Chlorochromate (PCC). Among the reagents reported to cleave 2-substituted furans into 4-oxoalkenals, PCC is quite effective for providing *trans* isomers in acceptable yields (60–70%) (Scheme 49).[178]



Scheme 49

Dimethyldioxirane. Dimethyldioxirane can convert 5-unsubstituted furans bearing ester moieties to *cis* 4-oxoalkenes.[179] Notably, under these conditions, it is also possible to obtain unstable compounds, such as *cis* 4-oxo-2-pentenals **67** (R = H) (Scheme 50).[43]

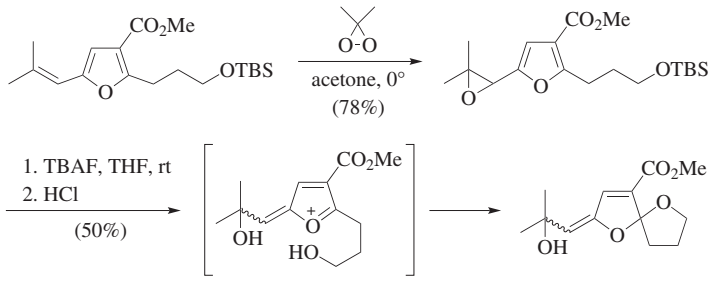


67

R = H, Me, $AcOCH_2$, $(MeO)_2CH$, $Me_2(TMSO)C$, $PhthHNCH_2$

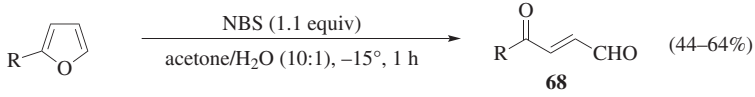
Scheme 50

DMDO also serves as an oxidant for reactions of furan derivatives that contain alkene substituents. However, in reactions of deactivated furans bearing electron-withdrawing substituents, the double bond is epoxidized preferentially without oxidation of the heterocyclic ring (Scheme 51).[180] As a result, it is possible to achieve high chemoselectivity between double bonds and furan rings based on activation and deactivation of the heterocycle towards oxidation.



Scheme 51

N-Bromosuccinimide. The use of bromine in pyridine has also been reported to oxidize 2-substituted furans,[181] albeit with some limitations.[182] In contrast, a reasonably broad array of furans undergo oxidation with NBS in pyridine to yield *trans* 4-oxoalkenals. Substrates containing different protecting groups (such as MOM–acetals[183]) and other functional groups (such as free hydroxyl groups and esters,[184] the 4-methoxyphenyl group,[185] silyl ethers,[182] and double bonds[186]) are compatible with these oxidation conditions, but in some cases mixtures of (*E*)/(*Z*) isomers are formed.[187] The use of NBS in 10:1 acetone/water with 2-alkylfurans also provides *trans* 4-oxoalkenals **68** (Scheme 52).[188]

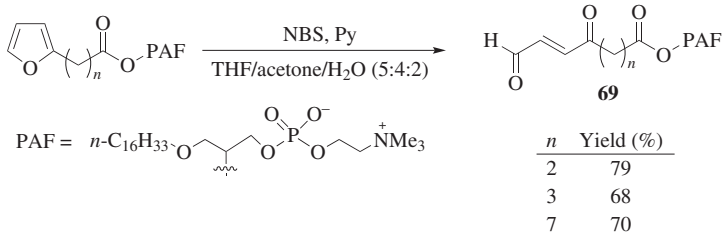


68

R = Et, *n*-Pr, *n*-Bu, *n*-C_5H_{11}

Scheme 52

A variety of bioactive phospholipids have been synthesized by using oxidation reactions of furans that form a 4-oxoalkenal unit as a key step. In these cases, oxidations have been carried out using NBS in the presence of pyridine in 5:4:2 THF/acetone/H_2O at −20° to generate the corresponding *trans* 4-oxoalkenals **69** in 68–80% yields without oxidation of the sensitive aldehyde group (Scheme 53).[189] Notably, the same aldehydes do not survive when the reactions are carried out using *m*-CPBA,[190] although the formation of a *cis* 4-oxoalkenal from a 2,3-fused furan derivative has been reported.[191]

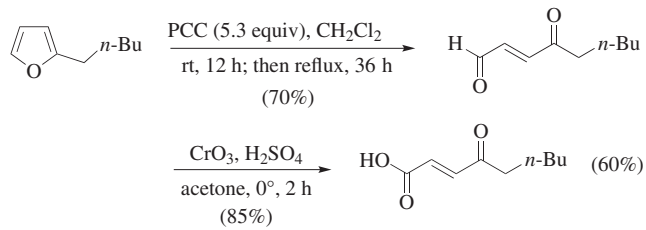


n	Yield (%)
2	79
3	68
7	70

Scheme 53

The same NBS procedure is used to prepare several targets bearing the typical phosphatidylcholine unit, which survives under the reaction conditions.[192,193] Identical reaction conditions are applied to simpler 2-alkylfurans to obtain the corresponding aliphatic 4-oxo-2-alkenals.[194]

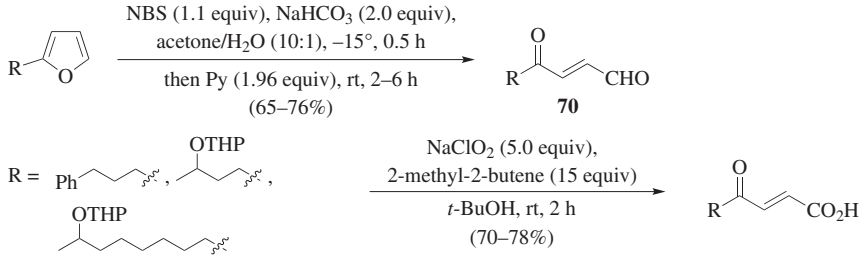
4-Oxoalkenoic Acids and Derivatives. As described above, oxidations of substituted furans with a variety of reagents invariably leads to formation of either 1,4-dioxoalkenes or 4-oxoalkenals, depending on the number and position of the substituents. In some cases, further in situ oxidation of a formed aldehyde function is possible under the reaction conditions,[195] but mixtures of compounds at different levels of oxidation are usually obtained.[196] Consequently, direct, clean oxidations to generate 4-oxoalkenoic acids are a difficult objective in this area. Some exceptions are found in *m*-CPBA promoted oxidations of fused furan derivatives, in which the use of 2 equivalents of the oxidant produces the corresponding *cis* 4-oxoalkenoic acids,[191] although in low yield.[197] Instead, it is usually preferable to transform 2-substituted furans into 4-oxoalkenoic acids by utilizing a two-step sequential oxidation process. Sometimes the intermediate aldehyde is isolated but most often the second oxidation step is carried out in a one-pot procedure. Jones' reagent in combination with PCC is found to be convenient for this purpose,[179] as exemplified by the oxidation of 2-pentylfuran to the antibiotic (*E*)-4-oxonon-2-enoic acid in 60% overall yield (Scheme 54).[178]



Scheme 54

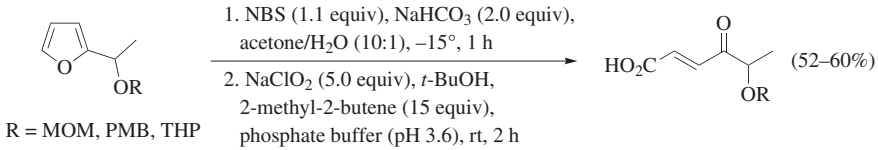
The most popular combination of reagents for this purpose employs sodium chlorite in the presence of an excess of 2-methyl-2-butene as chlorine scavenger as

the second oxidant, which follows initial furan ring cleavage promoted by NBS in an aqueous medium.[198] The use of an excess of 2-methyl-2-butene leads in some cases to quantitative yields in the second oxidation step,[186] but resorcinol can also be used as an additive in reactions carried out in an NaH_2PO_4 buffer solution.[183] A weak base such as pyridine or sodium bicarbonate is used as a scavenger of HBr generated in the reaction.[199] Under these conditions, furan cleavage is complete within 2 hours at −15°, but further reaction at ambient temperature is needed to isomerize the initially obtained *cis* dicarbonyl compound to the *trans* enal **70** (Scheme 55).[182]



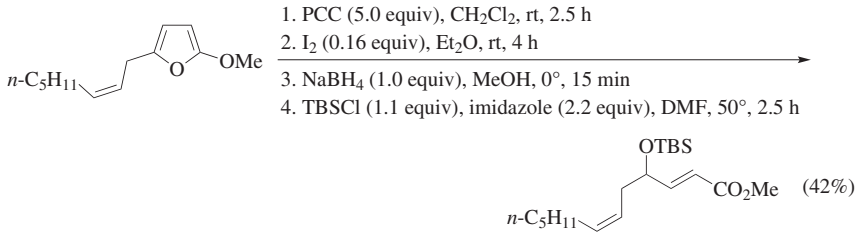
Scheme 55

From a synthetic point of view, the use of two different oxidation conditions avoids prolonged reaction times and expands the array of functionalities that can be tolerated in this transformation. For example, the oxidation reaction conditions described above are compatible with furans that contain MOM acetals[184] and 4-methoxybenzyl protecting groups (Scheme 56).[185] The versatility of the method has been demonstrated by its use in the preparation of bioactive phospholipids.[193]

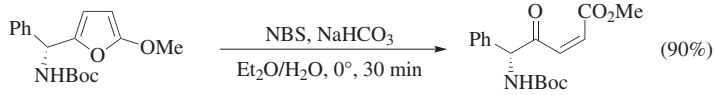


Scheme 56

Oxidation of 2-alkoxy-5-substituted furans serves as a direct method to prepare 4-oxoalkenoates. The oxidizing agent is the same as that used for 2,5-disubstituted furans, and ester products are formed in one step. Thus, both PCC (Scheme 57)[200] and NBS (Scheme 58)[201] are used for oxidation of 2-alkoxy-5-substituted furans, the latter being an effective choice for enantiomerically pure *N*-protected furfurylamines such as **71**.[202]



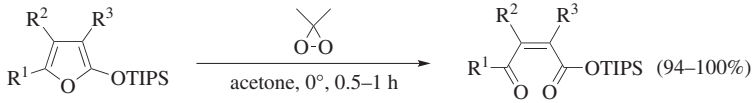
Scheme 57



71

Scheme 58

In a similar manner DMDO has been used to oxidize 2-siloxyfurans **72** to silyl esters **73** in high yields (Scheme 59).[203] As with 2,5-disubstituted furans, oxidations using NBS provide *trans* isomers while those promoted by dimethyldioxirane furnish *cis* isomers.



72

73

R^1 = H, Me
R^2 = H, Me, $BnOCH_2$, $ClCH_2$, *i*-Pr
R^3 = H, $PhCH_2$

Scheme 59

This process has been extended to PCC oxidations of 2-methylthiofurans to produce thiocarboxylates,[204] but longer reaction times (up to 24 hours) are needed and mixtures of *cis* and *trans* isomers are obtained.[205]

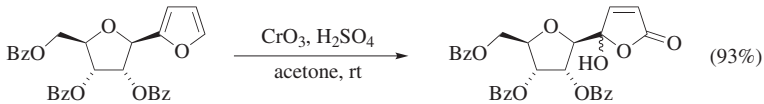
γ-Hydroxybutenolides. The *cis* 4-oxoalkenoic acids **74** exist in equilibrium with the corresponding γ-hydroxybutenolides **75** (ring tautomers) (Scheme 60),[206] but under acidic conditions γ-hydroxybutenolides are the only tautomers observed.

4-oxoalkenoic acid
74

γ-hydroxybutenolide
75

Scheme 60

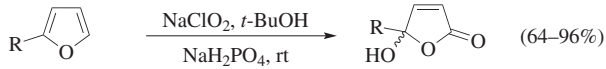
Thus, by forming 4-oxoalkenoic acids oxidatively in situ and selecting favorable reaction conditions, pH, substituents, and work-up conditions, the corresponding γ-hydroxybutenolides can be produced cleanly. For example, γ-hydroxybutenolides are obtained from 2-siloxyfurans by treatment with DMDO[207] followed by acid-catalyzed hydrolysis of the initially formed silyl-4-oxoalkenoate.[203] The conversion of 2-unsubstituted furans directly into γ-hydroxybutenolides is carried out by employing the same oxidizing agents used in the transformation of 2,5-disubstituted furans to 1,4-dioxoalkenes. A good example of this method is found in the chromic acid induced synthesis of butenolides **76** in the preparation of *C*-nucleosides (Scheme 61).[208]



76

Scheme 61

In a similar fashion, the formation of a butenolide has been reported to occur by reaction of magnesium monoperoxyphthalate (MMPP) with a 2,3,4-trisubstituted furan.[209] Nitrous acid has also been used for this purpose, but the yields are generally lower.[210] Oxidations of 2-alkylfurans using sodium chlorite under slightly acidic aqueous conditions furnish γ-hydroxybutenolides in high yields (Scheme 62).[211] These reaction conditions are compatible with the presence of several acid-sensitive protecting groups and can be employed to carry out reactions of substrates possessing free hydroxy groups.[212]

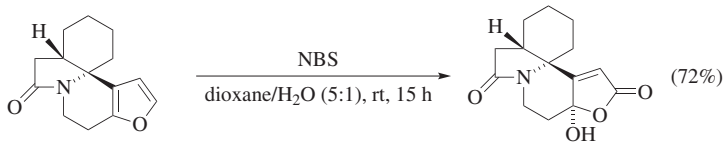


R = Me, *n*-C_5H_{11}, $TsO(CH_2)_4$, $THPO(CH_2)_4$, $TBSO(CH_2)_4$,
Me(CHOTBS)$(CH_2)_2$, $P_CO_2C(CH_2)_3$
P_C = 2-lysophosphatydylcholine

Scheme 62

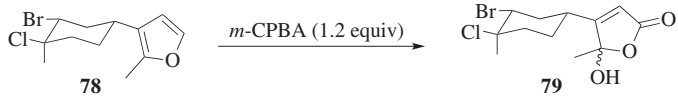
Some success has been achieved in preparing γ-hydroxybutenolides by using an excess of NBS in an aqueous medium,[213] as exemplified by the reaction of the

polycyclic substrate **77** (Scheme 63),[214] which produces an advanced intermediate in the synthesis of *Erythrina* alkaloids. A similar result is obtained in studies targeted at tetra-*nor*-terpenoids where NBS in methanol along with microwave irradiation is employed to promote the key oxidation process.[215]



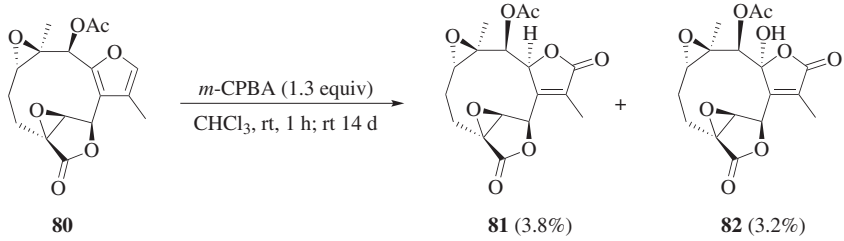
Scheme 63

m-CPBA is an ideal reagent for oxidation of the terpenoid-derived dihalide **78**, producing butenolide **79** in a study aimed at establishing the absolute configuration of the natural product (Scheme 64).[216]



Scheme 64

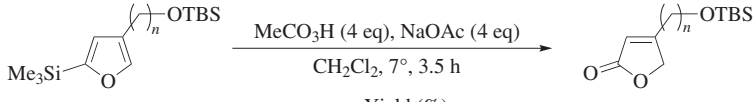
In other cases, such as in the *m*-CPBA induced oxidation of zeylanidine (**80**), mixtures of the expected lactone **81** and the γ-hydroxybutyrolactone **82** are obtained (Scheme 65).[217] However, a glucosyl butenolide is formed in 70% yield under very similar conditions,[161] which have also been employed in a reaction sequence used to confirm the absolute configuration of glaucescenolide, a natural γ-hydroxybutyrolactone.[218]



Scheme 65

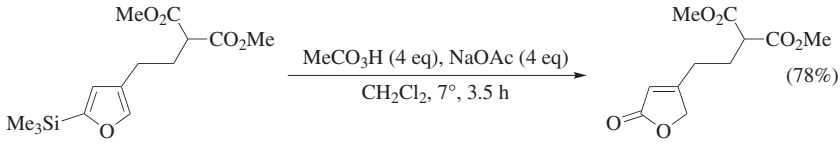
Reactions of 3-(silyloxyalkyl)- and 3-bis(methoxycarbonyl)propyl-2-trimethylsilyl furans with peracetic acid yield the corresponding butenolides (Schemes 66 & 67).[219]

3-Alkenyl-2-trimethylsilylfurans react under these conditions to form butenolides almost exclusively if the alkene is less than trisubstituted.[220]



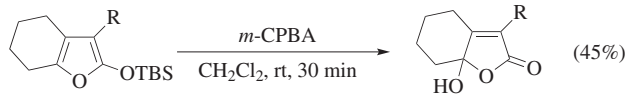
n	Yield (%)
1	75
2	88

Scheme 66



Scheme 67

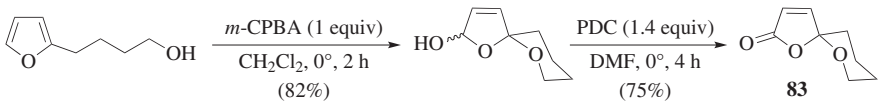
On the other hand, oxidations of 2-siloxyfuran derivatives with *m*-CPBA lead to generation of γ-hydroxybutyrolactones through a pathway involving concomitant desilylation at C2 of the furan ring (Scheme 68),[221] a process that does not take place when DMDO is employed as oxidant.[203] Reactions of 3,4-unsubstituted 5-alkyl-2-siloxyfurans produce silyl 4-oxoalkenoates in up to 11% yield. These oxoalkenoates can be converted to the expected γ-hydroxybutyrolactones upon treatment with dilute HCl in THF. The reaction can also be performed with enantiomerically pure substrates.[222]



R = H, Me

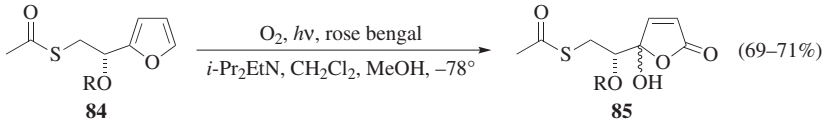
Scheme 68

When hydroxy substituents are present in furan side-chains, oxidations with *m*-CPBA yield lactols and a second oxidation step with PDC is required to obtain the corresponding lactones. This sequence is exemplified in the reaction of 4-(furan-2-yl)butan-1-ol from which 1,6-dioxaspiro[4,4]dec-3-en-2-one (**83**) is obtained (Scheme 69).[223]



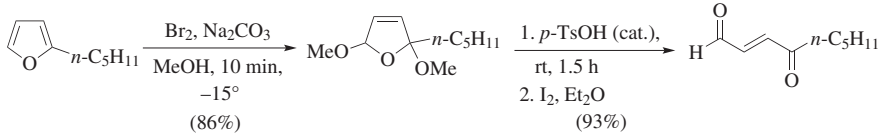
Scheme 69

Similarly, photoxygenation of an enantiomerically pure furan derivative bearing a hydroxyl group at the γ-position, followed by treatment with acetic anhydride in pyridine, leads to formation of a 2.7:1 mixture of epimeric γ-spiroketal-γ-lactones.[224] Photoxygenation of siloxy derivatives **84** using rose bengal as a sensitizer affords γ-hydroxybutenolides **85** in good yields (Scheme 70).[225]



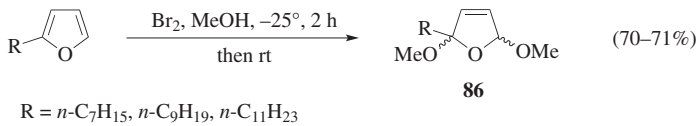
Scheme 70

2,5-Dialkoxy-2,5-dihydrofurans. *Bromine in Methanol.* Oxidation of furan derivatives in alcohol-containing solvents (methanol in most cases) is an excellent method for preparing protected 1,4-dicarbonyl derivatives in the form of 2,5-dialkoxy-2,5-dihydrofurans. Indeed, the main interest of these compounds resides in the fact that they are masked 1,4-dioxoalkenes that can be liberated by treatment with 2 N HCl,[226] HCl in THF/H_2O,[227] or catalytic amounts of 4-toluenesulfonic acid (Scheme 71).[228] Careful hydrolysis under mild conditions (0.005 M H_2SO_4) leads to partial hydrolysis of the bis-acetal moiety.[229,230]



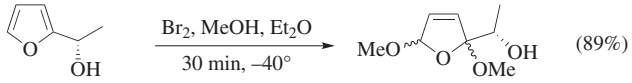
Scheme 71

Oxidations with bromine in methanol serve as efficient methods for converting 2-substituted furans to 2,5-dimethoxy-2,5-dihydrofurans **86** (Scheme 72) in processes known as the Clauson–Kaas reaction.[231,232] In addition, a variety of alcohols such as ethanol, *n*-propanol, and *n*-butanol can be employed in place of methanol without reducing the yield, and dichloromethane[233–235] and diethyl ether[236] can be used as cosolvents.[237]



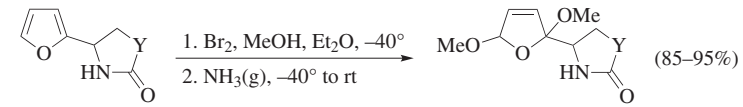
Scheme 72

The oxidation reaction of furfuryl alcohol using bromine in methanol produces a very useful synthetic intermediate, 2,5-dimethoxy-2-hydroxymethyl-2,5-dihydrofuran.[238,239] Also, racemic[240,241] and enantiopure forms (Scheme 73)[242,243] of methyl furfuryl alcohol undergo bromine-promoted oxidation in methanol containing diethyl ether as the cosolvent.[244]



Scheme 73

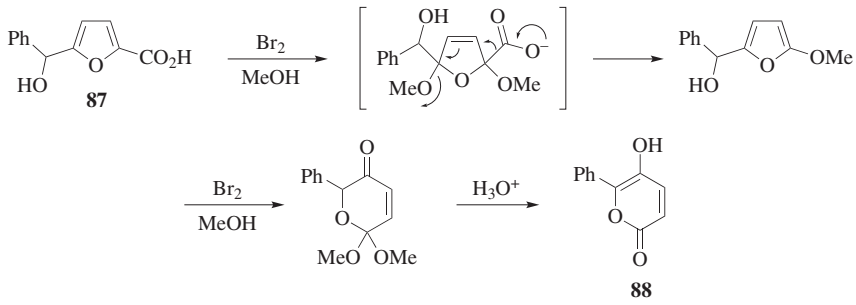
The same type of reaction can be carried out with a variety of substrates including substituted[226] and unsubstituted *N*-phthaloyl-[245] and *N*-acyl furfuryl amines (Scheme 74).[246] In all cases, the process is fully compatible with common protecting groups, such as benzyl ethers,[32] esters,[247,248] phosphonates[249] and acetals.[250] In general, 1:1 mixtures of stereoisomers are obtained.[251] In addition, the presence of substituents on the furan ring does not affect the reaction and thus 2,5-disubstituted[252] and 3,4-disubstituted furans can be employed as substrates.[253]



Y = CH_2, $(CH_2)_2$, O

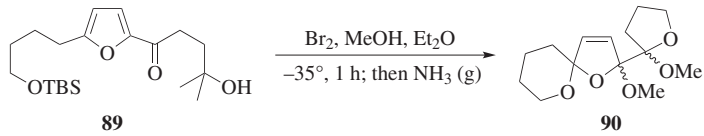
Scheme 74

Treatment of 5-(α-hydroxybenzyl)furoic acid (**87**) with bromine in methanol under basic conditions results in a reaction that occurs with concomitant decarboxylation. A second oxidation step in this process produces 5-hydroxy-2-pyranone **88**, through a rearrangement promoted by the hydroxyl group in the intermediate (Scheme 75).[146]



Scheme 75

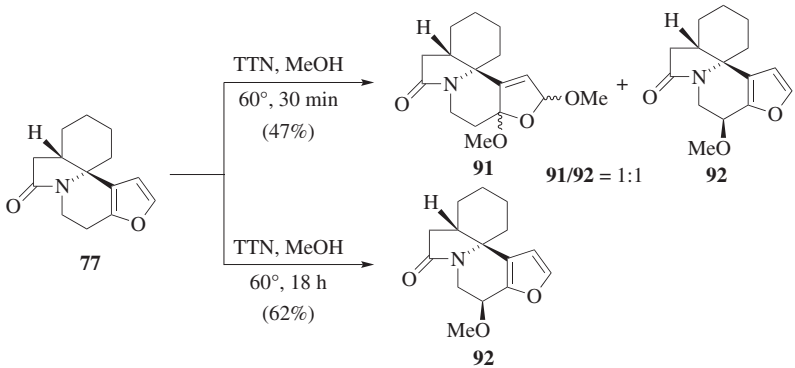
Oxidation of furan **89** using bromine in methanol with diethyl ether as a cosolvent and at low temperature, followed by treatment with ammonia leads to formation of the 2,5-dialkyl-2,5-dioxy-2,5-dihydrofuran derivative **90**. Under these conditions, the TBS protecting group does not survive and its loss yields an alcohol that promotes formation of the spirocyclic ketal **90** (Scheme 76).[254]



89 **90**

Scheme 76

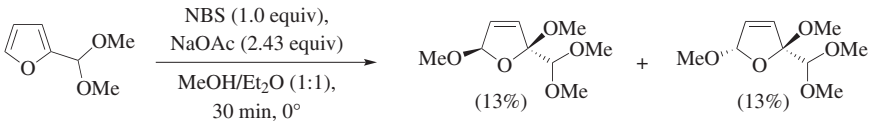
In contrast to the oxidation described above, treatment of furan **77** with thallium trinitrate (TTN) leads to production of **91** in 47% yield as a 1:1 mixture of isomers along with 50% of recovery of the starting material (Scheme 77). Prolonged oxidation (18 h) of **77** under the same conditions affords **92** as a single product in 62% yield, suggesting that **92** is formed by a secondary reaction of **91**.[255]



77 **91** **92** **92**

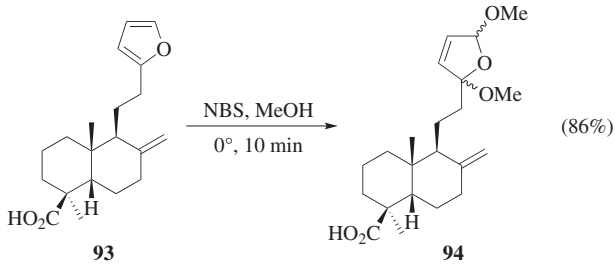
Scheme 77

N-Bromosuccinimide. Treatment of furfural dimethyl acetal with NBS in 1:1 methanol/diethyl ether in the presence of sodium acetate leads to formation of the corresponding dimethoxy derivative as a 1:1 mixture of isomers in 26% yield (Scheme 78).[256]



Scheme 78

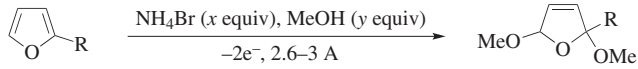
Enantiomerically enriched furan derivative **93** subjected to these conditions produces an approximately 1:1 mixture of stereoisomeric 2,5-dimethoxy dihydrofurans **94** (Scheme 79).[257] Analogous reactions take place under electrochemical or chemical (bromine in methanol) oxidation conditions.[258,259]



Scheme 79

Oxidations of 3-substituted and 3,4-disubstituted furans with NBS in ethanol provide 2,5-diethoxy dihydrofurans in essentially quantitative yields by reactions that are tolerant of a variety of substituents on the furan ring and appended functional groups.[260] The hydroxyl moiety participating in formation of the acetal functional group can be from the alcohol solvent or from the same molecule. In the latter case, spiro compounds are generated in a manner that is similar to oxidations with bromine in methanol illustrated above.[120]

Electrochemical Oxidation. Electrochemical oxidation of furans in the presence of an alcohol is one of the first and most used methods for preparing 2,5-dialkoxy-2,5-dihydrofurans. The reaction was initially reported in 1952 by Clauson-Kaas, who described the electrochemical dimethoxylation of several 2-substituted furans[261,262] Electrolytic oxidations of furan and 2-methylfuran with ammonium bromide as the electrolyte and in methanol as the solvent are carried out by using an electrolysis cell consisting of a hollow brass cylindrical cathode and a hollow graphite cylindrical anode. The average current employed is 2.6 A, with an average temperature of 12°. Under these conditions the products are formed in 72% and 49% yields, respectively, on a multigram scale (0.25–0.36 mol of starting materials) (Scheme 80).[263] Other electrolytes such as sodium bromide[264] can also be employed in these processes.

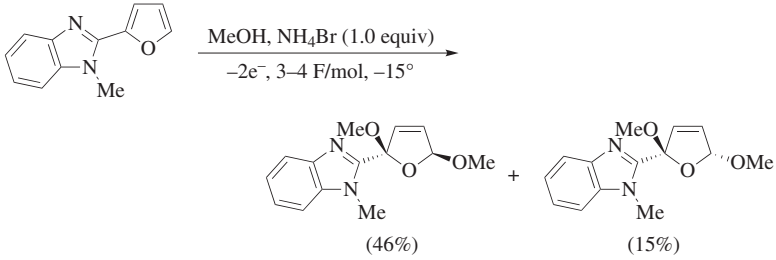


R	*x*	*y*	Yield (%)
H	.05	7.5	72
Me	.06	4.2	49

Scheme 80

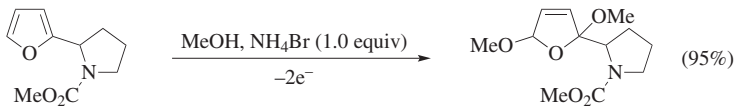
Electrolytic methoxylation has been carried out with *N*-benzoyl furfurylamine[265] and polyfunctionalized furans using a similar protocol, showing the compatibility

of the method with ester and acetal groups.[266] Some anomalous oxidation products have been observed in electrochemical oxidations of 2,5-dialkylfurans in acetic acid, but the expected 2,5-dimethoxy-2,5-dihydrofurans are obtained when the reactions are performed in methanol.[267] The presence of aromatic or other conjugated 2-substituents causes formation of anomalous products that either have dimeric structures or are structures in which one methoxy group is introduced into the furan ring.[268] In spite of these issues, electrochemical oxidations of 2-(2-benzimidazolyl)furans proceed in the anticipated manner (Scheme 81).[269] If aromatic and heteroaromatic substituents are not conjugated with the furan ring, oxidation proceeds to give the corresponding 2,5-dialkoxy-2,5-dihydrofuran derivatives.[270]



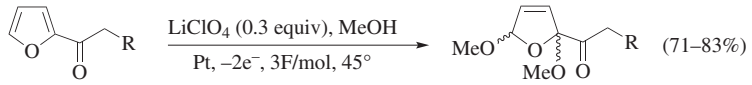
Scheme 81

Dihydrofuryl pyrrolidines and piperidines have been prepared in high chemical yields using electrochemical oxidations (Scheme 82).[271] The reactions tolerate oxygen-containing functionality and, more interestingly, can be carried out on 100 g scales to give the products in very high yields.[272]



Scheme 82

It is not always necessary to apply the theoretical amount of electricity in order bring reactions to completion. For example, by using tetraethylammonium perchlorate in methanol, 3-substituted-2,4-dimethylfurans have been oxidized to generate the corresponding 3-substituted-2,4-dimethyl-2,5-dimethoxy-2,5-dihydrofurans in high yields after passing only 2.78 F/mol of electricity through the solution.[273] Similarly, electrochemical oxidations of furanyl ketones **95** in methanol using lithium perchlorate as the electrolyte, platinum electrodes, and 3 F/mol of electricity afford the corresponding dihydrofuran derivatives **96** in high yields (Scheme 83).[274]

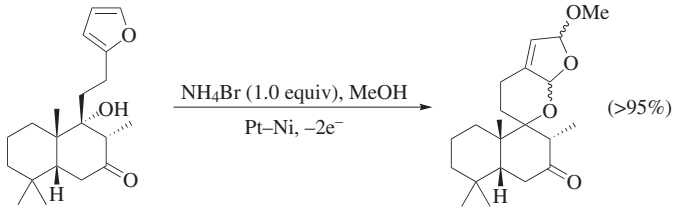


95 **96**

R = *n*-C_3H_7, *n*-C_5H_{11}, *n*-C_7H_{15}, *n*-C_9H_{19}

Scheme 83

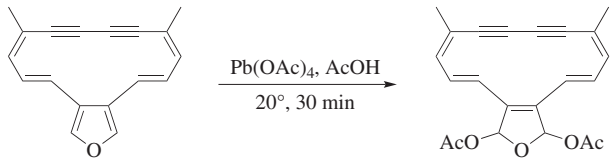
Electrochemical oxidation of the natural product hispanolone (**97**) using the typical system comprised of ammonium bromide, methanol, a platinum anode, and a nickel cathode affords the spiro-tetracyclic compound **98** in high yield (Scheme 84). This reaction can be extended to several similar compounds.[121]



97 **98**

Scheme 84

Other Oxidants. Other oxidizing agents such as lead tetraacetate have been employed in oxidations of a furan that forms a functionalized macrocycle en route to preparation of annulenes. Because these reactions are conducted in acetic acid, the corresponding 2,5-diacetoxy dihydrofurans **99** are produced (Scheme 85).[275,276]

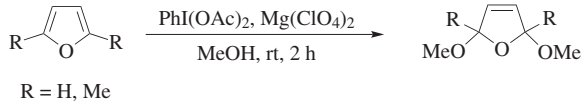


99

Scheme 85

2,5-Diethoxy-2,5-dihydrofurans are generated by oxidation of 2,5-disubstituted furans with hydrogen peroxide in aqueous ethanol in the presence of a catalytic amount of vanadyl sulfate. The reactions are conducted at 20°, but the products are isolated in only 12% yields.[277] Oxidations of furan and 2,5-dimethylfuran with

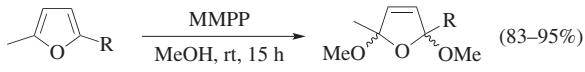
Dess–Martin periodinane in the presence of magnesium perchlorate in methanol leads to formation of 2,5-dimethoxydihydrofurans (Scheme 86).[70]



R = H, Me

Scheme 86

Similarly, if the reagent used in this process is magnesium monoperoxyphthalate (MMPP), excellent yields accompany oxidations of 5-substituted-2-methylfurans **100,** a reaction that has been demonstrated to take place through intermediate 1,4-dienones (Scheme 87).[37]

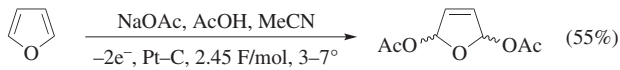


100

R = Me, *n*-C_5H_{11}, *n*-C_7H_{15}, *n*-C_8H_{17}, *n*-$C_{10}H_{21}$

Scheme 87

Oxidation of 2-furoic acid leads to formation of methyl 4,4-dimethoxybutanoate in 77% yield through a pathway involving decarboxylation and secondary oxidation of the intermediate 2,5-dialkoxy-2,5-dihydrofuran.[278] Anodic oxidation of furan can also be carried out in acetic acid (or in a mixture of acetic acid and acetonitrile) using sodium acetate and 2.45 F/mol of electricity to afford 2,5-diacetoxy-2,5-dihydrofuran (**101**) in 55% yield (Scheme 88).[279]



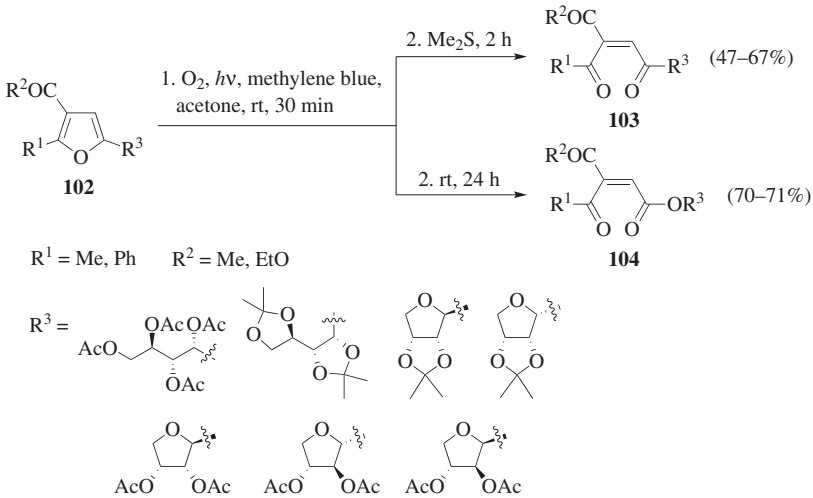
101

Scheme 88

Photooxygenation with Singlet Oxygen

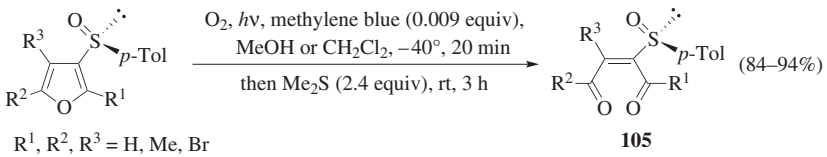
Photooxygenation reactions of furans with singlet dioxygen have been extensively studied[26,27,72,280] and analyzed in detail[281] with regard to their substituent dependence,[282,283] intermediates formed,[88,284,285] solvent effects,[286] and optimized reaction conditions.[287–289] Consequently, even though mixtures of products are often formed in these processes,[79,92,99] useful procedures for preparing 1,4-dicarbonyl compounds[290] and related derivatives such as butenolides[291] have emanated from these studies.[28]

Glycosyl furans **102** have been transformed using singlet oxygen mediated photooxygenation reactions through the corresponding endoperoxides to afford 1,4-dicarbonyl products (Scheme 89).[292] This process can be extended to furans bearing a hexose moiety[93] and a methoxycarbonyl function at the C5 position.[86] Formation of 1,4-dioxoalkenes **103** in these reactions is promoted by reaction of dimethyl sulfide with the intermediate endoperoxide. If dimethyl sulfide is not added to the reaction mixture after 1 mol of molecular oxygen is consumed, keto esters **104** are mainly generated by Baeyer–Villiger-type rearrangement of the intermediate endoperoxides.[94,292] Moreover, *cis* isomers of the products are transformed to the more stable *trans* isomers upon silica gel chromatography.[293] This same behavior has been observed for other substrates,[294] confirming that 2,5-disubstituted furans can undergo rearrangement reactions that generate esters upon photooxygenation at low temperature and followed by warming the reaction mixture.[295] Starting from 2-methoxyfurans, functionalized methyl *cis* 4-oxo-2-alkenoates can be prepared in a one-pot procedure by photooxygenation in methanol.[296] Singlet oxygen promoted photooxygenations afford both types of compounds chemoselectively depending on the reaction conditions employed. Moreover, these reactions can be carried out on furans that contain esters and acetals, and it is likely that the process will tolerate most other protecting and functional groups as well.[87]



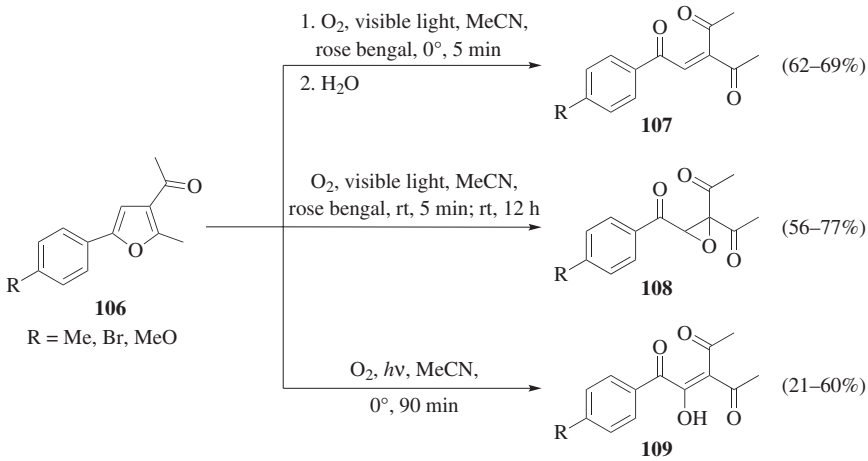
Scheme 89

Enantiomerically pure 1,4-dicarbonyl-2-(4-tolylsulfinyl)-2-alkenes **105** are generated by photooxygenation of the corresponding furans using methylene blue as sensitizer followed by treatment with dimethyl sulfide. Both methanol and dichloromethane can be used as solvents for these reactions and enantiomeric purities of the substrates are preserved in the products of the reactions (Scheme 90).[297]



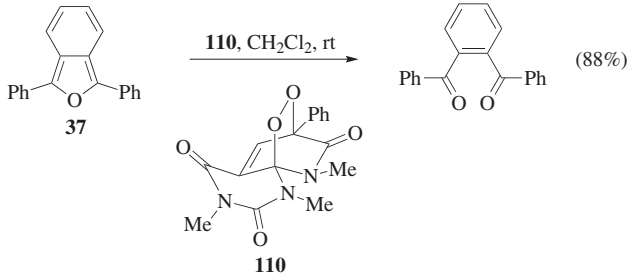
Scheme 90

Because of the mildness of the conditions used for these reactions, most functional groups remain intact. Direct photooxygenations of 3-acetyl-5-aryl-2-methylfurans **106** in acetonitrile in the presence of dry air and rose bengal yield 3-acetyl-1-aryl-2-pentene-1,4-diones **107** after aqueous work-up.[298] If the reaction mixture is kept at room temperature, epoxides **108** are obtained instead. The epoxides are also generated by base treatment of the intermediate hydroperoxy-dihydrofurans.[299] Several reaction conditions have been evaluated to bring about selective formation of either epoxides or 1,4-dioxoalkenes.[300] Direct UV light irradiation of the furans in the absence of additive was observed to promote formation of 3-acetyl-2-hydroxy-2-pentene-1,4-diones **109** (Scheme 91).[298]



Scheme 91

Isobenzofurans undergo similar singlet oxygen promoted reactions. For example, 1,3-diphenylisobenzofuran undergoes photooxidation to form 1,2-dibenzoylbenzene in quantitative yield.[301] However, if norbornene is present in the reaction mixture as the solution containing the intermediate endoperoxide is warmed, the yield of the 1,2-dibenzoyl product decreases to 73%, and norbornene epoxide is observed as a byproduct.[302] Higher yields and more selective reactions take place when reactions of 1,3-diphenylisobenzofuran are conducted using singlet oxygen generated from chemical precursors, in particular the pteridin-2,4,7-trione-6,8′-endoperoxide (**110**) (Scheme 92).[303]

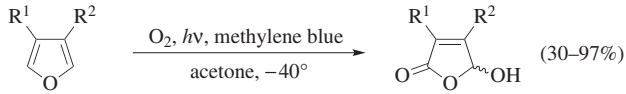


Scheme 92

Photooxygenation reactions of furan derivatives aimed at the preparation of 4-oxoalkenals have not yet been explored in detail, but in one of the few examples studied, a high yield of the product is observed (Scheme 93),[304] suggesting that similar substrates can undergo these transformations.

Scheme 93

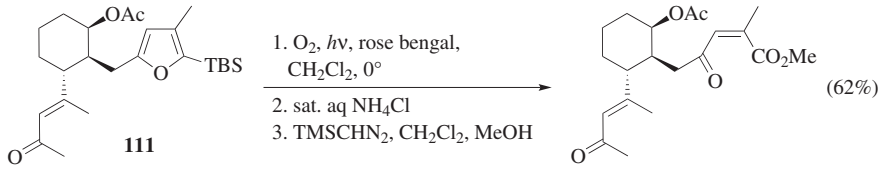
Although γ-hydroxybutenolides are generated in photooxygenation reactions of furans carried out under a variety of conditions, these processes often produce side products. In some cases the low chemical yields are not caused by the reaction itself but by the instability of the products. Among those reactions that take place in high yields, and therefore are practical, are the conversions of 3,4-disubstituted furans to γ-hydroxybutenolides promoted by photooxygenation in acetone (Scheme 94).[291]



R^1 = H, MeO_2C, Et_2NOC, PhCO, Ac
R^2 = H, Et_2NOC

Scheme 94

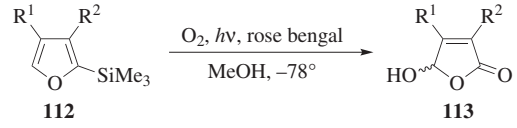
4-Oxoalkenoates are formed in photooxygenation reactions of 2-silyl-substituted furans, exemplified by **111** (Scheme 95).[305] Performing these photooxygenations in methanol generates butenolides directly.[306] Silyl esters resulting from these processes are quantitatively converted into γ-hydroxybutenolides by methanolysis.[91]



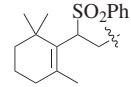
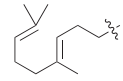
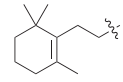
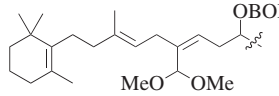
Scheme 95

In addition to the examples presented above, others exist in which photooxidations of simple furan substrates take place with moderately high efficiencies. The substrates for these processes, including isobenzofuran,[76] 2-benzimidazolylfuran,[307] 2,5-diarylfurans,[308] fused furans,[309] and macrocyclic furan-containing compounds,[310] all react to generate the corresponding 4-oxoalkenoates.

2-(Trimethylsilyl)furans **112** react to form γ-hydroxybutenolides **113** in very high yields upon exposure to singlet oxygen (from rose bengal sensitization) for a few minutes at ambient,[306] low (−17°),[311] and very low (−78°) temperatures.[312,313] Identical results are observed when methylene blue is used as the photosensitizer.[314] Moreover, this process can be made compatible with substrates that contain alkene moieties by properly adjusting the flow rate of oxygen and concentration of substrates (Scheme 96).[315,316] Notably, reactions of substrates that do not contain trimethylsilyl groups take place in lower yields and longer reaction times are needed for completion.



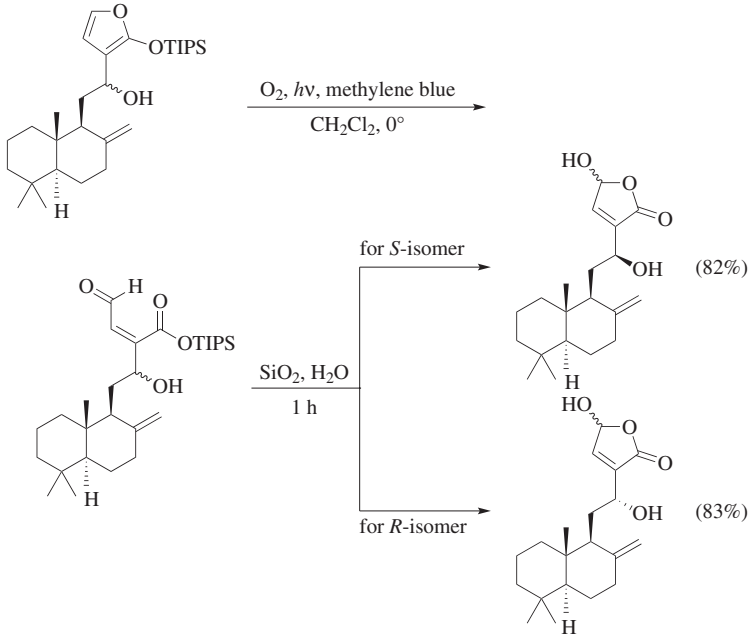
112 **113**

R^1	R^2	Yield (%)
H	$TMSOCH_2$	94
$TMSOCH_2$	H	91
H		93
H		93
H		93
	H	89

Scheme 96

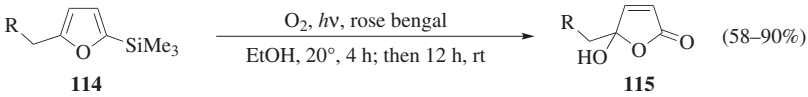
Photooxidation reactions of 2-*tert*-butyldimethylsilyl-substituted furans can be promoted by using tetraphenylporphyrin as a photosensitizer,[317] conditions in which

the presence of several functional groups such as acetals are tolerated.[318,319] When a triisopropylsilyl group is present at C2 of the furan ring, the open-chain 4-oxosilyl alkenoate is generated, although the γ-hydroxybutenolide can be formed by in situ hydrolysis of the silyl ester (Scheme 97).[320]



Scheme 97

It is likely that the same pathway is followed in the reactions of 2-trimethylsilylfurans, but the higher lability of the trimethylsilyl group prevents isolation of the silyl ester.[321] Similarly, a 4-oxo(*tert*-butyldimethylsilyl)alkenoate is produced from the corresponding 2-*tert*-butyldimethylsilyl furan derivative and the silyl ester group can be transformed in situ into a methyl ester by desilylation with TBAF in the presence of methyl iodide.[322] Site selectivity can also be achieved by introducing a formyl group instead of the trimethylsilyl group at C2, but mixtures of butenolides and 4-oxoalkenoates are obtained in some cases.[323] In contrast, photooxidation reactions of 5-substituted-2-silylfurans **114** in ethanol generate γ-hydroxybutenolides **115** in high yields (Scheme 98).[324] Similar reactions of 5-glycosylfurans produce glycosyl-butenolides in high yields.[325]

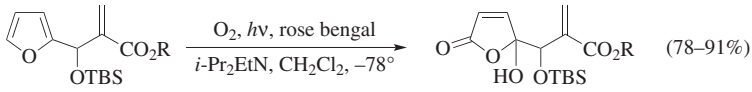


114 **115**

R = HO, AcO, BnO, AcNH, PhCONH, phthalimidyl

Scheme 98

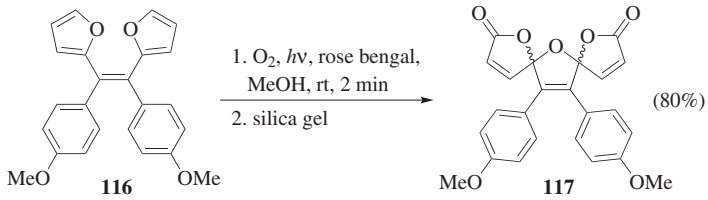
Reactions of 3-alkylfurans with singlet oxygen (generated by irradiation of polymer-bound rose bengal in the presence of molecular oxygen at −78°) in the presence of a hindered base yields 3-alkyl-4-hydroxybutenolides in moderate to high yields.[326] The site-selective formation of only γ-hydroxybutenolides in these processes is a consequence of the fact that, at low temperatures, base-catalyzed decomposition of the intermediate endoperoxides is favored over thermal decomposition. The use of a hindered base is crucial for ensuring site-selective removal of the hydrogen at C1 on the endoperoxide.[327] Hydroxyl groups in the substrate must be protected to avoid undesired fragmentation reactions (Scheme 99).[89] Bi- and polycyclic fused furans also undergo site-selective formation of butenolides owing to the steric restraints imposed by the substituents.[80] Fragmentation processes may also result in unexpected butenolides.[85]



R = Me, Et, *n*-Bu, dodecyl, benzyl, cinnamyl, allyl, chloroethyl

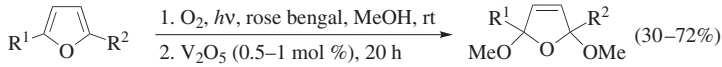
Scheme 99

Bis-spirobutenolides can be prepared by photooxygenation of bis-furans, exemplified by 1,2-difurylalkene **116**, in methanol followed by silica gel treatment. The process consists of a cascade sequence in which a double photooxygenation of **116** is followed by dehydration and spirocyclization to yield bis-spiroketal **117** (Scheme 100).[96] Formation of highly substituted bis-spirobutenolides is possible using photoxygenation of difuryl compounds, which undergo sequential additions of singlet oxygen to afford diendoperoxides that form the final products.[95]



Scheme 100

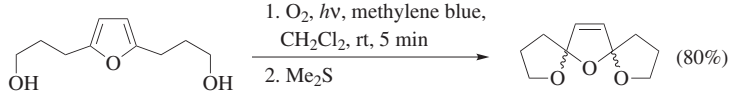
Photooxygenation reactions of 2,5-disubstituted furans in methanol, followed by treatment with a catalytic amount of vanadium pentoxide, produce 2,5-dimethoxy-2,5-dihydrofurans as mixtures of *cis/trans* isomers (Scheme 101).[328] The formation of 2,5-dialkoxy-2,5-dihydrofurans can also take place by controlled addition of alcohols to endoperoxides formed in situ through photooxygenation of furans in alcoholic medium, and in the presence of triphenylphosphine.[329] Similarly, 2,5-diethoxy-2,5-dihydrofurans are generated by photooxygenations of these substrates in an ethanol/acetone mixture. However, in this solvent system the reaction affords up to seven products, considerably limiting its synthetic utility.[92]



R^1 = H, Me
R^2 = Me, Et, $CH_3COCH_2CH_2$

Scheme 101

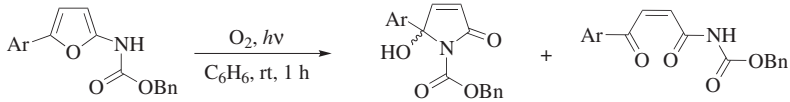
Photooxidation reactions of 2,5-disubstituted furans take place more cleanly when hydroxyl groups are present in the side chains. For example, furan **118** is converted into **119** in a one-pot, singlet oxygen-mediated, cascade process (Scheme 102).[330] The use of dimethyl sulfide is crucial for promoting reduction and ketalization of the intermediate spirocyclic hydroperoxide formed in this process by cleavage of the initially formed endoperoxide through intramolecular attack of a hydroxyl group. With unsymmetrical bis-spiroketals, induction of the second ketalization step by acid treatment is sometimes needed.



118 **119**

Scheme 102

2-Furylcarbamates **120** are transformed to 5-hydroxy-3-pyrrolin-2-ones **121** by irradiation in the presence of oxygen. The initially formed products **121** are in equilibrium with the corresponding *cis* γ-keto amides **122**. The results of a ^{1}H NMR study show that the presence of electron-withdrawing nitro groups in the aromatic ring linked at C5 of the furan ring stabilize the pyrrolinone isomer **121** (Scheme 103).[331] The process has been extended to 5-(alkoxymethyl)furyl carbamates, which react to



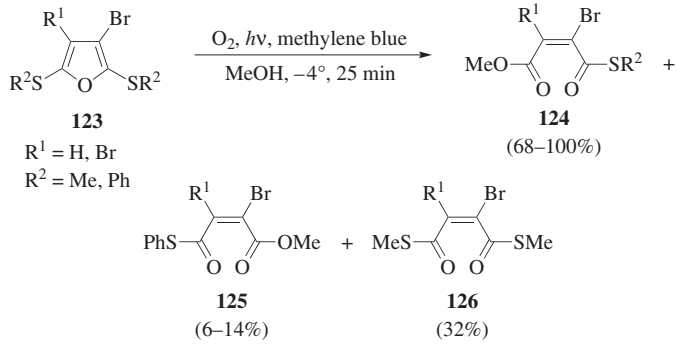
120 **121** **122**

Ar	**121** + **122** Yield (%)	**121/122**
Ph	41	81:19
4-$MeOC_6H_4$	42	50:50
4-MeC_6H_4	34	67:33
4-ClC_6H_4	36	88:12
4-$O_2NC_6H_4$	77	100:0
3-$MeOC_6H_4$	32	87:13
3-ClC_6H_4	36	92:8
3-$O_2NC_6H_4$	41	100:0
2-MeC_6H_4	16	20:80
2-ClC_6H_4	35	89:11

Scheme 103

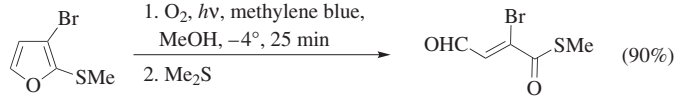
form products that generally show a marked preference for existence as pyrrolinone tautomers.[332]

Methylene blue sensitized photooxygenations of 3-bromo-2,5-bis(thio)furans **123** lead to the formation of *O,S*-thiomaleates **124** in high yields (Scheme 104).[333] The thioester moiety in the products is formed predominantly at the site adjacent to the bromine substituent, although the alternative thiomaleates **125** are obtained to some extent and the bis-thioesters **126** are obtained in one case (for R^1 = H, R^2 = Me). Finally, this reaction is not affected by the addition of reducing agents such as dimethyl sulfide, thiourea, and triphenylphosphine.



Scheme 104

The photooxidation reaction of 3-bromo-2-(methylthio)furan yields (*E*)-2-bromo-4-oxobutenethioate as the only product (Scheme 105).[333] In contrast, reaction of the 2,3-bis(thio)furan analog gives a γ-thiobutyrolactone in high yield.

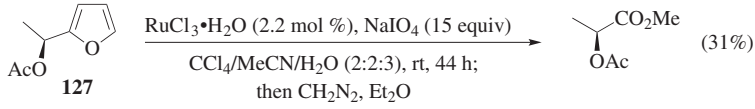


Scheme 105

Oxidations to Carboxylic Acids

Oxidations with Ruthenium Tetroxide. Complete oxidation of the furan ring of 2-substituted furan derivatives results in the formation of carboxylic acids. This transformation can be accomplished using a variety of oxidizing reagents, among which ruthenium tetroxide is the most common. Since its first introduction as an organic oxidant[334] the ability of ruthenium tetroxide to oxidize arenes has been demonstrated.[115,335] An improved procedure for the oxidation of phenyl groups, in which acetonitrile is used as solvent,[336] was successfully applied to the oxidation of furans and other heterocycles.[113] The optimal procedure to generate ruthenium

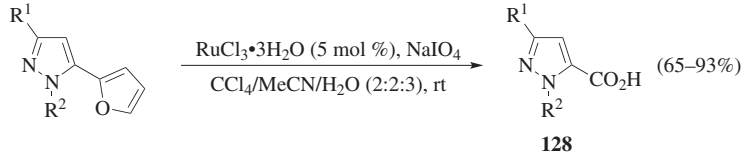
tetroxide involves the use of a catalytic amount (2.2 mol %) of ruthenium(III) chloride in the presence of an excess (4–30 equivalents) of sodium periodate with a 2:2:3 mixture of carbon tetrachloride/acetonitrile/water as the solvent. Under these conditions oxidation of the enantiomerically pure furan derivative **127** takes place without loss of enantiomeric purity, although in only 31% yield (Scheme 106).[113]



Scheme 106

These reaction conditions are tolerated by an extensive array of hydroxyl, protecting groups including alkyl,[337] benzyl,[338] and silyl[339] ethers, acetals,[340] and esters.[113,337] The use of ruthenium(III) chloride to generate ruthenium tetroxide is also possible in the presence of various nitrogen protecting groups including trifluoroacetyl,[341] benzyl,[341] 4-methoxybenzyl,[338] tosyl,[342] phosphinoyl,[343] and carbamates including *tert*-butoxycarbonyl[344,345] and benzyloxycarbonyl derivatives.[346] Interestingly, the oxidation reaction is also compatible with labile *N*,*O*-acetals.[347,348] Most of the transformations probed have employed enantiomerically pure compounds, thus demonstrating that the oxidation protocol is extremely useful in asymmetric
synthesis.

Oxidations of furans with ruthenium(III) chloride in the presence of sodium periodate is chemoselective with respect to other aromatic heterocyclic nuclei, such as the pyrazole ring,[349] making the method applicable to the preparation of a variety of fluorinated pyrazole derivatives **128** (Scheme 107).[350,351]

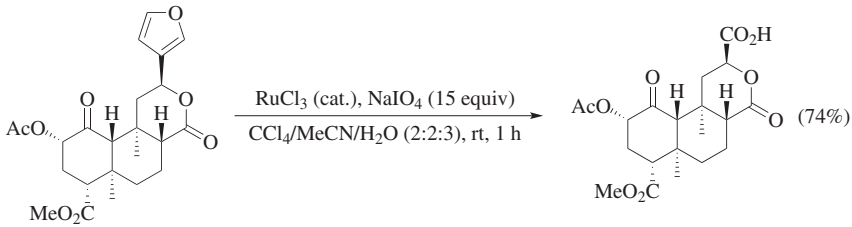


R^1 = CF_3, CF_3CHF, CF_3CH_2, MeCHF, CF_2HCH_2, CH_2FCH_2
R^2 = Me, 3-NC-4-FC_6H_3

Scheme 107

Similarly, 2-furylpyrazolines are transformed into 2-carboxypyrazolines using this oxidant. In these cases, while the reaction conditions are tolerated by *N*-benzoyl groups, the *N*-trifluoroacetyl group is lost during the oxidation reaction.[352]

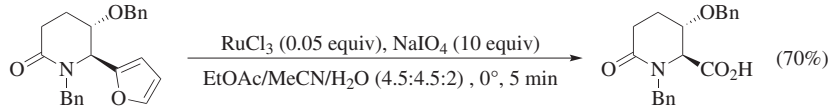
Oxidation of the furan ring to a carboxylic acid functionality also takes place with 3-substituted furans. For example, salvinorin (**129**), isolated from *S. divinorum*,[353] is readily oxidized to the corresponding carboxylic acid in 74% yield (Scheme 108).[233]



129

Scheme 108

Although a 2:2:3 carbon tetrachloride/acetonitrile/water mixture is commonly used as the solvent for ruthenium tetroxide oxidations of furans, the reaction can also be successfully carried out in other solvents. For example, a combination of 5 mol % of ruthenium(III) chloride in 1:1 acetonitrile/water can be used for this purpose.[354] Although replacement of carbon tetrachloride by dichloromethane increases reaction times up to 2 hours,[342] high yields are obtained.[355] A 1:1:1 acetonitrile/dichloromethane/water mixture has been employed in efficient (up to 90%) oxidations of 2-furan derivatives containing spiroketal units.[356,357] Other solvent combinations can be employed for this process, as exemplified by oxidation of the sugar-containing *N*-sulfonyl furfurylamines in 1:0.04:0.7 water/dichloromethane/acetonitrile,[358] but reaction times up to 1.5 h are needed for oxidations that are carried out in 2:2:3 acetonitrile/ethyl acetate/water at room temperature.[348] In contrast, in 4.5:4.5:2 acetonitrile/ethyl acetate/water the same reaction only requires 5 min at 0° for completion (Scheme 109).[359]

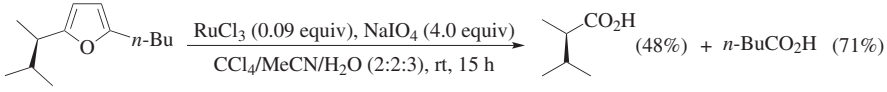


Scheme 109

High yields are also observed in ruthenium tetroxide promoted furan oxidations carried out in a biphasic system comprised of 1:1 ethyl acetate/water. These conditions, which make the reactions slightly exothermic, can be applied to the oxidation of 2,3-disubstituted furans.[360] The reaction is efficient when different ratios of the solvents are employed (for example, from 3:1:4 to 0:1:1 hexane/ethyl acetate/water and in 2:2:3 carbon tetrachloride/methanol/water). Even though ideal results are obtained when these reactions are run in the most versatile solvent system comprised of 1:3:4 hexane/ethyl acetate/water, substantial variations are observed for different substrates. As a consequence, no one set of optimized conditions can be prescribed for this process.

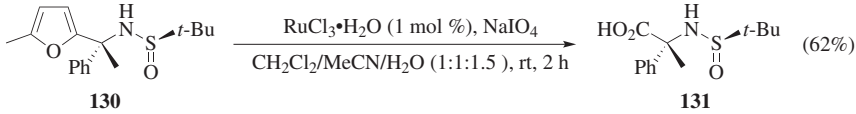
Oxidations of 2,5-disubstituted furans with catalytic amounts of ruthenium(III) chloride in the presence of an excess of sodium periodate afford the corresponding carboxylic acids in which one of the side-chains is lost.[354] When the C2 and C5

positions are occupied by similar alkyl chains, mixtures of products are produced (Scheme 110).[361] For example, with 2-methyl-5-substituted furans, the carboxylic acid is obtained along with acetic acid.



Scheme 110

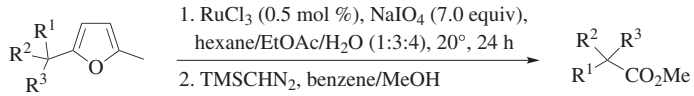
Oxidation of 5-methyl-*N*-sulfonyl furfurylamine **130** utilizing this oxidant leads to formation of the *N*-sulfinyl amino acid **131** in 62–69% yield (Scheme 111).[342] Similarly, 5-(methoxycarbonyl)-*N*-acetyl furfurylamines provide *N*-acetyl-α-amino acids in good yields.[362]

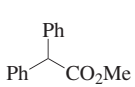


130 **131**

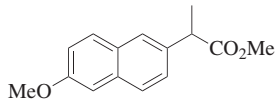
Scheme 111

The regioselective nature of oxidations of 2-arylmethyl-5-methylfurans has been explored in detailed studies probing the effects of solvents and number of equivalents of sodium periodate. In 1:3:4 hexane/ethyl acetate/water with 0.5 mol % of ruthenium(III) chloride and 7.0 equivalents of sodium periodate, the furan ring in the 2,5-disubstituted substrates is oxidized selectively on the side not containing phenyl or naphthyl substituents (Scheme 112).[363]

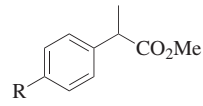




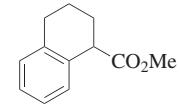
(87%)



(65%)



R	Yield (%)
MeO	92
BnO	96
CbzHN	86
Me	74
Ph	89

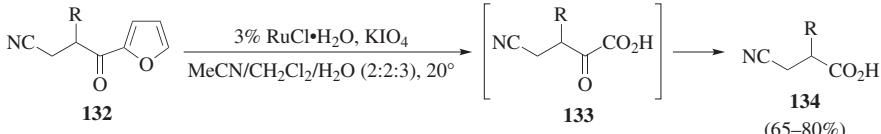


(85%)

Scheme 112

In addition, enantiomerically pure 2-methoxyfurans are oxidized without loss of enantiomeric purity.[364] Sodium periodate can be replaced as the primary oxidant

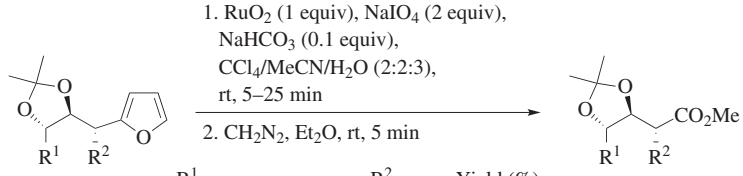
in this process by periodic acid. Under the latter conditions ($RuCl_3$, H_5IO_6, 2:2:3 carbon tetrachloride/acetonitrile/water, 10 minutes, room temperature) *N*-benzyl and *N*-benzyloxycarbonyl protecting groups are not affected.[365] An interesting decarboxylative oxidation reaction takes place when the furanyl ketones **132** are oxidized with ruthenium(III) chloride in the presence of potassium periodate. In this process, the initially formed pyruvic acid derivatives **133** undergo secondary oxidative decarboxylation to form acids **134** (Scheme 113).[366]



R = Me, Et, *n*-Bu, *s*-Bu, *n*-C_6H_{13}, *n*-C_5H_{11}, *c*-C_6H_{11}, $BnO(CH_2)_4$, $TMSCH_2$

Scheme 113

Ruthenium tetroxide can also be generated using ruthenium(IV) oxide and sodium periodate. No particular differences are observed in efficiencies when reactions are promoted using ruthenium(III) chloride or ruthenium(IV) oxide as the source of ruthenium, although the latter reagent has traditionally been utilized in carbohydrate chemistry[367–370] where a variety of protecting groups are employed. Indeed, oxidations using either ruthenium(IV) oxide or ruthenium(III) chloride are fully compatible with silyl,[368] benzyl, and allyl ethers,[369] and MOM acetals.[371] Isopropylidene acetals also tolerate typical oxidation conditions as do both oxygen[372] and nitrogen[373] functionalities (Scheme 114),[370,374,375] and *N,O*-acetals.[376]

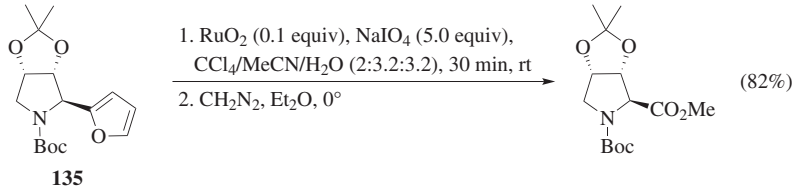


R^1	R^2	Yield (%)
H	MeO	69
H	BocNH	78
$BnCH_2O$	BocNH	56
$TBSO(CH_2)_4CHMe$	BocNH	65

Scheme 114

As with ruthenium(III) chloride, oxidative cleavage employing ruthenium(IV) oxide can be performed in the presence of amino groups, monoprotected as carbamates,[373–375] tosylamines,[376,377] and benzamides,[378,379] as employed in an expeditious synthesis of amino acids from furfurylamines.[380] *N*-Hydroxy amino

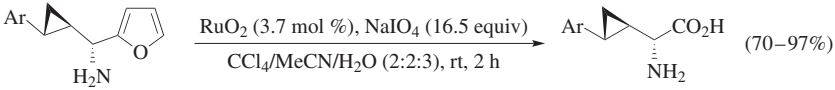
acids are also prepared using this method because the N–O bond is not affected by the reaction conditions.[381] Cyclic amino acids can be prepared from the corresponding 5-furyl-*N*-Boc-2-pyrrolidinones[382] and 2-furyl-*N*-Boc-2-pyrrolidines **135** (Scheme 115).[383]



135

Scheme 115

The use of ruthenium(IV) oxide enables chemoselective oxidations of the furan ring in the presence of other aromatic rings.[384] Notably, free amino groups can sometimes survive the reaction conditions as exemplified by the formation of amino acids **136** in high yields (Scheme 116).[385]



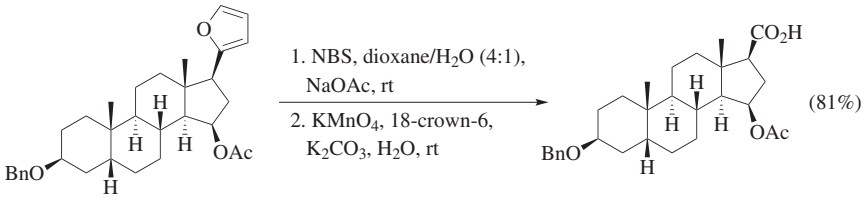
Ar = Ph, 2-ClC$_6$H$_4$, 3-MeC$_6$H$_4$, 4-MeOC$_6$H$_4$, 2-naphthyl

136

Scheme 116

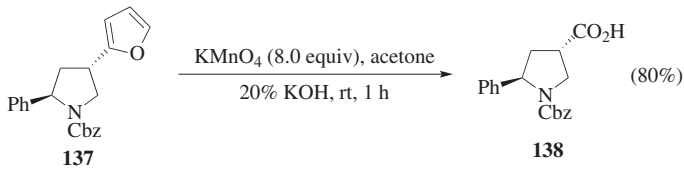
In summary, oxidative cleavage reactions of furans with ruthenium tetroxide does not depend on the method of generation of the oxidant, and either ruthenium(III) chloride or ruthenium(IV) oxide can be used for this purpose. In addition, several solvent systems can be employed, lending flexibility when substrate solubility is an issue. No matter what reaction conditions are used, the process displays excellent compatibility with a great variety of oxygen and nitrogen protecting groups, making this a method of high synthetic utility.

Oxidations with Potassium Permanganate. Potassium permanganate is an alternative oxidant that can be employed in furan ring cleavage reactions. This oxidant is generally useful for the oxidation of heterocyclic compounds.[386] The combination of NBS in dioxane/water followed by in situ oxidation with a catalytic amount of potassium permanganate in the presence of an excess of sodium periodate has been employed to transform a steroidal furan derivative into the corresponding carboxylic acid (Scheme 117).[387]



Scheme 117

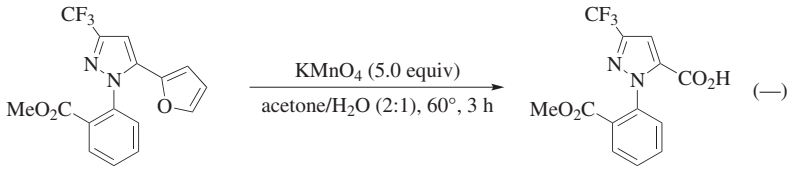
Arylfurans are converted into benzoic acid derivatives by the action of potassium permanganate in *tert*-butanol/water at reflux for several hours.[388] Milder conditions (room temperature, 1 hour) are sufficient for converting enantiomerically pure *N*-Cbz-2-phenyl-4-(2-furyl)pyrrolidine (**137**) into the corresponding β-proline derivative **138** (Scheme 118).[389]



137 **138**

Scheme 118

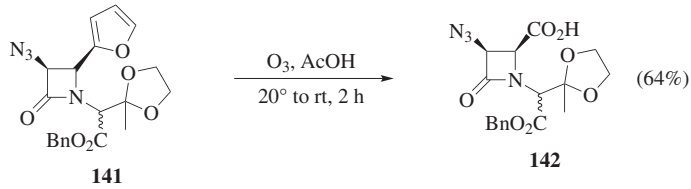
The oxidizing power of potassium permanganate prevents its use with substrates bearing sensitive functional groups even when catalytic amounts of oxidant and controlled reaction conditions are utilized. Nevertheless, this oxidant is useful in the oxidation of 3-(2-furyl)pyrazolyl derivatives of biological importance. For example, an excess of potassium permanganate promotes oxidation of pyrazole **139** to the corresponding carboxylic acid **140** in high yield (Scheme 119).[390] Finally, potassium permanganate is compatible with aromatic rings containing different functional groups such as azides,[391] nitrile,[392] and ester moieties.[393]



139 **140**

Scheme 119

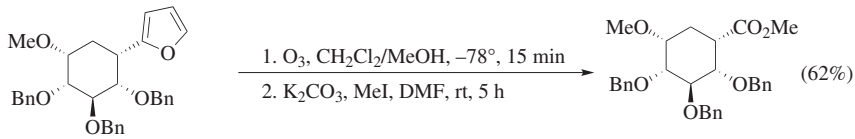
Oxidations with Ozone. The process of oxidizing furans to give carboxylic acids by the action of ozone has been known for more than 50 years.[100,101] No systematic studies have been performed on this process but numerous examples illustrate its high synthetic utility. For example, oxidation of the highly functionalized β-lactam **141** to produce carboxylic acid **142** takes place smoothly by treatment with a stream of ozone in acetic acid at room temperature (Scheme 120).[394]



141 **142**

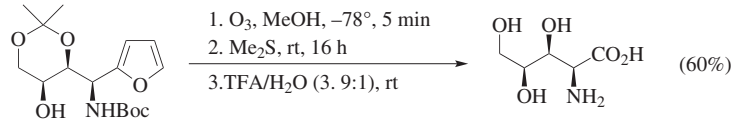
Scheme 120

Ozone-induced oxidations can be carried out in anhydrous methanol[395] at −30° and in dichloromethane/methanol at −78°. The carboxylic acid is isolated by simply warming the reaction mixture to room temperature and evaporating the solvent. In general, the methyl ester is formed in situ by treatment with diazomethane, trimethylsilyldiazomethane, or methyl iodide in a basic medium (Scheme 121).[396] The mildness of these reaction conditions, including a simple work-up procedure, has contributed to the popularity of furan oxidations through ozonolysis in carbohydrate chemistry.[397] A variety of protecting groups (acetals, benzyl, esters, ethers, etc.) may be present[398] in the substrate without being affected by the ozonolysis conditions.[399]



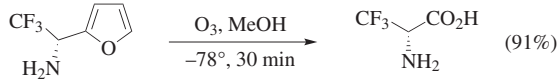
Scheme 121

In a similar fashion, warming the reaction mixture to room temperature after ozonolysis at −78° can be followed by treatment with triphenylphosphine[400,401] or dimethyl sulfide[111] to promote decomposition of the ozonide. Unprotected hydroxyl groups are preserved under these reaction conditions. Several stereoisomers of 4-hydroxyleucine are obtained from the corresponding *N*-Boc-1-(2-furyl)-1,3-amino alcohols using this technique.[402] The ozonolysis of the furan ring is also possible in the presence of free amino and hydroxyl groups,[403,404] although in one example only a 30% yield was obtained.[405] Ozone oxidations can also be carried out on substrates possessing labile 1,3-acetonides.[400,406] This procedure is particularly convenient when other acid-labile groups are present because it is possible to carry out an in situ deprotection step subsequent to the oxidation (Scheme 122).[407]



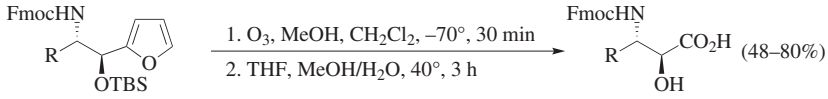
Scheme 122

Ozonolysis of furans in dichloromethane at low temperature permits preservation of the integrity of amino protecting groups, such as *N*-Boc,[408,409] *N*-Cbz,[410] *N*-Fmoc,[411,412] *N*-benzoyl,[379] cyclic carbamates,[413] and lactams.[414] Interestingly, this oxidation is also compatible with the presence of free amino groups, as demonstrated by the process shown in Scheme 123.[385,415]



Scheme 123

On the other hand, partial cleavage of a *tert*-butyldimethylsilyl group is observed in the ozonolysis of **143** caused by migration of the silyl group to the newly formed carboxylic acid moiety.[411] For this reason, a one-pot deprotection is carried out to yield *N*-protected α-hydroxy-β-amino acids in high yields (Scheme 124).[412]

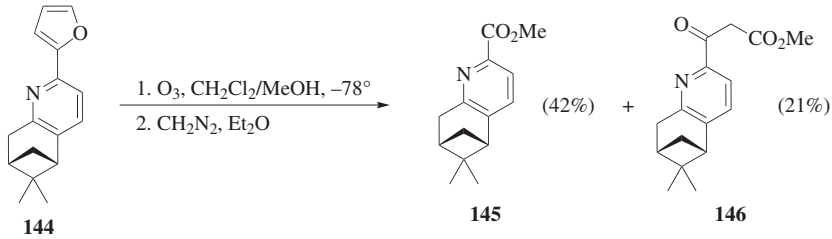


143

R = H, Me, *i*-Pr, *i*-Bu, Ph, Bn

Scheme 124

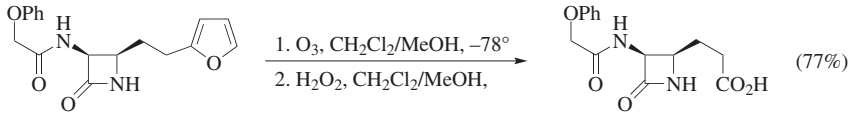
Ozone-promoted oxidation of 2-furylpyridine **144** forms nicotinic acid **145**, although this process is accompanied by formation of the incompletely oxidized by-product **146** (Scheme 125).[416]



144 **145** **146**

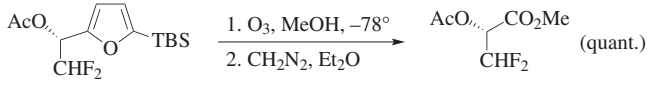
Scheme 125

Multifunctional furans containing a cyclopropyl ring, a benzene unit and a free amino group are oxidized in high yields through ozonolysis in dichloromethane at low (−78°) temperature.[385] However, oxidative work-up with hydrogen peroxide, which enables rapid generation of the carboxylic acid (Scheme 126), is not tolerated by free amino groups.[417] Bis-furan derivatives are oxidized simultaneously at the two furan units providing dicarboxylic acids.[418,419]



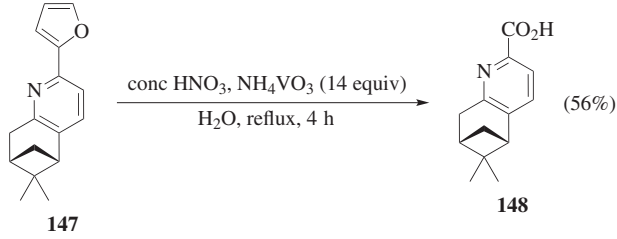
Scheme 126

Ozonolysis reactions of chiral furans containing C2 silyl groups take place with complete preservation of enantiomeric purity (Scheme 127).[420] In contrast, whereas 2-acyl furans yield mixtures of the expected keto acid and the corresponding decarboxylated derivatives,[421] 2-methyl-5-(trifluoromethylcarbonyl)furan reacts with ozone to form the α-keto ester in good yield.[422]



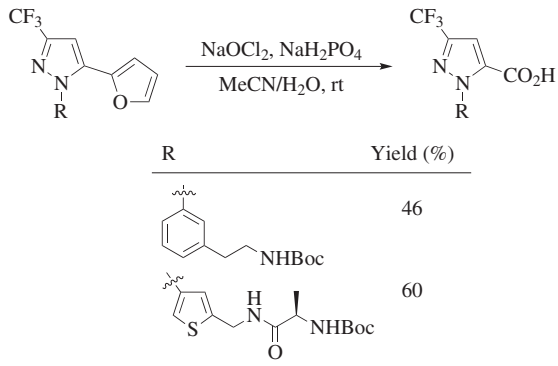
Scheme 127

Oxidations with Other Oxidants. Oxidation reactions of furans to generate carboxylic acids can be performed using photooxidation in methanol, but low yields are common in these reactions.[307] To avoid this problem, oxidations of the substrates exemplified by **147** can be carried out using nitric acid in the presence of ammonium vanadate (Scheme 128).[423] Under these conditions, carboxylic acid **148** is formed as the only product in 56% yield.



Scheme 128

2-Pyrazolylfuran derivatives have been oxidized using sodium chlorite under conditions that do not affect several functional groups, including benzene[424] and heteroaromatic ring systems like thiophenes (Scheme 129).[425]

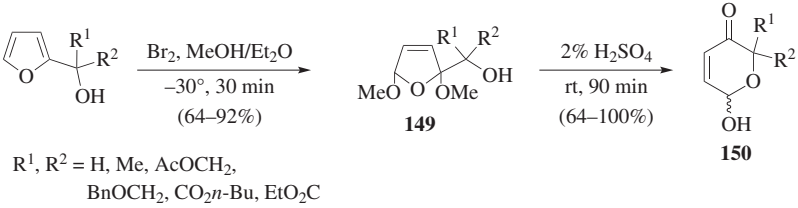


Scheme 129

The Achmatowicz Reaction

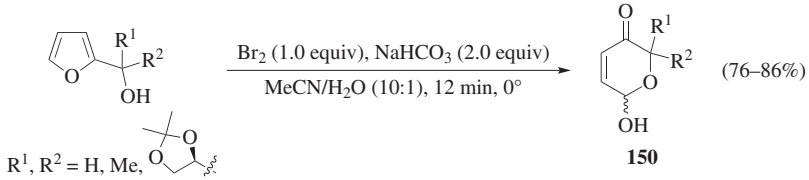
The Achmatowicz reaction, the oxidative conversion of furfuryl alcohols to 6-hydroxy-2*H*-pyran-2-ones, can be achieved with substrates bearing multiple substituents on side chains and the furan ring. Thus, the synthetic utility of this method is determined by availability of methods for oxidizing the furan ring. In this process, oxidation generates the corresponding 1,4-dicarbonyl compound that undergoes in situ cyclization involving the hydroxy group at the α-position.

Bromine in Methanol. The original procedure reported by Achmatowicz[31] involves oxidation of a furan derivative using bromine in methanol to give a dimethoxy dihydrofuran **149**. Acid hydrolysis of **149** then produces the rearranged 2*H*-pyran-2-one **150** (Scheme 130).[426,427]



Scheme 130

The reaction involving bromine also proceeds at −78° and the hydrolysis can be performed using 10% aqueous sulfuric acid at room temperature.[428] The overall transformation can be accomplished in one pot by treating the furfuryl alcohol with a stoichiometric amount of bromine in a solvent containing a few equivalents of water (Scheme 131).[429]

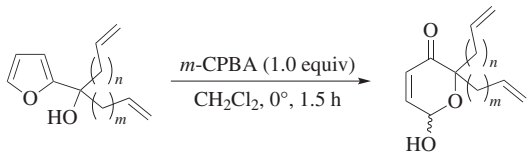


150

Scheme 131

Solvents have little influence on the reaction and, as a result, both protic (alcohols and carboxylic acids) and aprotic (diethyl ether, dioxane, acetone, acetonitrile, DMF) solvents can be used. In all cases, reactions take place at 0° and are complete in less than 2 minutes, typically generating products in essentially quantitative yields. When tetrahydrofuran/water serves as the solvent and reactions are performed at 5°, the yields are lower.[430] Moreover, the resulting epimeric mixtures of products can be silylated in situ using *tert*-butyldimethylsilyl chloride to form a chromatographically separable mixture (3:1) of α- and β-epimers at C2. The undesired β-epimer can be readily separated and recycled by sequential deprotection/protection to give the α-epimer in 67% overall yield after two recycles.[431]

***m*-Chloroperoxybenzoic Acid.** Oxidations of furfuryl alcohols with peroxyacetic acid or *m*-CPBA produce the corresponding 6-hydroxy-2*H*-pyran-3(6*H*)-ones in one step and without the need for a secondary hydrolysis step.[432,433] This reaction is general for a variety of furans containing alkyl and aryl substituents as side chains.[434–437] In a similar fashion, substrates with steroid side chains are smoothly oxidized by *m*-CPBA[438] utilizing several reaction protocols.[439,440] With simple furfuryl alcohols, reactions are nearly always carried out in dichloromethane at 0°, are complete within 1 hour, and produce products in high yields as mixtures of isomers.[441–445] Highly substituted substrates require reaction times of up to 12 hours.[446] The oxidation procedure is compatible with substrates containing double bonds (Scheme 132),[310,447,448] and a furan substrate in which an epoxide is present reacts to give the product in 94% yield.[449] High yields also attend reactions of substrates containing several protecting groups such as TBS and benzyl ethers.[444,450]

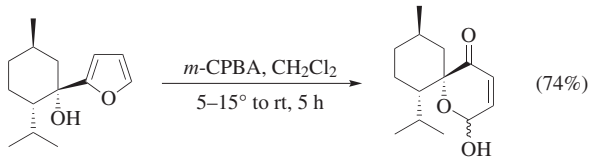


m	*n*	Yield (%)
2	1	58
2	2	58
3	1	55
3	2	59
3	3	56

Scheme 132

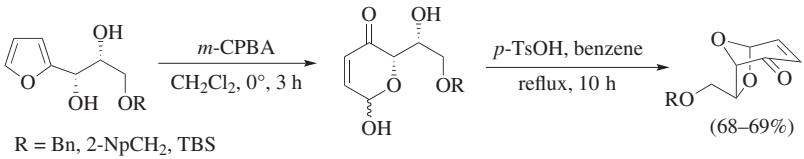
β-Phosphinoyl furfuryl alcohols are also oxidized in high[451] to moderate chemical yields.[452]

In general, substitution on the furan ring does not affect the yield of the reaction. In addition, the process takes place smoothly with more diverse substrates to generate highly substituted 2*H*-pyran-3(6*H*)-ones.[442,453] Cyclic tertiary furyl carbinols can also be easily oxidized using *m*-CPBA to form spiro derivatives (Scheme 133).[452,454,455]

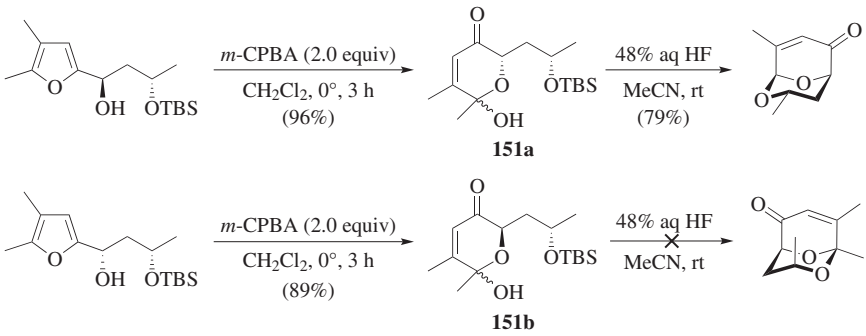


Scheme 133

With furans possessing a hydroxyl group on a side chain, it is possible to induce formation of a bicyclic product by prolonged acid treatment following the oxidation step (Scheme 134).[456,457] In reactions of enantiomerically pure substrates that generate new stereocenters, high levels of diastereoselectivity are observed.[458,459] 4,5-Disubstituted furans give products such as **151a** and **b**. Only **151a**, derived from the corresponding *anti* adduct, forms the corresponding hemiacetal. No reaction is observed for **151b** as a consequence of unfavorable 1,3-diaxial interactions in the final product (Scheme 135).[453]

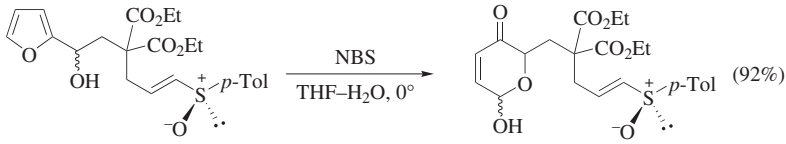


Scheme 134



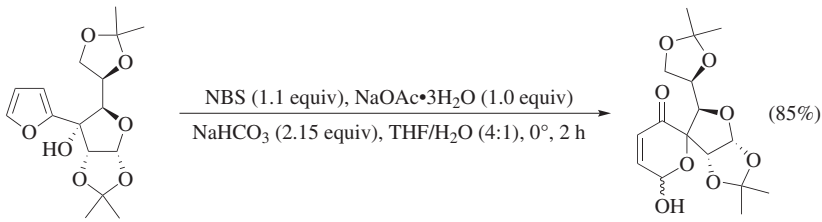
Scheme 135

***N*-Bromosuccinimide.** Furfuryl alcohols react rapidly with *N*-bromosuccinimide in the presence of water to produce 6-hydroxy-2*H*-pyran-3(6*H*)-ones in high yields.[435] *N*-Bromosuccinimide in 4:1 tetrahydrofuran/water effects oxidations of a variety of furfuryl alcohols. The typical reaction conditions employed for these processes[460] are compatible with hydroxyl protecting groups including acetals,[461,462] silyl ethers,[463–469] and esters,[470–472] as well as typical carbamates[473–475] that are used as amine protecting groups (Scheme 136).



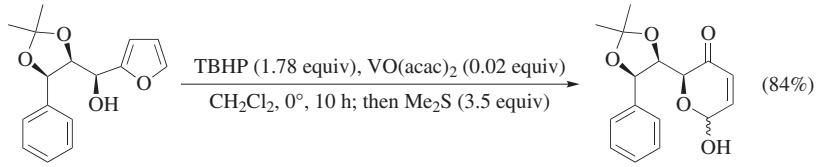
Scheme 136

Double[476–478] and triple[479] bonds are also compatible with furan oxidation using *N*-bromosuccinimide. Moreover, the method has been applied to solid-phase synthesis of compound libraries.[151,480] In one case, selective acylation of the resulting mixture of hemiacetals formed at low (−78°) temperature results in a dr >20:1.[481] NBS oxidation of a furanyl sugar at room temperature gives a 1:1 mixture of anomers. Spiro compounds can also be produced using this process if there is an appropriate substituent on the side chain[482] or on the furan ring[483] (Scheme 137).



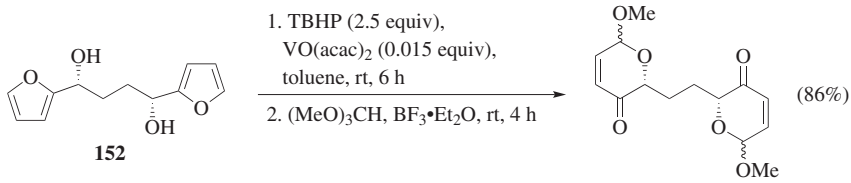
Scheme 137

***tert*-Butyl Hydroperoxide.** *tert*-Butyl hydroperoxide (TBHP) and a catalytic amount of vanadyl diacetylacetonate serve as another oxidizing system for transforming furfuryl alcohols into 6-hydroxy-2*H*-pyran-3(6*H*)-ones.[484,485] A proposed mechanism for this process involves initial epoxidation of a double bound of the furan ring followed by vanadium-promoted epoxide ring opening and rearrangement to form the final products via a *cis* 1,4-dicarbonyl intermediate.[486] These conditions enable oxidation of a furan ring in the presence of a labile acetonide group (Scheme 138).[487–493] Several types of furan derivatives, including aliphatic and aromatic derivatives, can be effectively oxidized using these conditions.[494–499]



Scheme 138

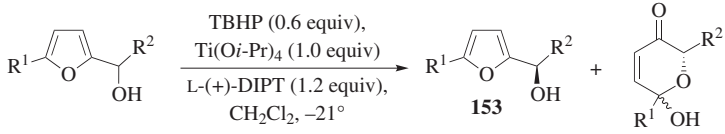
When other oxidizable groups are present in the substrate, the use of lower temperatures results in a greater degree of chemoselectivity.[10,500–502] In addition, under the reaction conditions, double bonds,[503–506] including dienes[507] and allenes, remain unreactive.[508] Implementation of these reaction conditions along with the inclusion of acetic anhydride in the reaction mixture enables the conversion of furan substrates to mixtures of 6-acetoxy epimers.[509] Similarly, in situ methylation with methyl orthoformate in the presence of boron trifluoride etherate can be used to generate 6-methoxy derivatives.[40,510] The procedure has been applied in two-directional syntheses starting with bis-furan derivatives such as **152** (Scheme 139).[511,512]



152

Scheme 139

Replacement of the vanadium catalyst with 10 mol % of titanium isopropoxide and 15 mol % of D- or L-tartrate enables catalytic, asymmetric, kinetic resolution of racemic furfuryl alcohols.[513] Various enantiomerically enriched 2-furylcarbinols **153** have been prepared in addition to 6-hydroxy-2*H*-pyran-2-ones **154** using stoichiometric amounts of both titanium isopropoxide and L-(+)-diisopropyl tartrate (DIPT).[514] Under these conditions excellent enantioselectivities are observed except for the reaction of the *tert*-butyl derivative (Scheme 140).

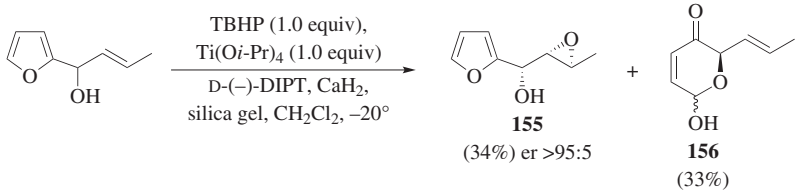


153 **154**

R^1	R^2	Time (h)	**153** Yield (%)	**153** er	**154** Yield (%)
H	Me	24	32	>95:5	53
H	*n*-C_5H_{11}	25	42	>95:5	53
H	*i*-Pr	25	39	>95:5	55
H	*t*-Bu	40	41	58:42	58
H	Ph	40	42	>99:1	44
Me	*n*-C_5H_{11}	6	45	>95:5	55

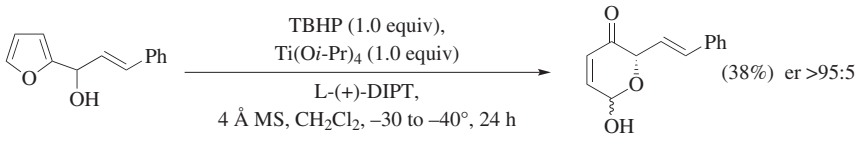
Scheme 140

When an excess of *tert*-butyl hydroperoxide is employed, higher product yields are obtained by carrying out the reaction in the presence of 5–10 mol % of calcium hydride and 10–15 mol % of silica gel.[515] The kinetic resolution process is applicable to substrates containing double bonds since only the furan ring is oxidized.[516,517] However, it is possible to adjust the reaction conditions so that both resolution and epoxidation of the double bond occur. For example, whereas oxidation of a furfuryl alcohol with 0.5 equivalents of *tert*-butyl hydroperoxide produces only a 4% yield of the epoxidation product **155**, using 1.0 equivalent of oxidant increases the yield of **155** to 34% without affecting the degree of enantioselectivity (Scheme 141).[518]



Scheme 141

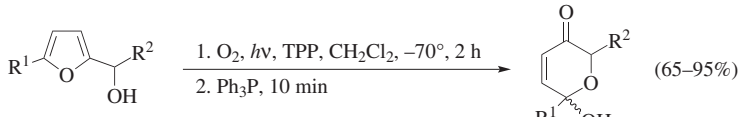
Kinetic resolution based synthesis of enantiomerically pure 2-alkenyl-6-hydroxypyran-3-ones such as **156** can be carried out under reaction conditions in which the double bond is not altered, followed by a second conventional oxidation (*tert*-butylhydroperoxide/vanadyl acetylacetonate) of the resolved alkenyl furfuryl alcohol.[476,519] High levels of enantioselectivity are realized using 20 mol % of titanium isopropoxide/L-(+)-diisopropyl tartrate, although under these conditions only the resolved furfuryl alcohol is recovered from the reaction mixture.[520] In contrast, catalytic conditions (10 mol % of titanium isopropoxide and 15 mol % of L-(−)-diisopropyl tartrate) at −40° enable isolation of the enantiomerically enriched (er 97:3) 6-hydroxypyran-3-one in moderate yield (31%) as a 69:31 mixture of epimers.[521] These conditions are applicable to sequential kinetic resolution of difuryl derivatives[522] and desymmetrization of *meso* compounds.[523] By executing the reaction at −40° in the presence of molecular sieves, alkenyl pyranones are obtained with high levels of enantioselectivity (Scheme 142).[524]



Scheme 142

Photooxygenation. The photooxygenation reactions of alkenyl furfuryl alcohols, which produce 6-hydroxypyran-3-ones in high yields,[525] are generally carried out

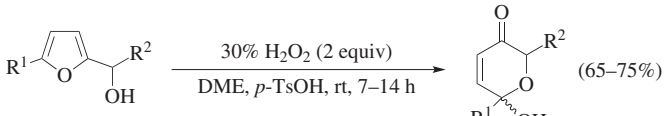
using either rose bengal, TPP, or methylene blue as sensitizers (Scheme 143).[526] Irradiation is typically followed by treatment of the product mixture with an excess of triphenylphosphine or dimethyl sulfide.[527,528] These reaction conditions are also compatible with the presence of double bonds in the molecule.[529]



R^1 = H, Me, $HOCH_2$, $AcOCH_2$, $PhCOCH_2$
R^2 = H, Me, Et, Ph, *n*-$C_{11}H_{23}$

Scheme 143

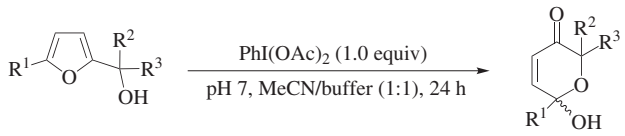
Hydrogen Peroxide. Treatment of furfuryl alcohols with hydrogen peroxide in the presence of *p*-toluenesulfonic acid (PTSA) affords furfuryl hydroperoxides, which in the presence of excess oxidant (2.0 equivalents) give rise to 2,6-disubstituted 6-hydroxy-2*H*-pyran-3(6*H*)-ones (Scheme 144).[530] The formation of these products results from two sequential oxidations of the starting materials.[531] On the other hand, by using hydrogen peroxide in the presence of titanium silicalite 1 (TS-1) in acetonitrile as a solvent, 6-hydroxy-3-pyranones are generated through the intermediacy of dicarbonyl derivatives formed via the conventional Achmatowicz reaction mechanism.[48] Oxidations of 5-methyl-substituted furfuryl alcohols proceed in low yields (20%) in marked contrast to oxidations of 5-unsusbtituted compounds (80–93%).



R^1 = H, Me
R^2 = *n*-C_5H_{11}, *n*-C_6H_{13}, *n*-C_8H_{17}

Scheme 144

Other Oxidants. The Achmatowicz reaction of furylcarbinols promoted by dimethyldioxirane is compatible with the presence of double bonds.[532] The use of hypervalent iodine reagents can also be used to transform these substances into 6-hydroxy-3-pyranones, as emplified by the iodosobenzene diacetate (IBDA)-induced formation of the hydroxy-2*H*-pyran-3(6*H*)-ones shown in Scheme 145.[533]



R^1	R^2	R^3	Temp (°)	Yield (%)
H	H	Me	50	30
Me	H	Me	rt	50
Me	H	Et	rt	50
H	H	*n*-Bu	50	30
Me	H	*n*-Bu	rt	50
H	*c*-C_6H_{11}	*c*-C_6H_{11}	50	40
Me	*c*-C_6H_{11}	*c*-C_6H_{11}	rt	76
Me	H	*n*-$C_{10}H_{21}$	rt	70

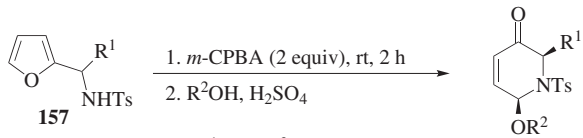
Scheme 145

Other oxidants capable of promoting formation of 6-hydroxy-3-pyranones from furfuryl alcohols include pyridinium chlorochromate (PCC)[534] and sodium chlorite.[535] Electrochemical oxidation is also effective for this purpose.[536]

The Aza-Achmatowicz Reaction

Oxidation of furfuryl amines affords the corresponding 6-hydroxy-1,2-dihydropyridin-3(6*H*)-ones, provided that the nitrogen is properly substituted. Since the resulting heterocycle contains a potentially labile hemiaminal group, the presence of electron-withdrawing groups on nitrogen is needed to increase stability of the dihydropyridinone ring system. As a consequence, the so-called aza-Achmatowicz reaction[33] is limited to furfuryl amides, sulfonamides, and carbamates. This condition does not limit the synthetic utility of the process, whose products are widely applicable as building blocks in the preparation of a great variety of nitrogen-containing compounds. Solid-phase techniques have also been applied for carrying out this reaction.[537]

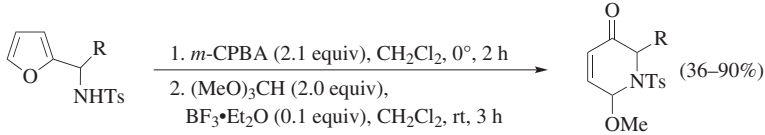
***m*-Chloroperoxybenzoic Acid.** Treatment of *N*-tosyl furfurylamines **157** with *m*-CPBA in dichloromethane for 2 hours at room temperature yields 2,6-dihydro-1*H*-pyridin-3-ones as single diastereomers.[538] These substances are often unstable and therefore are treated with an alcohol in the presence of a catalytic amount of sulfuric acid (Scheme 146)[538]or cerium(IV) salts[539]to give the corresponding alkoxy derivatives.



R^1	R^2	Yield (%)
H	*i*-Pr	83
n-Bu	Et	82
n-Bu	*i*-Pr	54

Scheme 146

The hydroxyl groups in these products can be converted into ethers by treatment with methyl[540,541] or ethyl[542,543] orthoformate in the presence of boron trifluoride etherate (Scheme 147). These reaction conditions are fully compatible with the presence of other protecting groups, including silyl ethers,[541,544,545] esters,[546] and acetals.[547] An alternative to the protection of the hydroxyl group is an in situ oxidation to form the corresponding lactams.[437]

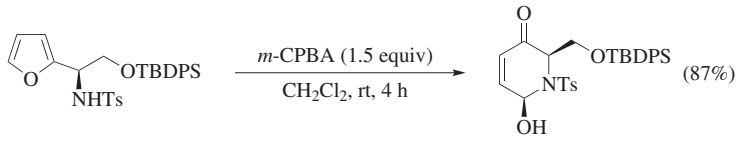


R = H, Me, Et, *i*-Pr, *n*-Pr, *i*-Bu, *n*-Bu

Scheme 147

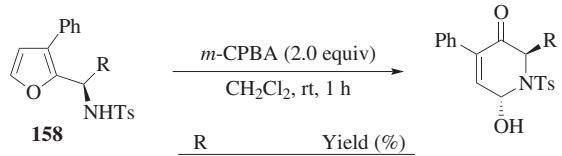
The stabilities of 6-hydroxy-2,6-dihydro-1*H*-pyridin-3-ones are strongly substituent dependent. Some of these substances are sufficiently stable to be purified using column chromatography on silica gel,[548] and to be stored at room temperature.[549] When alkyl substituents are present at C2 of the furan, in situ protection of the hydroxy group is advisable,[550–552] although these compounds can be purified by using silica gel pretreated with a phosphate buffer.[405]

Trans isomers of 6-methoxy-2-methyl-1-tosyl-1,6-dihydro-2*H*-pyridin-3-ones are formed preferentially in these processes, but the *cis* isomers can be generated as a consequence of the $A^{1,3}$-strain involving the tosyl group, which forces the methoxy and the methyl groups to adopt pseudoaxial orientations.[553,554] Indeed, even in products containing bulkier groups on the ring, such as a dioxolane ring[555] or a *tert*-butyldiphenylsiloxy group,[556] *cis* isomers predominate (Scheme 148).



Scheme 148

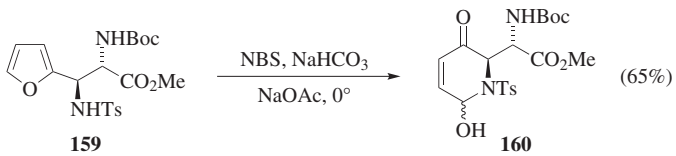
Thus, reactions of enantiomerically pure phenyl furfuryl-*N*-tosylamines **158** produce 4-phenyl *trans* isomers in very high yields (Scheme 149).[557]



R	Yield (%)
$TMSCH_2$	94
$AcOCH_2CMe_2$	83

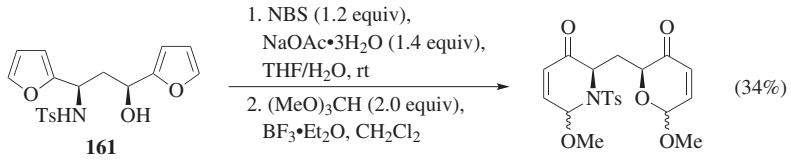
Scheme 149

***N*-Bromosuccinimide.** Treatment of racemic *N*-tosyl-furylglycinol with *N*-bromosuccinimide at 0° for 4 hours yields 83% of the oxidized product *trans*-*N*-tosyl-2-hydroxymethyl-6-hydroxy-1,2-dihydropyridin-3(6*H*)-one.[558] A mixture of *N*-bromosuccinimide, sodium bicarbonate, and sodium acetate has been employed to oxidize diamino acid **159** to produce the dihydropyridone **160** in 65% yield (Scheme 150).[559] Actually, a 5:1 mixture of **160** and its side chain epimer is obtained, indicating that some epimerization of the α-amino group takes place in this process. However, in a manner that is similar to that described above, the *cis* isomers of 6-methoxy-2-methyl-1-tosyl-1,6-dihydro-2*H*-pyridin-3-ones are formed as a consequence of the $A^{1,3}$-strain of the tosyl group, which forces the methoxy and methyl groups to adopt pseudoaxial orientations.[553,554] Even with bulkier groups like a dioxolane ring[555] or a *tert*-butyldiphenylsiloxy group,[556] the formation of the *cis* isomers predominates. In addition to *N*-tosyl furfurylamines, *N*-benzyloxycarbonyl derivatives can be used as substrates in these reactions,[560] which produce mixtures of *cis* and *trans* isomers even when bulky substituents are present.[561] If an excess of *N*-bromosuccinimide is used, further oxidation occurs to produce pyridines.[154]



Scheme 150

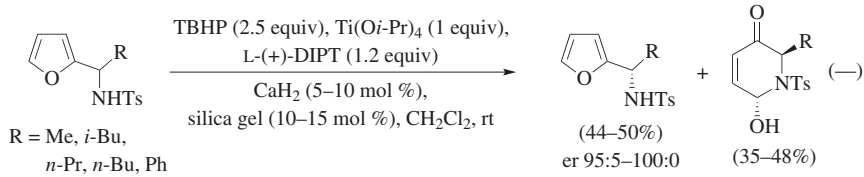
As previously discussed (Scheme 147), in situ formation of the corresponding methoxy derivatives can take place by secondary reactions with trimethyl orthoformate in the presence of boron trifluoride etherate.[562] With the difurfuryl alcohol derivative **161**, *N*-bromosuccinimide promotes simultaneous Achmatowicz reactions on both furan moieties, which serves as a critical step in the synthesis of disaccharide mimetics (Scheme 151).[563] The same transformation takes place with the corresponding *anti* isomer of **161**.



161

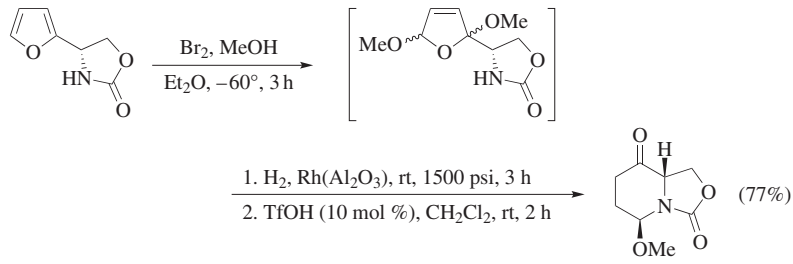
Scheme 151

***tert*-Butyl Hydroperoxide.** Oxidations of furfuryl alcohols using the modified Sharpless asymmetric epoxidation reagent can also be used for preparing enantiomerically enriched furfuryl amides by way of a kinetic resolution.[515] In general, up to three days are needed for the reaction to go to completion.[564] With *N*-tosylfurfurylamines, the (*S*) enantiomer is slower-reacting when L-(+)-diisopropyl tartrate is employed and, thus, (6*R*)-dihydropyridones are obtained in enantiomerically pure form (Scheme 152).[565] Using the enantiomeric D-(+)-diisopropyl tartrate causes the (*R*)-enantiomer to be slower-reacting.[566] The efficiency of this kinetic resolution process is not affected by the presence of isolated double bonds, which are not oxidized.[42]



Scheme 152

Bromine in Methanol. A variety of furfuryl amines bearing sulfone or carbonyl groups on the nitrogen atom are oxidized to give dimethoxy dihydrofurans by the action of bromine in methanol. Cyclization of these compounds occurs to form 3-piperidinones under acidic conditions after catalytic hydrogenation of the (*Z*) double bond (Scheme 153).[246] The procedure is applicable to cyclic substrates, furnishing 3,8-dioxoindolizidines[567,568] and carbacephems precursors.[33]

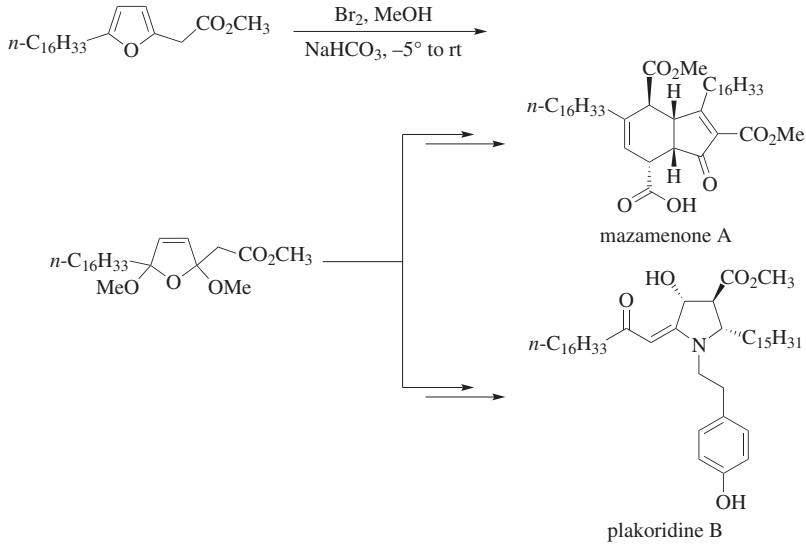


Scheme 153

APPLICATIONS TO SYNTHESIS

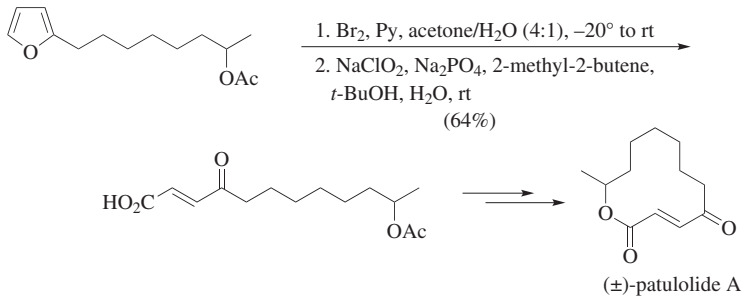
Synthesis of 1,4-Dioxo Compounds

The scope and synthetic potential of employing the furan ring as a C_4 synthon has been amply demonstrated in a number of synthetic studies. All of the possible transformations of this heterocycle into 1,4-dicarbonyl compounds have been employed in routes for the total synthesis of a variety of substances. For example, efficient routes using bromine in methanol oxidations have been developed to prepare a host of alkaloids[248] and marine natural products of biological interest such as mazaminones[251,252] and plakoridines[229,230] (Scheme 154).



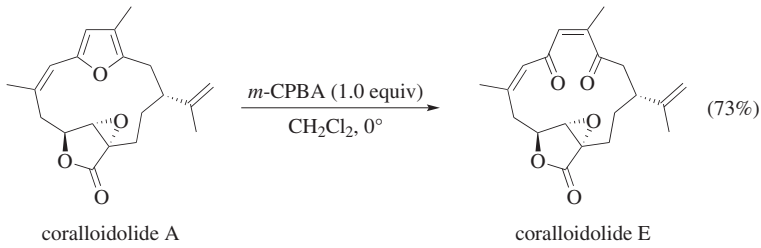
Scheme 154

Reactions of furans with bromine in other solvents have also been applied to the synthesis of the macrocyclic lactones tylonolide[142] and patulolide (Scheme 155).[181]



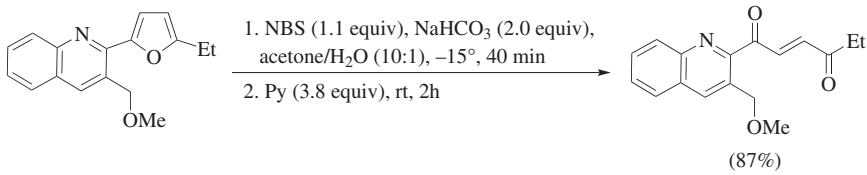
Scheme 155

Preparation of the latter target was also accomplished by employing a *m*-CPBA oxidation of a furan derivative.[197] Indeed, the use of *m*-CPBA has been extended to the synthesis of diverse targets such as aphidicolin,[158,159] endesmanolides,[191] and coralloidolide E (Scheme 156).[157]



Scheme 156

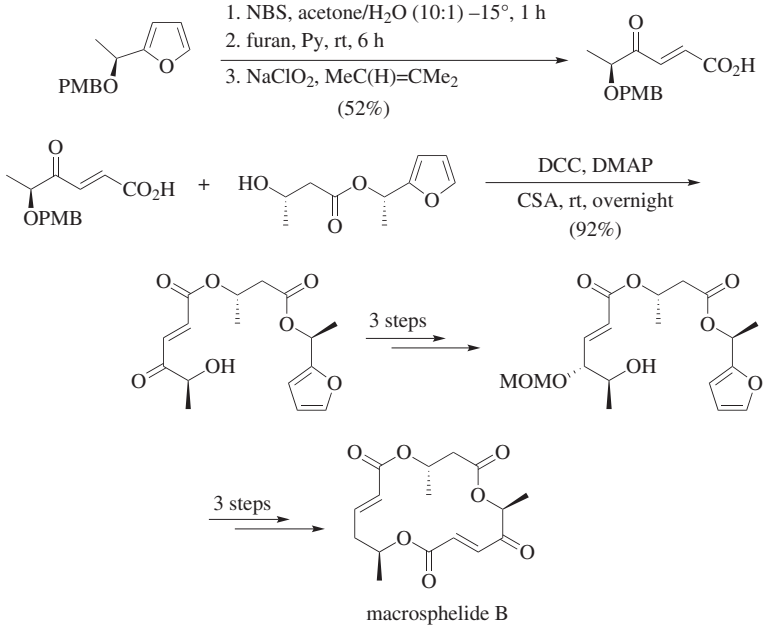
Conversions of 2,5-disubstituted furans into the corresponding dioxoalkenes by the action of *N*-bromosuccinimide in pyridine has been used to prepare precursors of the alkaloid nothapodytine (Scheme 157).[150]



Scheme 157

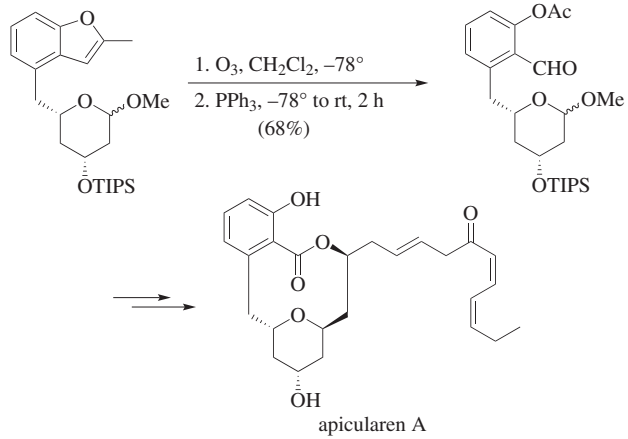
The convenient protocol for converting 2-substituted furans into 4-oxoalkenoic acids, involving oxidation with *N*-bromosuccinimide and further oxidation of the 4-oxoalkenal formed with sodium chlorite, has been applied to the synthesis of a variety of macrolides. The presence of several 4-oxoalkenoic acid moieties in these compounds makes the furan oxidation approach highly attractive. Among the macrolides synthesized by utilizing this method are brefeldin,[183] (+)-aspicilin,[198] the antibiotic

(−)-A26771B,[186] and macrosphelides A and B (Scheme 158),[185,569] C and D,[570] and H and G.[571]



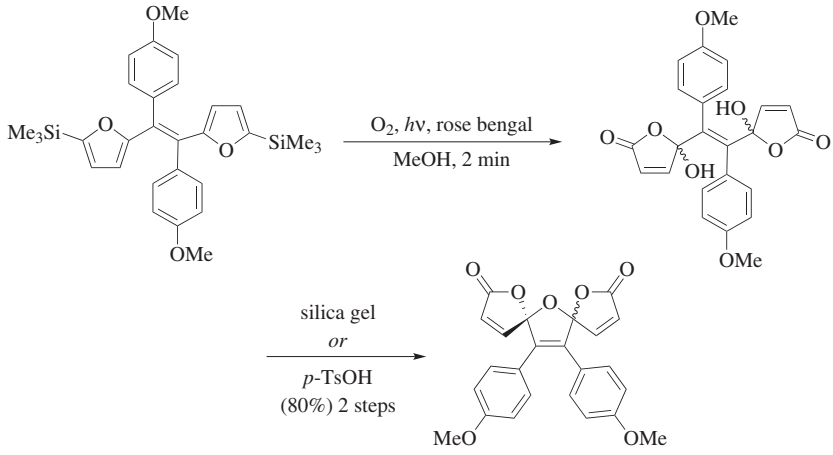
Scheme 158

Conversion of a 2-methyl-4-substituted benzofuran into a 2-substituted 6-acetoxybenzaldehyde using ozonolysis at low temperature followed by treatment with triphenylphosphine has been employed as a key step in the synthesis of the antimicrobial agent apicularen A (Scheme 159).[572]



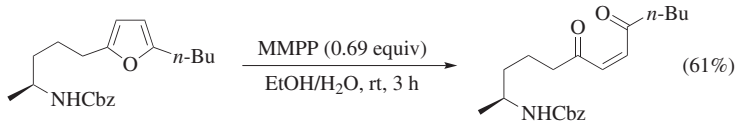
Scheme 159

Biomimetic syntheses of natural products from the litseaverticillol and prunolide families have been designed based on photooxygenations of furan derivatives (Scheme 160).[95] Similarly, photooxygenations of 2-(trimethylsilyl)furan derivatives have been used in synthetic pathways to prepare (+)-premnalene A and its 8-epimer.[314]



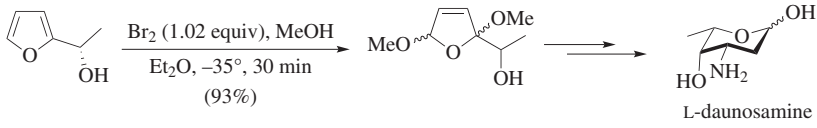
Scheme 160

Transformations of a 2,5-disubstituted furan into the corresponding 1,4-dioxoalkene by employing magnesium monoperoxyphtalate (MMPP) as the oxidant is a key step in the synthesis of the alkaloid monomorine (Scheme 161).[141]



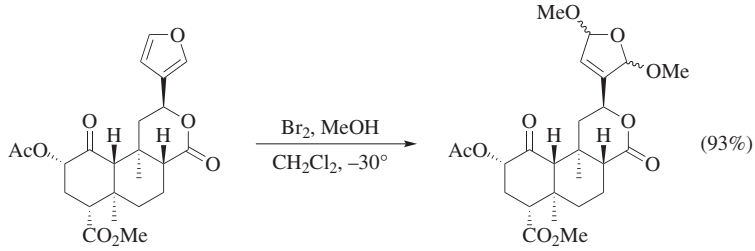
Scheme 161

Bromination of 1-(2-furyl)ethanol in methanol to afford the corresponding 2,5-dimethoxydihydrofurans is used as the first step in the synthesis of racemic daunosamine and related amino sugars.[240] The same process using an enantiomerically pure starting material leads to L-daunosamine (Scheme 162).[241]



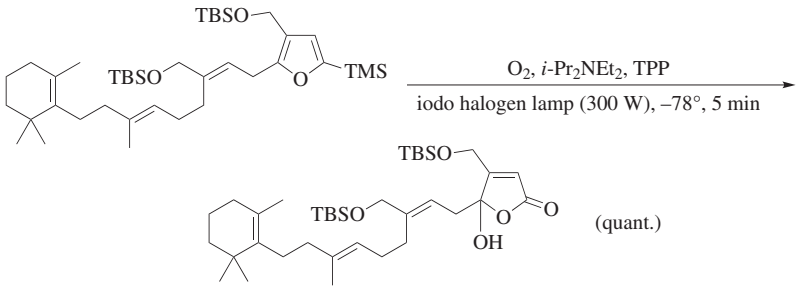
Scheme 162

Routes for the total synthesis of neopatulin[238] and patulin[239] begin with oxidations of furfuryl alcohols utilizing bromine in methanol. The formation of 2,5-dimethoxydihydrofurans in this way has also been employed in the synthesis of phytoalexins[264] and several diterpenes[233–235] from *Salvia divinorum* (Scheme 163).



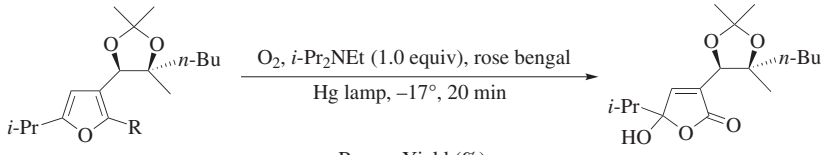
Scheme 163

Conversions of furans into 4-hydroxybutenolides offer direct entry to the synthesis of a broad number of polyoxygenated natural products and related compounds. Among the various methods for carrying out this transformation, photooxygenation is ideal because it serves as a powerful tool to increase the molecular complexity of the system in one step and in high yields.[28] A chemoselective photooxygenation reaction of a 2-(trimethylsilyl)furan has been used in the first synthesis of the marine natural product (*E*)-neomanoalide (Scheme 164).[315] A similar transformation establishes the structure of gloeosporone.[319]



Scheme 164

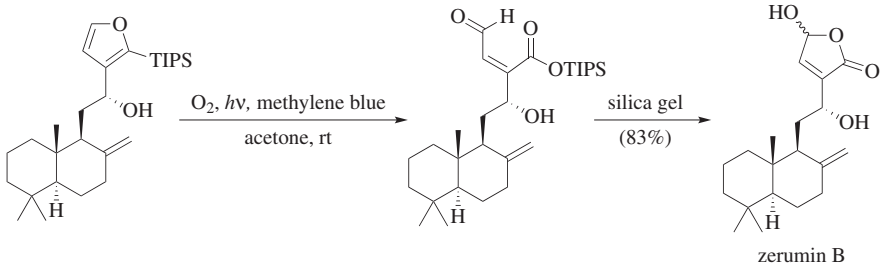
Photooxygenation of a trisubstituted 2-(trimethylsilyl)furan derivative is a key step in the synthesis of PI-091, a platelet aggregation inhibitor (Scheme 165).[311,318]



R	Yield (%)
H	60
TMS	99

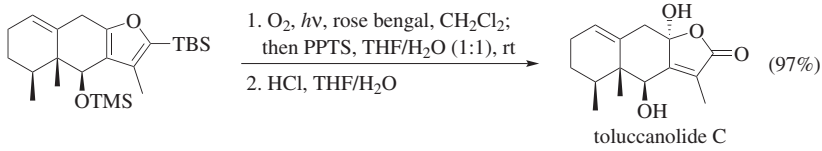
Scheme 165

Similarly, the photooxygenation of a 2-(triisopropyl)furan leads to a late-stage precursor of (+)-zerumin B and (+)-12-epizerumin B (Scheme 166).[320]



Scheme 166

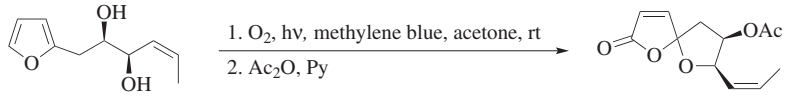
Biomimetic syntheses of bis-sesquiterpene lactones have been developed based on photooxygenations of 2-(trialkylsilyl)furans.[312] Using this method, dimeric biatractylolide and biepiasterolide[222,313] as well as furanoeremophilane sesquiterpenoids such as toluccanolide C (Scheme 167)[573] are readily prepared.



Scheme 167

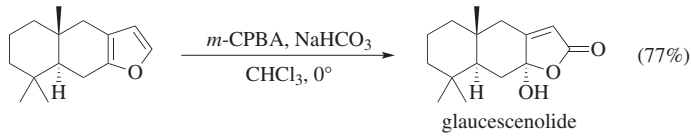
The spirocyclic core of the prunolides, cytotoxic marine products, can be constructed using photooxygenation reactions of bis(2-trimethylsilylfurans) in methanol.[96] In the same manner, γ-spiroketal lactone precursors for pyrenolide D and the anticancer natural product crassalactone D, are accessible by irradiation

promoted reaction of 2-(2,3-dihydroxyalkyl)furans in the presence of oxygen and methylene blue followed by dehydration (Scheme 168).[224]



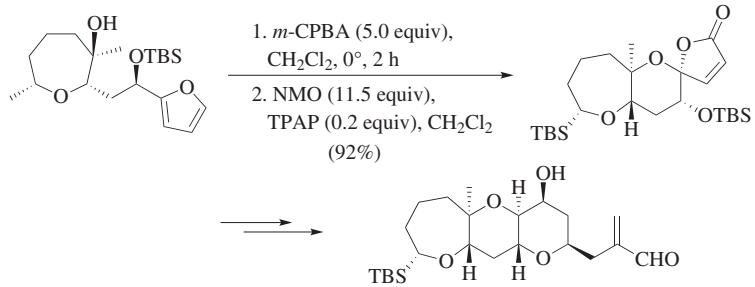
Scheme 168

(+)-Crassalactone D can also be prepared by a sequence using *m*-CPBA to oxidize a furan precursor.[574] Oxidation with *m*-CPBA is a key step in the synthesis of glaucescenolide, a cytotoxic sesquiterpenoid, and confirms its absolute configuration (Scheme 169).[218]



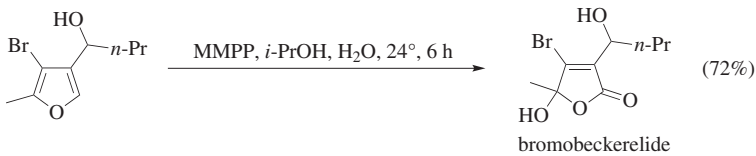
Scheme 169

The ABC ring system of hemibrevetoxin B is synthesized by oxidizing a furan ring with *m*-CPBA with subsequent oxidation of the resulting spirocyclic hemiacetal (Scheme 170).[575]



Scheme 170

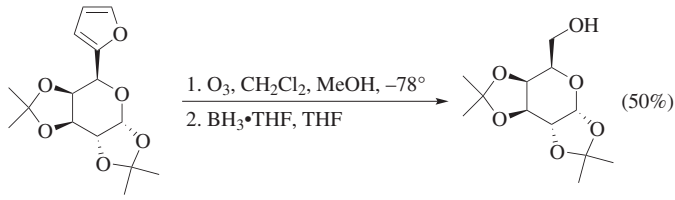
A total synthesis of racemic bromobeckerelide is accomplished in five steps from 5-methylfurfural using a photooxidation promoted by magnesium monoperoxyphtalate (MMPP) as a final step (Scheme 171).[209]



Scheme 171

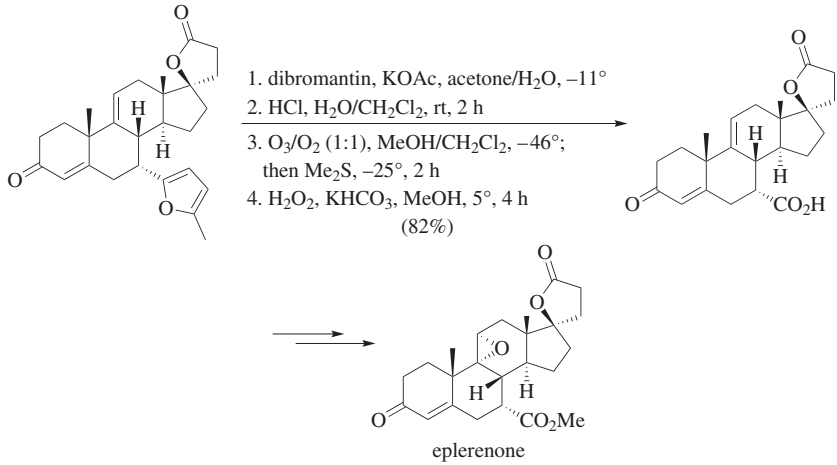
Oxidations to Carboxylic Acids

The synthetic equivalence of a furan ring and a carboxylic acid has been exploited in carbohydrate chemistry and related fields. For example, ozonization of a 2-furyl glycoside and further reduction is used as a key step in the synthesis of hikosamine, the undecose part of hikizimycin, an antibacterial and antihelmintic agent (Scheme 172).[397]



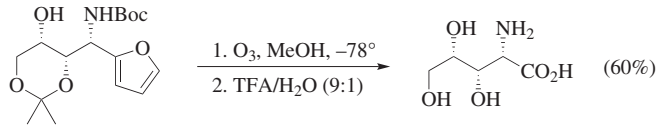
Scheme 172

On the other hand, direct ozonolysis of the furan ring in an attempted synthesis of eplerenone, a new drug for cardiovascular indications, was unsuccessful, necessitating prior treatment with HOBr (generated in situ from dibromantin) followed by ozonolysis of the resulting *trans* enedione to achieve carboxylic acid unmasking (Scheme 173).[107]



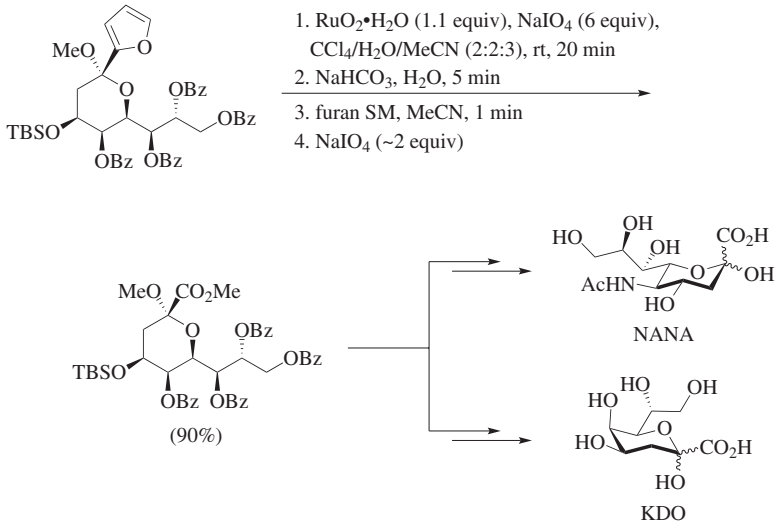
Scheme 173

Ozonization of an *N*-Boc-polyhydroxylated furfurylamine produces an advanced intermediate in the synthesis of polyoxamic acid, a component of the nucleoside antibiotic polyoxins (Scheme 174).[404,407]



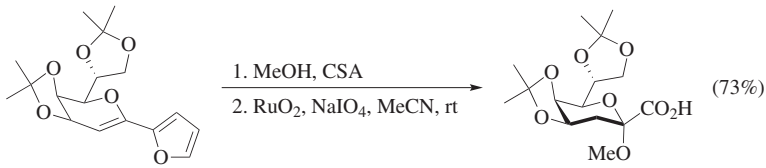
Scheme 174

Several higher ulosonic acids, including the important *N*-acetylneuraminic acid (NANA), are accessible through a strategy based on the use of a furan ring as a carboxylic acid surrogate. 2-Furylsugars are used as key intermediates and transformation of the furan ring into a carboxylic acid group is achieved using ruthenium tetroxide generated from ruthenium(IV) oxide and sodium periodate. To preserve the integrity of several protecting groups, the reaction is carried out in the presence of sodium bicarbonate as a buffer (Scheme 175).[368]



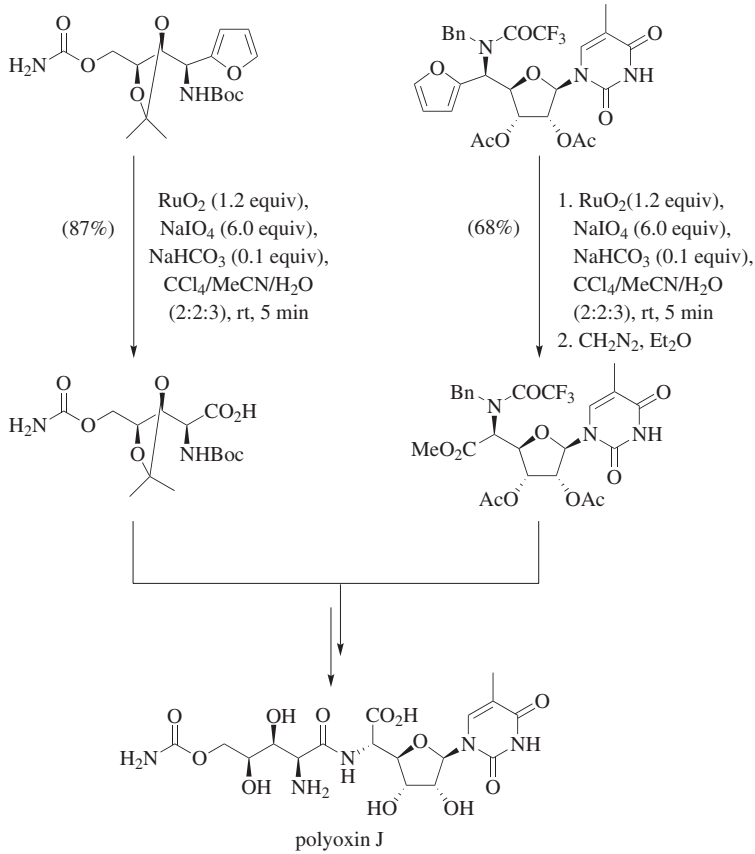
Scheme 175

A similar synthesis of 3-deoxy-D-manno-2-octulosonic acid (KDO) has been achieved using 2-furylglycals as intermediates (Scheme 176).[370]



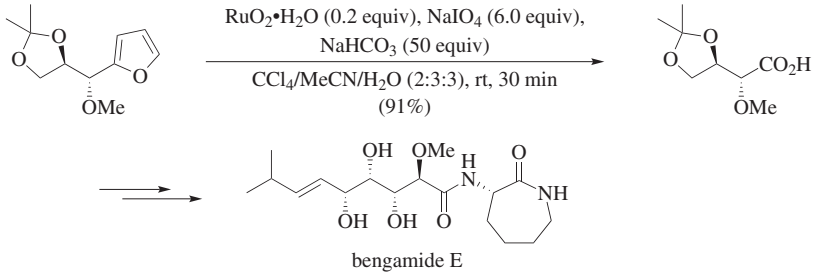
Scheme 176

A strategy based on the use of furan as the synthetic equivalent of a carboxylic acid has been designed for a total synthesis of polyoxin J, a dipeptide nucleoside antibiotic. Both fragments, polyoxamic acid,[374] and thymine polyoxin C[381] are stereoselectively constructed from furan derivatives, which are oxidized with ruthenium tetroxide in a late stage of the synthesis.[346] Further coupling of those fragments results in the formation of polyoxin J (Scheme 177).[341] A similar strategy is applied to the preparation of other polyoxins[358] and related nikkomycins.[378]



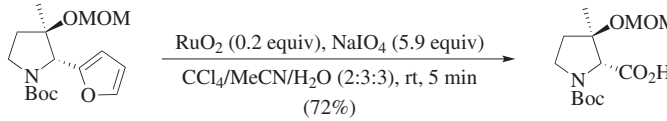
Scheme 177

Other dipeptides, such as bengamide E, a marine natural product, are prepared by oxidation of a furan precursor using ruthenium tetroxide to form a carboxylic acid (Scheme 178).[372]



Scheme 178

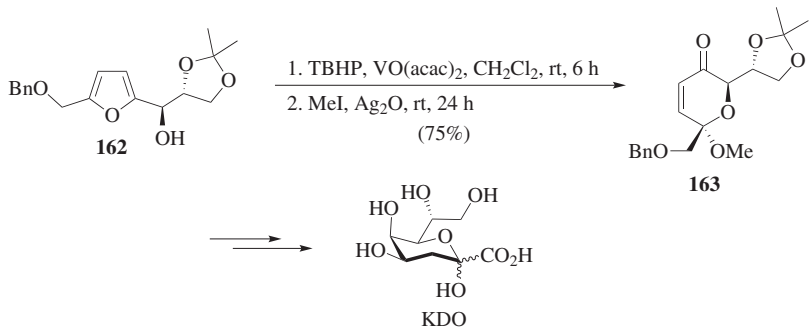
The complete degradation of the furan ring to a carboxylic acid by the action of ruthenium tetroxide has also been employed in the synthesis of members of the cyclothreonamides,[348] another family of marine natural products, as well as in the preparation of naturally occurring substituted proline fragments of more complex compounds (Scheme 179).[371]



Scheme 179

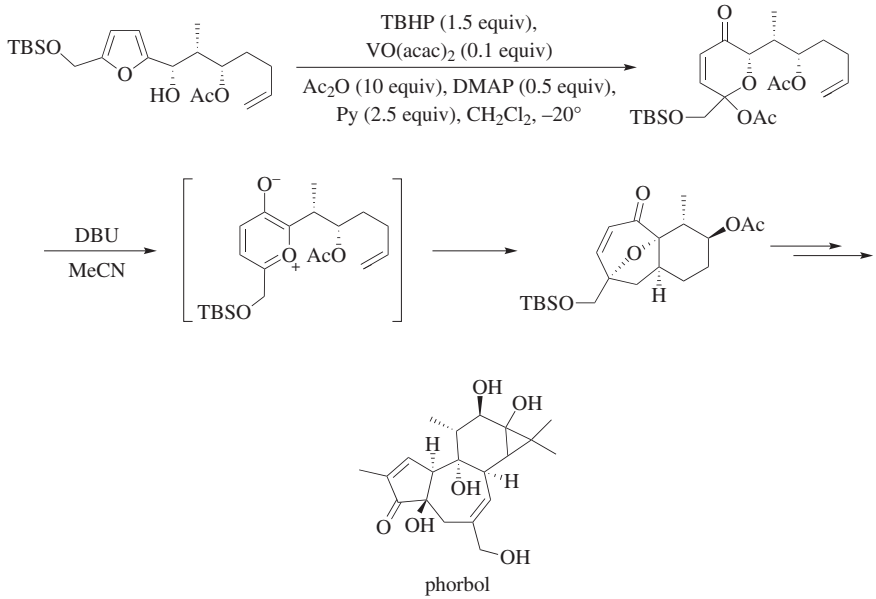
The Achmatowicz Reaction

The Achmatowicz reaction has enjoyed considerable synthetic application because it is atom economic and simultaneously introduces several important functionalities that enable further transformations. Indeed, the reaction was initially described as a de novo entry to higher carbohydrates[31] because of the excellent possibilities it offered for the synthesis of the so-called hexenuloses.[576,577] For example, the intermediate **163** in the synthesis of monosaccharide 3-deoxy-D-manno-2-octulosonic acid (KDO) is available from furan precursor **162** through use of the Achmatowicz reaction promoted by TBHP in the presence of a catalytic amount of vanadyl acetylacetonate ($VO(acac)_2$) (Scheme 180).[488]

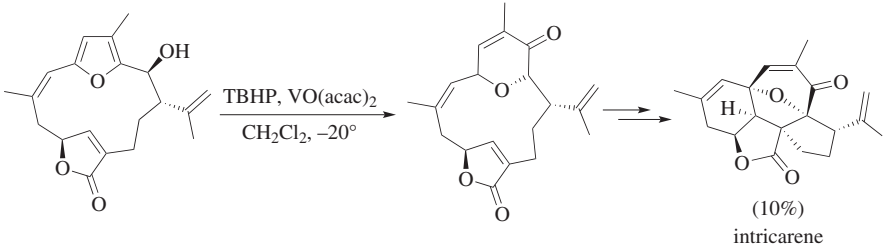


Scheme 180

The Achmatowicz reaction of 5-substituted furfuryl alcohols, promoted by TBHP/VO(acac)$_2$, has also been used in the formal synthesis of the diterpene phorbol (Scheme 181),[509] daphnetoxins,[496] the C_{27}–C_{38} and C_{44}–C_{53} subunits of norhalichondrin B,[505] and a biomimetic synthesis of the polycyclic diterpene (+)-intricarene (Scheme 182).[10]

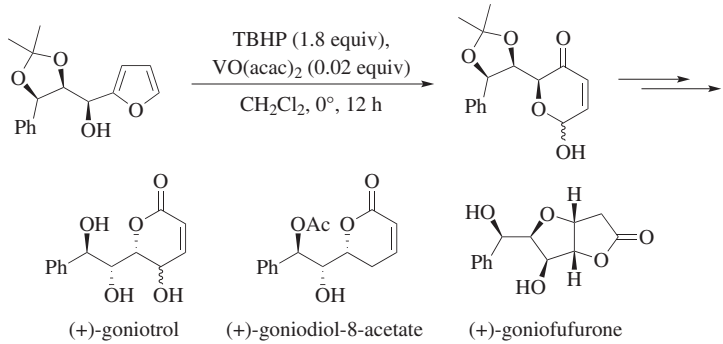


Scheme 181



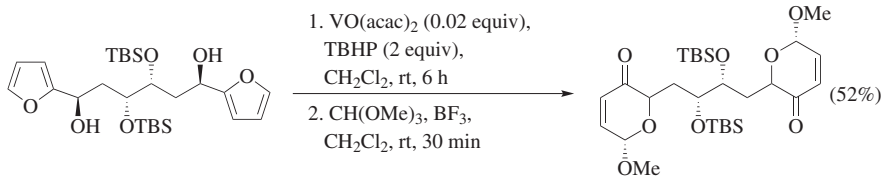
Scheme 182

A total synthesis of the natural antitumor styryl lactones (+)-goniodol-8-acetate,[487] (+)-goniotrol, and (+)-goniofufurone[578] are achieved in a stereoselective manner via treatment of a polyhydroxylated furfuryl alcohol with TBHP/VO(acac)$_2$ at 0° (Scheme 183).



Scheme 183

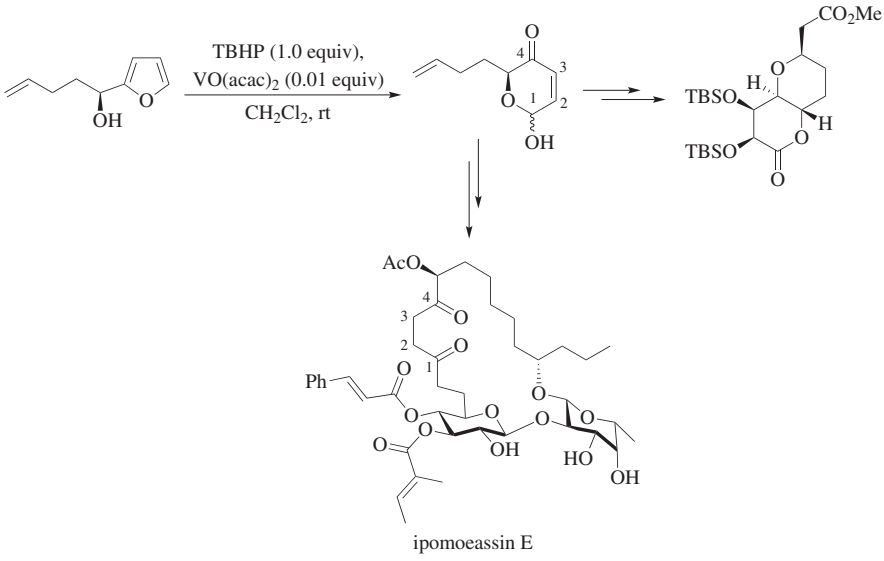
The fungal metabolite mycoepoxydiene is obtained by employing oxidative rearrangement of a furfuryl alcohol using the conditions described above.[495] The related natural product (−)-1893A is also accessible by the same process.[507] A two-directional synthesis of the C_{58}–C_{71} fragment of palytoxin was designed based on a C2-symmetrical dipyranone obtained via a double Achmatowicz reaction of a bis-furan derivative (Scheme 184). Two equivalents of TBHP are necessary for completion of the reaction.[512]



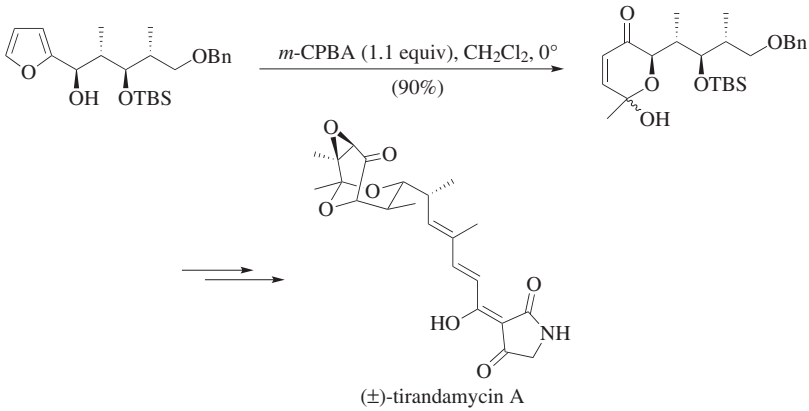
Scheme 184

Ipomoeassin E is prepared using an enantiomerically pure alkenyl furfuryl alcohol as starting material through treatment with TBHP/$VO(acac)_2$ in dichloromethane (Scheme 185).[504] The same initial step is employed in a synthesis of the C_1–C_{15} domain of the marine macrolide halichondrins.[506]

The Achmatowicz transformation carried out using *m*-CPBA as the oxidizing reagent has been used in the synthesis of racemic tirandamycin A (Scheme 186)[442] and pheromones from the olive fruit fly[441] and hepialid moth.[453]

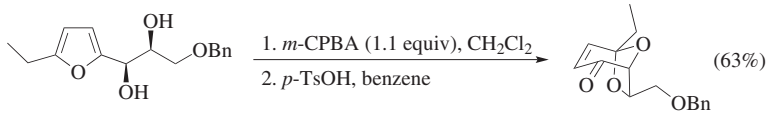


Scheme 185



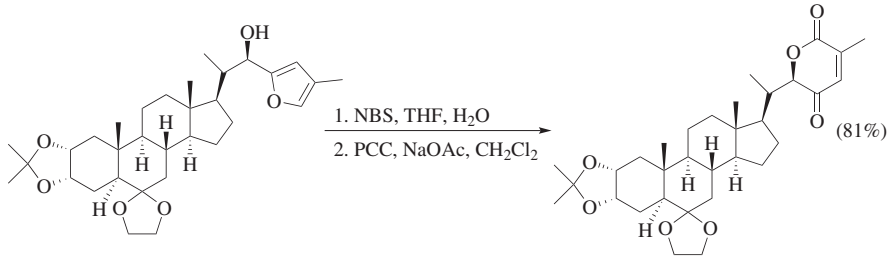
Scheme 186

The reaction of a polyhydroxylated 2,5-disubstituted furan with *m*-CPBA in dichloromethane is a key step in a synthesis of (−)-exo-isobrevicomin (Scheme 187).[458]



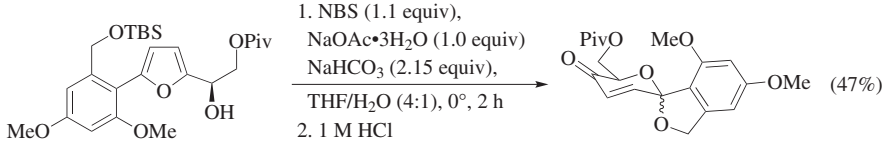
Scheme 187

The steroid castasterone is obtained using a route involving treatment of a furan intermediate with NBS in THF/H_2O (Scheme 188).[461] The same reaction, but in a buffered medium, is used as the first step in syntheses of important α,β-unsaturated lactones such as isoaltholactone,[579] (*R*)-(−)-argentilactone,[580] basiliolide B,[581] and phomopsolides C,[582] D,[462] and E.[583]



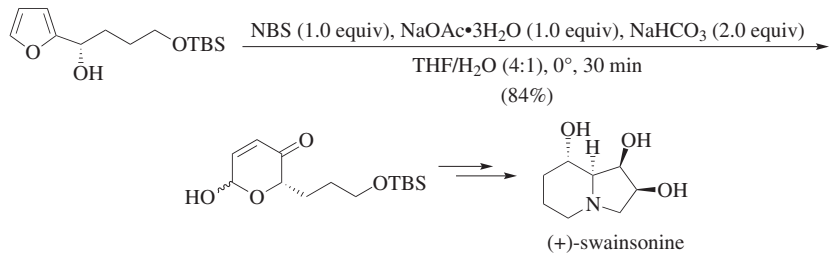
Scheme 188

The starting materials required for the synthesis of the *C*-arylglycoside tricyclic spiroketal nucleus of the antifungal agents papulacandins are obtained by implementation of the Achmatowicz reaction using NBS/water systems and 5-aryl-2-(1,2-dihydroxyethyl)furans (Scheme 189).[483]



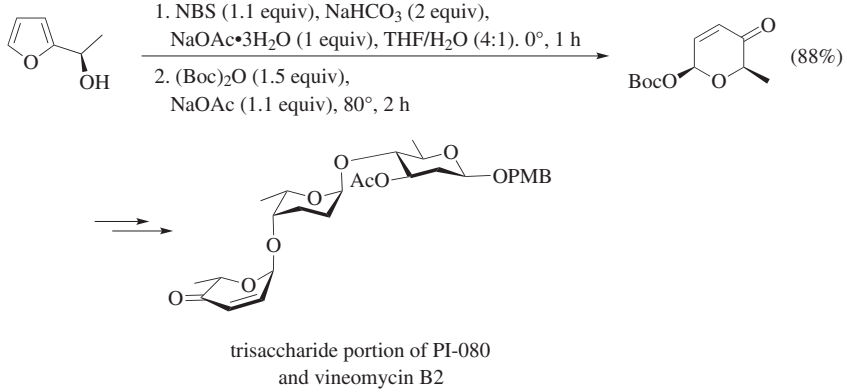
Scheme 189

A de novo synthesis of both enantiomers of the alkaloid (+)-swainsonine relies on the use of an Achmatowicz reaction of a furfuryl alcohol as the initial step to construct a C_6-substituted pyranone precursor of the final product (Scheme 190).[469]



Scheme 190

Complex carbohydrate-containing substrates are accessible using NBS-promoted Achmatowicz reactions of enantiomerically pure α-methyl furfuryl alcohol. Following this approach, syntheses of the trisaccharide subunit of landomycins A and E,[498] and the trisaccharide portion of PI-080 and vineomycin B2 (Scheme 191)[499] have been accomplished.

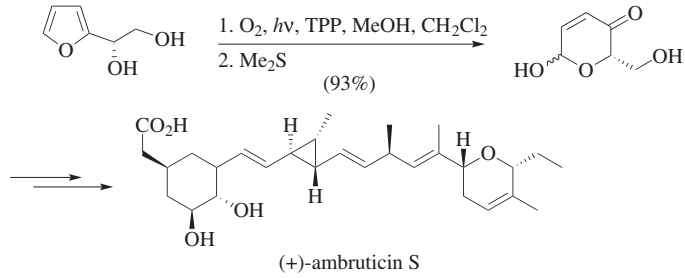


trisaccharide portion of PI-080
and vineomycin B2

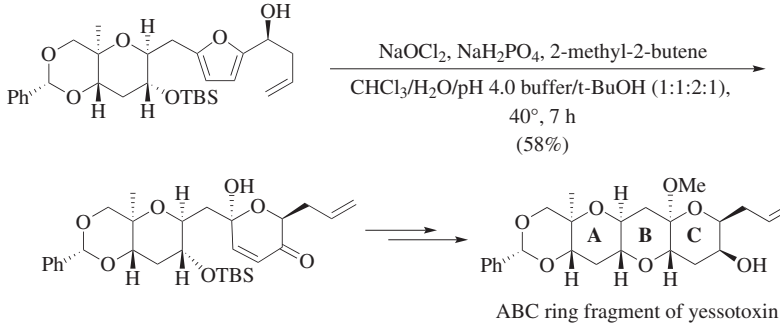
Scheme 191

Other oxidants have also been employed for the Achmatowicz reaction and applied in synthetic pathways. Photooxygenation of (α-hydroxymethyl)furfuryl alcohol, promoted by tetraphenylporphirin (TPP), is the first step in a total synthesis of (+)-ambruticin S (Scheme 192).[527] The antibiotic (+)-macbecin I is accessed in a similar way,[431] as is the (+)-Prelog–Djerassi lactone.[428]

The synthesis of the complex structure of the marine polyether toxin yessotoxin is addressed through use of an Achmatowicz approach that employs sodium chlorite as the oxidizing agent. In this approach, the ABC ring fragment is prepared in the manner illustrated in Scheme 193.[535]

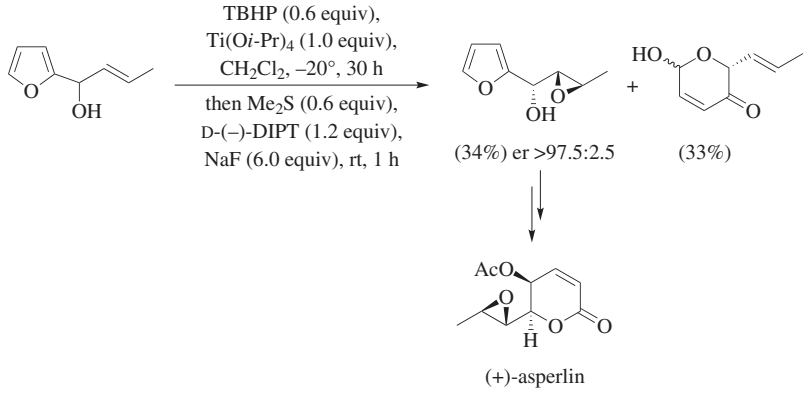


Scheme 192



Scheme 193

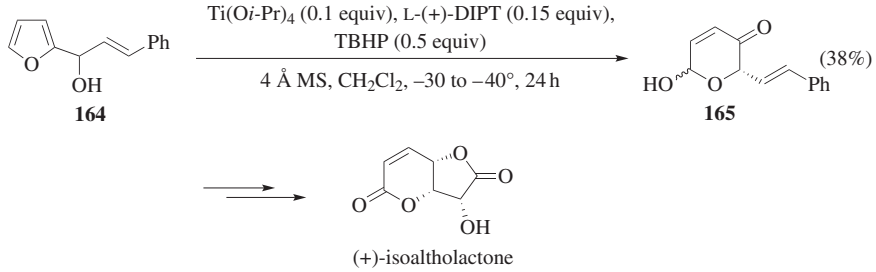
Kinetic resolution of racemic furfuryl alcohols achieved by treatment with TBHP in the presence of L-(+)-diisopropyl tartrate and titanium isopropoxide has been used for the preparation of an enantiomerically enriched starting material required for the synthesis of (+)-asperlin (Scheme 194).[518] In a similar way, an enantiomerically pure



Scheme 194

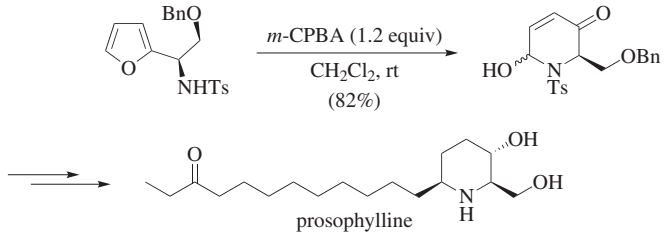
furfuryl alcohol with >95:5 er is obtained using this procedure in a route for preparation of the 14-membered bis-lactone grahamimycin A.[184]

Treatment of alkenyl furfuryl alcohol **164** under kinetic resolution conditions results in the formation of pyranone **165**, which is a precursor of (+)-isoaltholactone (Scheme 195).[524]



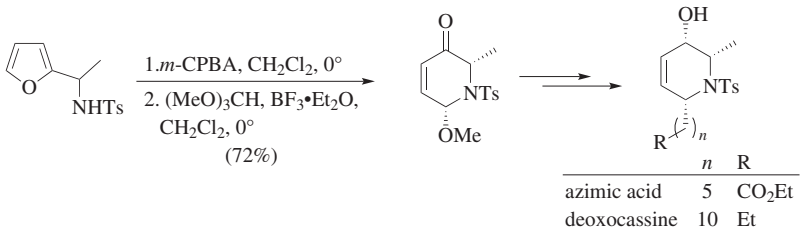
Scheme 195

The aza-Achmatowicz reaction[33] has enormous synthetic potential, including obtaining enantiomerically enriched compounds through kinetic resolution.[34] Oxidation of a furfurylamine derivative with *m*-CPBA is used as the starting step in a synthesis of (+)-deoxoprosophylline[542] and prosophylline (Scheme 196).[543] This method is applicable to solid-phase synthesis, although it has been used only to prepare racemic targets.[537]

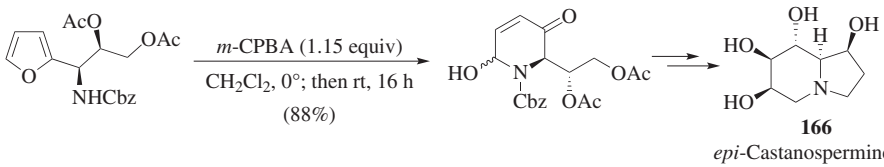


Scheme 196

Hydroxylated piperidine alkaloids, like azimic acid, spicigenine, cassine, and deoxocassine are prepared in racemic form through oxidation of *N*-tosyl furfurylamines mediated by *m*-CPBA (Scheme 197).[551,552] The same type of oxidation can be applied to the generation of several azasugars including mannojirimycin,[549] *epi*-indolizidine 223A,[553] indrizidine 223AB,[405] 8a-*epi*-swainsonine,[561] and *epi*-castanospermine (**166**) (Scheme 198).[546]

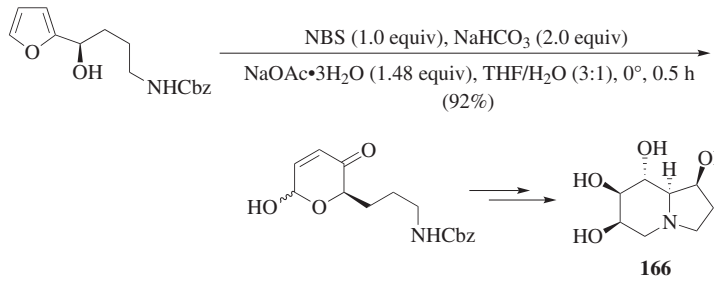


Scheme 197



Scheme 198

Swainsonine[42] and deoxymannojirimycin[564] are obtained in enantiomerically pure forms by performing kinetic resolution of a furfuryl tosylamide as a key step. *epi*-Castanospermine (**166**) is also prepared from a furfuryl amine through treatment with aqueous NBS at 0°[463] and in the presence of sodium acetate (Scheme 199).[473]



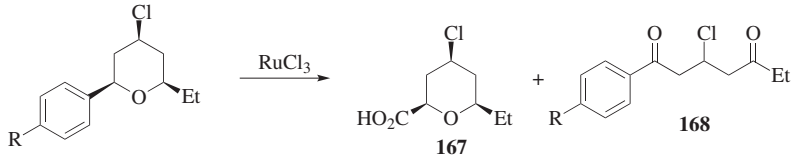
Scheme 199

COMPARISON WITH OTHER METHODS

The utility of furan ring cleavage reactions is heightened by the fact that no alternative C_4 synthons exist that can be used to generate 1,4-dioxo derivatives or functionalized heterocycles like 6-hydroxy-2*H*-pyran-3(6*H*)-ones and 6-hydroxy-1,2-dihydropyridin-3(6*H*)-ones. In addition, although there are several methods for generating carboxylic acids from other functional groups, these procedures cannot be considered to be competitive with oxidations of furans. However, several other functional groups can be oxidatively transformed to carboxylic acids, including

heteroaromatics, phenyl groups,[113] alkynes, and alkenes.[114] In all cases, the processes involve complete degradation, giving the carboxylic acids as final products. The same conditions ($RuCl_3$ or RuO_2, $NaIO_4$ in 2:2:3 CCl_4/MeCN/H_2O) are usually employed for all of these reactions,[336] with variations being found in only the reaction times and temperatures, which in some cases are as high as 70°.[584] Nevertheless, the use of other solvents like acetone[585] or the environmentally friendly dimethyl carbonate/water system[586] is also possible. Periodic acid[587–590] and sodium hypochlorite[590] can be used as primary oxidants instead of sodium metaperiodate.

The oxidation of benzene rings with ruthenium tetroxide is very sensitive to the nature of the ring substituents and site-selective oxidations can be performed when more than one aromatic ring is present in a molecule.[588] In general, the procedure is compatible with a variety of functional groups except for those sensitive to ruthenium oxidations and acidic media. In fact, oxidations of benzene rings with ruthenium(III) chloride in the presence of sodium periodate under classical conditions either are unsuccessful or low yielding when methoxymethyl and *tert*-butyldimethylsilyl ethers are present on the ring.[591] In the same study, the authors demonstrate that oxidation of phenyl groups are more efficient when an acetoxy group is present. The same conditions are compatible with nitrogen atoms protected as carbamates, which serve to prepare non-natural amino acids by using the phenyl group as a synthetic equivalent of a carboxylic acid.[592] The chemoselective oxidation of an aromatic ring in the presence of a tetrahydropyran is possible when the primary oxidant is changed from sodium periodate to periodic acid, and water is absent from the solvent system. When a benzene ring is activated by the presence of a methoxy group, complete chemoselectivity is observed as evidenced by the ratio of product **167** to product **168**. (Scheme 200).[593]



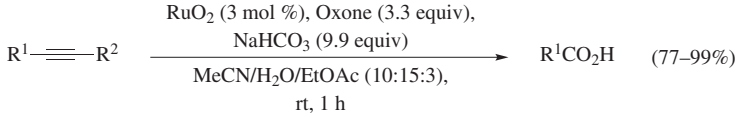
R	Co-Oxidant	Solvents	**167** + **168** Yield (%)	**167/168**
H	$NaIO_4$	H_2O/MeCN/CCl_4	—	0:100
H	H_5IO_6	MeCN/CCl_4	52	87:13
MeO	H_5IO_6	MeCN/CCl_4	72	100:0

Scheme 200

Oxidations of 2,5-disubstituted oxazoles with ozone, followed by treatment of the crude reaction mixture with sodium borohydride in methanol, afford carboxylic acids. This reaction takes place through an intermediate anhydride, which is transformed into the carboxylic acid by the action of the reducing agent.[594]

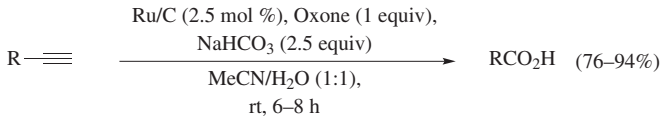
In addition to ruthenium tetroxide,[489] other oxidants have been used for transforming alkynes into carboxylic acids. These include ozone,[490–493] potassium

permanganate,[595,596] polyoxometals derived from molybdenum and tungsten,[597] [bis(trifluoroacetoxy)iodo]benzene,[598] and hydrogen peroxide in the presence of methyltrioxorhenium,[599] peroxotungsten compounds,[600] or under a basic medium.[601] A synthetically useful method for the oxidative degradation of alkynes to form carboxylic acids consists of a combination of ruthenium(IV) oxide, Oxone®, and sodium bicarbonate in a 10:15:3 acetonitrile/water/ethyl acetate mixture as the solvent (Scheme 201).[602] The reaction proceeds to completion at room temperature in 1 hour and high yields are obtained. The reaction conditions are compatible with the presence of phenyl groups and several protecting groups including benzyl and *tert*-butyldiphenylsilyl ethers.



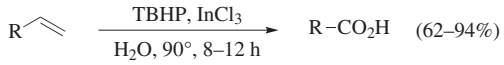
Scheme 201

Aromatic terminal alkynes are cleanly converted into carboxylic acids by the action of recyclable ruthenium supported on charcoal in the presence of Oxone® as the oxidant. The procedure, similar to that described above but using lesser amounts of the reoxidant and sodium carbonate, is also fully compatible with the presence of aromatic and heteroaromatic rings like thiophene (Scheme 202).[603] The reaction can be carried out on a 100 mmol scale.



Scheme 202

Alkynes also undergo oxidation to form carboxylic acids by the action of cobalt acetate bromide in the presence of air. Although the initial products are diketones, prolonged reaction times afford carboxylic acids.[604] Typically, alkenes are converted into carboxylic acids by ozonolysis followed by oxidative workup. A safer and more efficient method utilizes *tert*-butyl hydroperoxide and indium(III) chloride as the catalyst with water as the solvent.[605] Examples of several alkenes undergoing this process are illustrated in Scheme 203. The reaction can be extended to formation of more complex products.



R = Ph, 4-MeOC$_6$H$_4$, 4-ClC$_6$H$_4$, 1-naphthyl

Scheme 203

Oxidation of alkenes to yield carboxylic acids can also be carried out using ruthenium-based systems. Aqueous reactions can be performed in the presence of an emulsifing agent and under ultrasonic irradiation.[606] Several cosolvents can be used successfully in the oxidation of alkenes with ruthenium trichloride in the presence of sodium periodate.[607] However, it is possible to design ruthenium-based oxidation protocols of less than fully substituted alkenes that afford aldehydes rather than carboxylic acids.[608]

EXPERIMENTAL CONDITIONS

All oxidants must be handled with caution, as they can lead to flammable oxidation products. Although oxidants like tert*-butyl hydroperoxide,* meta*-chloroperoxybenzoic acid, dimethyldioxirane, and hydrogen peroxide can be used in water, peroxides are potentially flammable and/or explosive and may ignite fires when they come in contact with other materials, especially flammable solvents. Consequently, in many cases it is strongly recommended that an inert atmosphere be used. In addition these substances can cause skin and eye burns on contact. Bromine must be used with extreme caution because it can cause severe damage to the skin.*

In general, metal-based oxidants, such as ruthenium dioxide or trichloride, potassium permanganate, and lead tetraacetate, are toxic as a consequence of the presence of heavy metals. Thus, special care must be taken in their manipulation and disposal (avoid skin contact, inhalation, and, of course, ingestion).

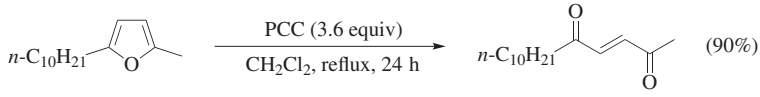
Ozone is a powerful oxidizing reagent and thus it reacts with unsaturated organic compounds, like furans, to form peroxides, which are unstable and can decompose violently. Ozonization reactions on the micro- and semimicro scale are carried out safely with a glass apparatus consisting of two separated chambers with inlet and outlet tubes.[609]

Photooxygenation reactions are usually carried out by generating singlet oxygen in situ. A solution of the sensitizer and substrate in an appropriate solvent (usually dichloromethane) is irradiated under an atmosphere of dry oxygen for the desired time at a given temperature ranging from −78° to room temperature. Irradiation is carried out in a Pyrex flask with halogen or tungsten lamps, using powers of 200–650W. Shallow, silvered Dewar flasks can be used for reactions carried at low temperatures. Preparative photooxygenations are best carried out with a low-power (150W) mercury high pressure lamp. An irradiation unit with an automatic oxygen consumption recording system and a cut-off filter (<380 nm) is also recommended.[79] A catalytic amount of a sensitizer is needed to promote the formation of singlet oxygen. Rose bengal and methylene blue are the most commonly used sensitizers although other compounds such as tetraphenylporphyrin can also be employed.

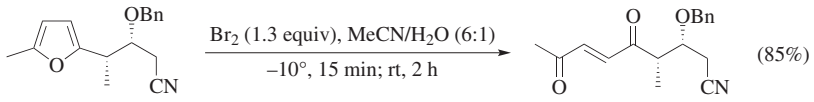
Special attention should be paid to oxidations carried out with NBS in the presence of water to avoid the formation of byproducts. In particular, the reaction temperature should be maintained below 5° and NBS must be added as a solid in order to promote the immediate consumption of the bromine liberated in situ. The oxidation of furan derivatives with *N*-bromosuccinimide is usually carried out in 4:1 tetrahydrofuran/water at 0° but has been conducted in 1:1 tetrahydrofuran/water[575] and ethyl acetate at reflux.[610] High yields are obtained when the reaction is carried out in the presence of sodium bicarbonate and sodium acetate.[579,582,583] Optimal conditions consist of employing 1.05 equivalents of NBS, 1.0 equivalent of sodium acetate, and 2.0 equivalents of sodium bicarbonate.[611] Under these conditions oxidations are carried out smoothly in less than 1 hour and in excellent yields.[580,581,612] If the oxidation is carried out in the presence of acetic anhydride, the corresponding acetoxypyranone is obtained directly[613] although a two-step procedure (oxidation and then acetylation) may afford a better overall yield.[614]

Electrochemical oxidations of furan derivatives are typically performed by passing a constant current of 4 A through an alcoholic (e.g. methanolic) solution containing the furan and an electrolyte until 4 F/mol of current is passed. Normally, ammonium bromide, tetraethylammonium perchlorate, sodium acetate, or lithium perchlorate are employed as electrolytes. A platinum anode encased in an ion-exchange membrane containing the electrolyte ions can also be used to avoid the use of added electrolyte.[615] In some instances 7–8 F/mol, twice the theoretical amount of electricity needed, are required to achieve good yields.[616] This amount of electricity is required in reactions involving polymer-supported materials, which typically give low yields. These reactions suffer from the intrinsic difficulty of obtaining direct contact between the polymer-bound substrate and the electrode.[617]

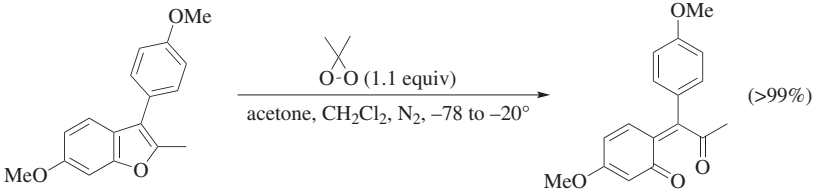
EXPERIMENTAL PROCEDURES



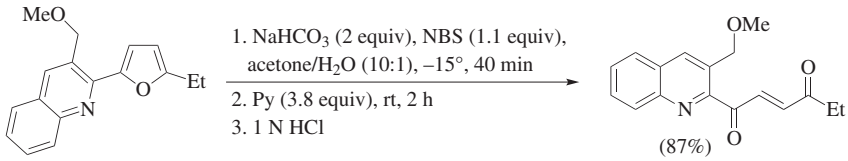
(*E*)-3-Pentadecene-2,5-dione [Oxidation of a Furan to a 1,4-Dicarbonyl Derivative with Pyridinium Chlorochromate].[618] 2-Methyl-5-decylfuran (1.10 g, 0.05 mmol), diluted with anhydrous CH_2C1_2 (10 mL), was added to a suspension of PCC (4 g) in anhydrous CH_2C1_2 (50 mL). The mixture was heated to reflux for 24 h and then filtered through a short pad of Florisil. The crude product obtained after removal of the solvent was chromatographed on SiO_2. Elution with hexane yielded (*E*)-3-pentadecene-2,5-dione (1.06 g, 90%): mp 68–69°; IR (CCl_4) 2970, 2872, 1680, 1620, 1360, 980 cm^{-1}; ^1H NMR (CCl_4) δ 6.77 (s, 2H), 2.60 (t, $J = 8$ Hz, 2H), 2.31 (s, 3H), 1.31 (s, 17H), 0.92 (m, 3H); EIMS (70 eV) (*m/z*): M^+ 238. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.44; H, 11.09.



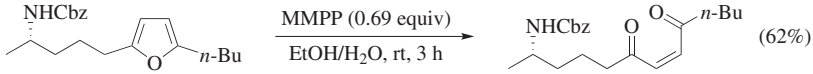
(3*R*,4*S*)-3-Benzyloxy-4-methyl-5,8-dioxonon-6-enenitrile [Oxidation of a Furan to a 1,4-Dicarbonyl Derivative with Bromine].[142] To a stirred solution of nitrile (200 mg, 0.74 mmol) in a 6:1 mixture of MeCN/H_2O (6 mL), bromine (154 mg, 0.96 mmol) in MeCN (2 mL) was added dropwise at −10°, and the reaction mixture was stirred at −10° for 15 min. The cooling bath was removed and the reaction mixture was stirred at rt for 2 h to complete *cis*/*trans* isomerization (TLC, hexane/EtOAc, 6:4). Brine was added, the aqueous layer was extracted with EtOAc, combined organic phases were dried ($MgSO_4$), evaporated, and purified by column chromatography (hexane/EtOAc, 7:3) to give the pure product as a yellow solid (180 mg, 85%): mp 59–61° (hexane/ether); $[\alpha]_D$ 5.15 (c 1.6, $CHCl_3$); IR (film) 3037, 2967, 2899, 2247, 1674, 1458, 1423, 1359, 1298, 1270, 1103, 1049, 996, 743, 700, 591, 477 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.35 (s, 5H), 6.88 (s, 2H), 4.73 (d, J = 11.4 Hz, 1H), 4.55 (d, J = 11.4 Hz, 1H), 3.97 (ddd, J = 4.8, 5.6, 6.8 Hz, 1H), 3.22 (dq, J = 6.8. 7.1 Hz, 1H), 2.68 (dd, J = 17.1, 4.8 Hz, 1H), 2.55 (dd, J = 17.1, 5.6 Hz, 1H), 2.34 (s, 3H), 1.26 (d, J = 7.1 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl^3$) δ 201.2, 197.7, 137.6, 136.8, 135.5, 128.6, 128.3 (4-Ph), 128.1 (3-Ph), 117.1, 75.0, 72.9, 48.7, 28.5, 20.9, 12.8 (4-Me); EIMS (*m*/*z*): $[M + H]^+$ 286; HRMS-EI (*m*/*z*): $[M + H]^+$ calcd for $C_{17}H_{19}NO_3$, 286.14408; found 286.144. Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.31; H, 6.73; N, 4.97.



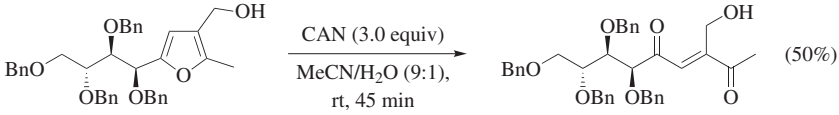
(*Z*)-3-Methoxy-6-[1-(3-methoxyphenyl)-2-oxopropylidene]-2,4-cyclohexadienone [Oxidation of a Furan to a 1,4-Dicarbonyl Derivative with Dimethyldioxirane].[38] A cooled (−78°) solution of dimethyldioxirane[619,620] in acetone (8 mL of a 0.067 M solution, 0.536 mmol), dried over molecular sieves at −20°, was rapidly added to a cooled (−78°), stirred solution of 6-methoxy-3-(4-methoxyphenyl)-2-methylbenzylfuran (134 mg 0.5 mmol) in anhydrous CH_2C1_2 (2 mL), under a N_2 atmosphere. The reaction temperature was allowed to increase to −20° while stirring until complete consumption of the benzo[b]furan was indicated by TLC. The solvent was evaporated (−20° at 0.01 mm Hg, 1–2 h) to yield 3-methoxy-6-[1-(3-methoxyphenyl)-2-oxopropylidene]-2,4-cyclohexadienone in quantitative yield: ^1H NMR ($CDC1_3$, −20°) δ 7.47–7.33 (m, 2H), 6.97–6.87 (m, 3H), 6.21 (dd, J = 2.2, 10.1 Hz, 1H), 5.71 (d, J = 2.3 Hz, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 2.29 (s, 3H); ^{13}C NMR ($CDC1_3$, −20°) δ 204.9, 185.4, 170.7, 161.3, 160.8, 131.8, 131.7, 126.6, 123.6, 122.2, 114.2, 101.5, 56.0, 55.4, 28.4.



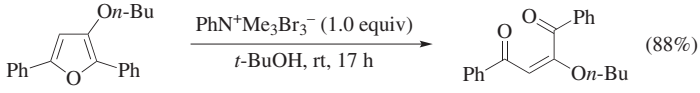
(*E*)-1-[3-(Methoxymethyl)quinolin-2-yl]-hex-2-ene-1,4-dione [Oxidation of a Furan to a 1,4-Dicarbonyl Derivative with *N*-Bromosuccinimide].[150] A solution of NBS (1.57 g, 8.8 mmol) in a 10:1 acetone/water mixture (11 mL) was added dropwise to a solution of the furan derivative (2.14 g, 8 mmol) and $NaHCO_3$ (1.34 g, 16 mmol) in the same solvent (32 mL) at −15°. After stirring for 40 min at −15°, pyridine (2.4 mL, 30 mmol) was added, and the reaction mixture was allowed to warm to rt. After 2 h at rt, the mixture was quenched with 1 N HCl to neutral pH and extracted with EtOAc (3 × 15 mL). The combined extracts were dried (Na_2SO_4) and evaporated, and the crude product was purified on silica gel (15% EtOAc/hexane) to yield (*E*)-1-[3 (methoxymethyl)quinolin-2-yl]-hex-2-ene-1,4-dione as a yellowish solid (1.97 g, 87%): mp 87° (EtOH); IR (neat) 2906, 1698, 1668 cm^{-1}; ^1H NMR ($CDC1_3$) δ 8.46 (d, J = 16.17, 1H), 8.45 (s, 1H), 8.17 (d, J = 8.46 Hz, 1H), 7.85 (d, J = 8.46 Hz, 1H), 7.74 (t, J = 7.35 Hz, 1H), 7.63 (t, J = 7.35 Hz, 1H), 7.13 (d, J = 16.17 Hz, 1H), 4.97 (s, 2H), 3.55 (s. 3H), 2.80 (q, J = 7.35 Hz, 2H), 1.18 (t, J = 7.35 Hz, 3H); ^{13}C NMR ($CDC1_3$) 201.2, 191.7, 150.2, 145.8, 137.6, 135.0, 134.6, 134.2, 132.7, 130.1, 129.9, 129.2, 127.6, 71.3, 59.0, 34.8, 7.8. EIMS (*m*/*z*): M^+ 283, 226, 195, 166; HRMS-EI (*m*/*z*): M^+ calcd for $C_{17}H_{17}NO_3$, 283.1208; found, 283.1204.



(2*S*)-2-(*N*-Benzyloxycarbonylamino)-6,9-dioxo-7-tridecene [Oxidation of a Furan to a 1,4-Dicarbonyl Derivative with Magnesium Monoperoxyphthalate].[141] To a solution of 2-((2*S*)-2-*N*-benzyloxycarbonylaminopentyl)-5-butylfuran (0.023 g, 0.067 mmol) in EtOH (0.3 mL) was added magnesium monoperoxyphthalate (0.023 g, 0.046 mmol) in water (0.3 mL) at rt and the mixture was stirred for 3 h. Addition of saturated aq $NaHCO_3$ solution to the mixture was followed by extraction with CH_2Cl_2 (2 × 3 mL). The combined organic layers were dried over $MgSO_4$, concentrated, and the residue was purified by silica gel column chromatography (hexane/EtOAc, 3:1) to provide (2*S*)-2-(*N*-benzyloxycarbonylamino)-6,9-dioxo-7-tridecene (0.015 g, 62%): $[\alpha]_D^{24}$ + 0.8 (c 1.50, $CHCl_3$); IR (neat) 3342, 2958, 1700, 1699, 1527 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34–7.26 (m, 5H), 6.25 (s, 2H), 5.06 (s, 2H), 4.52 (br d, J = 9.3 Hz, 1H), 3.58 (m, 1H), 2.54 (t, J = 6.9 Hz, 2H), 2.49 (t, J = 7.3 Hz, 2H), 1.61 (m, 2H), 1.46 (m, 2H), 1.38 (m, 2H), 1.35 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H), 0.85 (d, J = 4.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 202.7 (2C), 155.8, 136.6, 136.0, 135.2, 128.5 (3C), 128.0 (2C), 66.5, 46.8, 42.3, 41.8, 36.1, 25.5, 22.2, 21.2, 19.7, 13.8; HRMS (*m*/*z*): M^+ calcd for $C_{21}H_{29}NO_4$, 359.4593; found 359.4499.

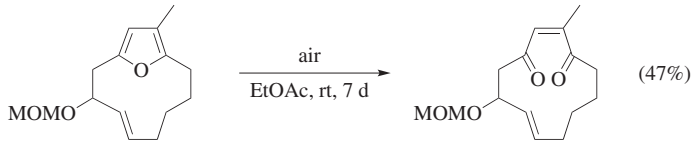


(6*S*,7*R*,8*R*,3*E*)-6,7,8,9-tetrakis(Benzyloxy)-3-(hydroxymethyl)non-3-ene-2,5-dione [Oxidation of a Furan to a 1,4-Dicarbonyl Derivative with Ceric Ammonium Nitrate].[132] To a stirred solution of (2-methyl-5-((1*S*,2*R*,3*R*)-1,2,3,4-tetrakis(benzyloxy)butyl)furan-3-yl)methanol (64 mg, 0.108 mmol) in $MeCN/H_2O$ (9:1, 5 mL) at rt, was added CAN (180 mg, 0.327 mmol, 3 equiv) over 45 min (adding 64 mg, 0.108 mmol, every 15 min). After the first addition, the initial red–orange color had faded to colorless. Further CAN was added and the mixture was stirred for 15 min. The reaction mixture was diluted with dichloromethane and washed successively with brine and H_2O (3 × 25 mL), dried (Na_2SO_4), and concentrated. The residue was purified by silica gel chromatography (Et_2O/petroleum ether, 1:3–1:1) to afford pure (6*S*,7*R*,8*R*,3*E*)-6,7,8,9-tetrakis(benzyloxy)-3-(hydroxymethyl)non-3-ene-2,5-dione as a colorless oil (50 mg, 50%): $[\alpha]_D^{25}$ – 34.6 (*c* 1, CH_2Cl_2); IR (neat) 3468, 1696, 1625 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32–7.24 (m, 20H), 6.56 (t, *J* = 1.9 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.52 (s, 2H), 4.40 (d, *J* = 11.1 Hz, 1H), 4.34 (d, *J* = 11.6 Hz, 1H), 4.22 (d, *J* = 3.4 Hz, 1H), 4.12 (br s, 2H), 4.06 (dd, *J* = 8.2 Hz, 1H), 3.84 (m, 1H), 3.80 (dd, *J* = 2.4, 10.7 Hz, 1H), 3.68 (dd, *J* = 3.9, 1H), 2.21 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 205.5, 200.6, 157.9, 138.2, 138.0, 137.7, 137.1, 128.3–127.5 (20C), 120.1, 84.8, 79.8, 77.5, 74.4, 73.4, 71.7, 71.3, 68.1, 63.0, 29.5; MS–FAB (*m*/*z*): $[M + Na]^+$ 631 (100%); HRMS–FAB (*m*/*z*): $[M + Na]^+$ calcd for $C_{38}H_{40}O_7$, 631.2671; found, 631.2644. Anal. Calcd for $C_{38}H_{40}O_7$: C, 75.00; H, 6.62. Found: C, 75.53; H, 6.55.

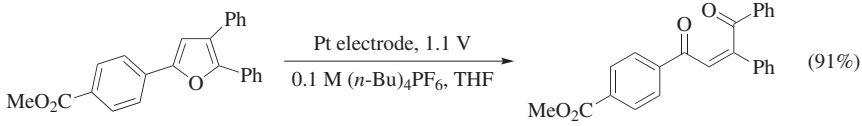


(*E*)-1,4-Diphenyl-2-hydroxy-2-butene-1,4-dione [Oxidation of a Furan to a 1,4-Dicarbonyl Derivative with Phenyltrimethylammonium Tribromide].[176] To a solution of 3-butoxy-2,5-diphenylfuran (292 mg, 1.0 mmol) in *t*-BuOH (10 mL) at rt, was added phenyltrimethylammonium tribromide (376 mg, 1.0 mmol). After being stirred for 17 h at rt the reaction mixture was treated with 0.5 M aq $Na_2S_2O_3$ and saturated aq NaCl, and subsequently extracted with EtOAc. The organic layer was washed with 0.5 M aq $Na_2S_2O_3$ and brine, and then was dried with $MgSO_4$. Removal of the solvent in vacuo afforded 1,4-diphenyl-2-hydroxy-2-butene-1,4-dione, which was purified by column chromatography on silica gel ($CCl_4/CHCl_3$, 3:2) to afford the pure title product (222 mg, 88%): IR (neat) 3381, 3065, 2926, 1681, 1600, 1566, 1490, 1449, 1358, 1320, 1267, 1181, 1144, 1100, 1076, 1053, 1026, 1001, 970, 899, 872, 832, 809, 774, 735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.14–7.25 (m, 10H), 6.85 (s, 1H). ^{13}C NMR ($CDCl_3$) δ 190.4, 187.0, 182.3, 134.2, 133.7, 133.4, 130.4, 128.8, 128.8, 128.6, 127.6, 96.2; HRMS (*m*/*z*): $[M + Na]^+$ calcd for $C_{16}H_{12}O_3$,

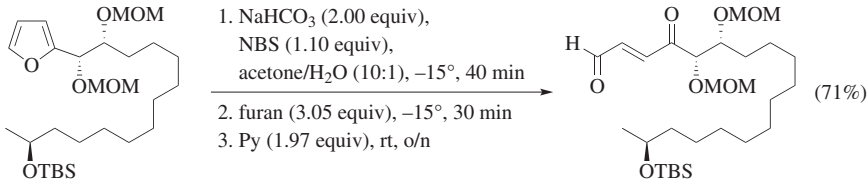
275.0679; found, 275.0678. Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.80. Found: C, 76.31; H, 4.92.



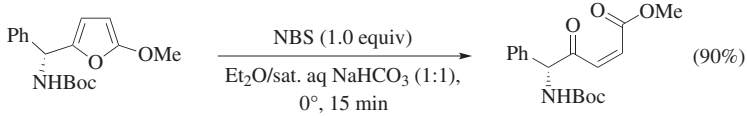
(2*Z*,7*E*)-6-(Methoxymethoxy)-2-methylcyclododeca-2,7-diene-1,4-dione [Oxidation of a Furan to a 1,4-Dicarbonyl Derivative with Air].[173] A stream of air was passed over a stirred solution of (*E*)-3-(methoxymethoxy)-11-methyl-13-oxabicyclo[8.2.1]trideca-1(12),4,10-triene (153.0 mg, 0.611 mmol) in EtOAc (6.1 mL) at rt for 7 d. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (hexanes/ether, 6:1–1:1–1:2) to afford the starting furan (31.2 mg) and (2*Z*,7*E*)-6-(methoxymethoxy)-2-methylcyclododeca-2,7-diene-1,4-dione (76.6 mg, 47%) as an oil: IR (film) 1694, 1612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.23 (d, J = 1.5 Hz, 1H), 5.69–5.61 (m, 1H), 5.59–5.24 (m, 1H), 4.71 (ABq, J = 6.8 Hz, 1H), 4.52 (ABq, J = 6.8 Hz, 1H), 4.49–4.41 (m, 1H), 3.35 (s, 3H), 2.86–2.73 (m, 2H), 2.38–2.31 (m, 3H), 2.01–1.96 (m, 1H), 1.92 (d, J = 12.1 Hz, 3H), 1.62–1.35 (m, 2H).



(*Z*)-Methyl 4-(4-Oxo-3,4-diphenylbut-2-enoyl)benzoate [Electrochemical Oxidation of a Furan to a 1,4-Dicarbonyl Derivative].[69] A bulk electrolysis was carried out using a tube-shaped Pt-web (52 mesh, diameter 1.5 cm, height 1.5 cm) working electrode, a Pt foil counter electrode, and an Ag/Ag^+ (10 mM $AgNO_3$) reference electrode. A THF solution (50 mL) containing 0.1 M Bu_4NPF_6 and methyl 4-(4,5-diphenylfuran-2-yl)benzoate (150 mg, 0.42 mmol) was electrolyzed at 1100 mV. The electrolytic solution was stirred continuously throughout the electrolysis process. The charge consumption (102.1 Coulombs) was calculated by integrating the current–time curve. The electrolyte was evaporated in vacuo, and the pure product was obtained after workup and chromatographic separation on silica gel (CH_2Cl_2/hexane, 2:1). (*Z*)-methyl 4-(4-oxo-3,4-diphenylbut-2-enoyl)benzoate was obtained (143 mg, 91%) as a white powder: mp 114–115°; IR (KBr) 1722, 1674, 1651 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 2H), 8.03 (d, J = 8.4 Hz, 2H), 7.99 (d, J = 7.8 Hz, 2H), 7.67 (s, 1H), 7.61–7.57 (m, 3H), 7.50–7.41 (m, 5H), 3.92 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 196.6, 187.9, 166.0, 155.8, 139.1, 136.9, 134.2, 133.7, 133.4, 130.8, 129.9, 129.2, 128.6, 128.5, 128.3, 127.1, 121.1, 52.5; HRMS–FAB (*m*/*z*): $[M + H]^+$ calcd for $C_{24}H_{18}O_4$, 371.1283; found 371.1292.

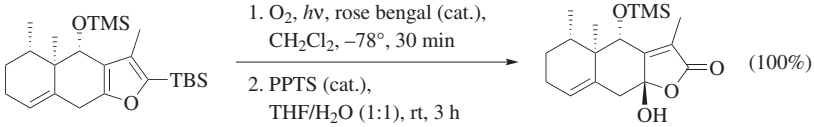


(2*E*,5*S*,6*R*,17*S*)-17-[(*tert*-Butyldimethylsilyl)oxy]-5,6-bis(methoxymethoxy)-4-oxo-2-octadecenal [Oxidation of a Furan to a 4-Oxoalkenal with *N*-Bromosuccinimide].[182] To a mixture of (1*S*,2*R*,13*S*)-2-(13-[(*tert*-butyldimethylsilyl) oxy]-1,2-bis(methoxymethoxy)-1-tetradecanyl)furan (793 mg, 1.54 mmol) and $NaHCO_3$ (258 mg, 3.08 mmol) in acetone/H_2O (10:1, 3 mL) was added NBS (304 mg, 1.69 mmol) dissolved in acetone/H_2O (10:1, 1.5 mL) at −15°. The mixture was stirred for 40 min, and furan (0.34 mL, 4.7 mmol) was added to quench excess NBS. After 30 min at −15°, pyridine (0.24 mL, 3.03 mmol) was added. The mixture was stirred at rt overnight and then was poured into phosphate buffer (pH 3.6) and EtOAc. The phases were separated, and the aqueous phase was extracted with EtOAc. The combined organic phases were dried over $MgSO_4$ and concentrated to give a residue that was purified by chromatography (hexane/EtOAc) to furnish (2*E*,5*S*,6*R*,17*S*)-17-[(*tert*-butyldimethylsilyl)oxy]-5,6- bis(methoxymethoxy)-4-oxo-2-octadecenal (584 mg, 71%): IR (neat) 1697, 1032, 835, 775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.77 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 16.0 Hz, 1H), 6.88 (dd, J = 16.0, 8.0 Hz, 1H), 4.72 (d, J = 7.0 Hz, 1 H), 4.70 (d, J = 7.0 Hz, 1H), 4.64 (d, J = 7 Hz, 1H), 4.57 (d, J = 7 Hz, 1H), 4.27 (d, J = 3 Hz, 1H), 3.95–3.87 (m, 1H), 3.81–3.69 (m, 1H), 3.37 (s, 3H), 3.26 (s, 3H), 1.76–1.12 (m, 20H), 1.10 (d, J = 6.0 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 6H); HRMS–CI (*m*/*z*): $[M + H]^+$ calcd for $C_{24}H_{54}O_7Si$, 531.3717; found, 531.3718.

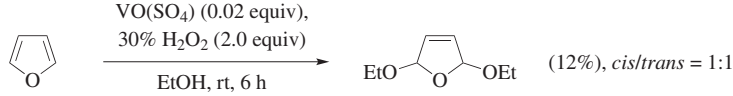


***tert*-Butyl (*Z*)-4-(Methoxycarbonyl)-2-oxo-1-phenylbut-3-enyl carbamate [Oxidation of a Furan to a 4-Oxoalkenoic Ester with *N*-Bromosuccinimide].[202]** To a stirred solution of the furan derivative (151.7 mg, 0.5 mmol) in diethyl ether (5 mL) was added saturated aq $NaHCO_3$ (5 mL). To the resulting biphasic solution was added NBS (89.0 mg, 0.5 mmol) over 15 min as a solid at 0°. When the addition was complete, the resulting clear solution was diluted with water and extracted with CH_2Cl_2. The organic extract was dried over Na_2SO_4 and filtered. After concentration, the residue was purified by column chromatography (EtOAc/hexane, 1:10–1:4). The 4-oxoalkenoic ester was obtained as a liquid (144 mg, 90%): IR (KBr) 3389, 2976, 2943, 1738, 1724, 1693, 1624, 1501, 1439, 1354, 1290, 1244, 1167, 1051, 891, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 7.39–7.29 (m, 5H), 6.32 (d, J = 12.2 Hz, 1H), 6.05 (d, J = 12.2 Hz, 1H), 6.03 (br s, 1H), 5.55 (br d, J = 6.2 Hz, 1H), 3.78 (s, 3H), 1.41 (br s, 9H); ^{13}C NMR ($CDCl_3$, 67.8 MHz)

δ 197.4, 165.6, 154.7, 137.8, 136.2, 129.1, 128.6, 128.0, 127.2, 79.9, 64.2, 52.3, 28.3; HRMS–ESI (*m*/*z*): $[M + Na]^+$ calcd for $C_{18}H_{23}NO_4$, 342.1312; found, 342.1312.

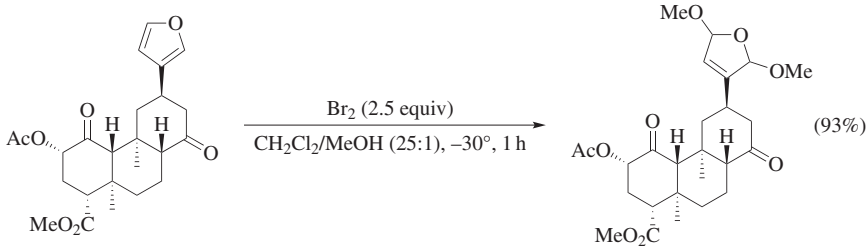


9*a*-Hydroxy-3,4*a*,5-trimethyl-4-trimethylsilyloxy-4*a*,5,6,7,9,9*a*-hexahydro-4*H*-naphtho[2,3-*b*]furan-2-one [Oxidation of a Furan to a γ-Butenolide with Singlet Oxygen].[573] A solution of 2-(*tert*-butyldimethyl)silyl-3,4*a*,5-trimethyl-4-trimethylsilyloxy-4,4*a*,5,6,7,9-hexahydronaphtho[2,3-*b*]furan (7.9 mg, 0.019 mmol) in CH_2Cl_2 (1.3 mL) containing a crystal of rose bengal was flushed with O_2, then was cooled to −78° and irradiated with a 300W tungsten lamp. After 30 min, a crystal of pyridinium *p*-toluenesulfonate in THF (1 mL) and water (1 mL) was added, and the mixture was stirred at rt for 3 h. The mixture was extracted with Et_2O (3 × 5 mL) and the combined extracts were concentrated to dryness. The residue was purified by silica gel column chromatography (hexane/EtOAc, 90:10) to yield 9*a*-hydroxy-3,4*a*,5-trimethyl-4-trimethylsilyloxy-4*a*,5,6,7,9,9*a*-hexahydro-4*H*-naphtho[2,3-*b*]furan-2-one (7.2 mg, 100%) as a colorless solid: mp 192–196°; IR (neat) 3347, 2957, 2922, 2852, 1740, 1694, 1435, 1306, 1253, 1232, 1204, 1121, 1086, 1062, 1013, 954, 909, 882, 840, 753 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.75 (br s, 1H), 4.47 (d, *J* = 2.0 Hz, 1H), 2.76 (s, 1H), 2.65 (d, *J* = 14.0 Hz, 1H), 2.54 (dd, *J* = 14.0, 2.0 Hz, 1H), 2.07–2.00 (m, 2H), 2.02 (d, *J* = 2.0 Hz, 3H), 1.82 (dtd, *J* = 16.0, 7.0, 3.0 Hz, 1H), 1.59–1.51 (m, 1H), 1.36 (dddd, *J* = 14.0, 10.0, 7.0, 7.0 Hz, 1H), 1.10 (d, *J* = 7 Hz, 3H), 0.88 (s, 3H), 0.17 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 172.0, 159.7, 134.8, 129.8, 124.4, 102.5, 78.4, 47.5, 46.2, 36.7, 28.6, 24.7, 18.5, 12.8, 9.2, −0.2; CIMS (*m*/*z*): $[M + H]^+$ 337, 319, 247, 229; HRMS–CI (*m*/*z*): $[M + H]^+$ calcd for $C_{18}H_{28}O_4Si$, 337.1835; found, 337.1820.

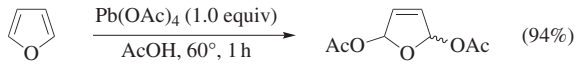


2,5-Diethoxy-2,5-dihydrofuran [Oxidation of a Furan to a 2,5-Dihydrofuran with Hydrogen Peroxide].[621] A mixture of furan (23.8 g, 0.35 mol), 30% H_2O_2 (75 mL, 0.70 mol), and vanadyl sulfate (2.1 g, 0.007 mol) in ethanol (100 mL) was stirred at rt for 6 h. The reaction mixture was extracted with Et_2O, and the extract was dried over sodium sulfate. The mixture was filtered, and the solvent was removed by distillation. Vacuum distillation of the residue gave 2,5-diethoxy-2,5-dihydrofuran (6.6 g, 12%) as a 1:1 mixture of *cis*/*trans* isomers: bp 70–75° (10 mm Hg), n_D^{20} 1.4340, d_4^{20} 1.0031; IR (neat) 1115, 1130, 1350, 1370, 1635, 2895, 2940, 2990 cm^{-1}; ^1H NMR ($CDCl_3$) δ (*cis* isomer) 6.07 (m, 2H), 5.68 (m 2H), 3.68 (m, 4H), 1.24 (m, 6H); (*trans* isomer) 6.07 (m, 2H), 5.68 (m, 2H), 3.68 (m 4H), 1.24

(m, 6H); ^{13}C NMR ($CDCl_3$) δ (*cis* isomer) 131.0 (2C), 105.9 (2C), 62.3, 14.9; (*trans* isomer) 131.4 (2C), 107.4 (2C), 62.7, 15.0; Anal. Calcd for $C_8H_{14}O_3$: C 60.74; H 8.92. Found: C 60.54; H 8.86.



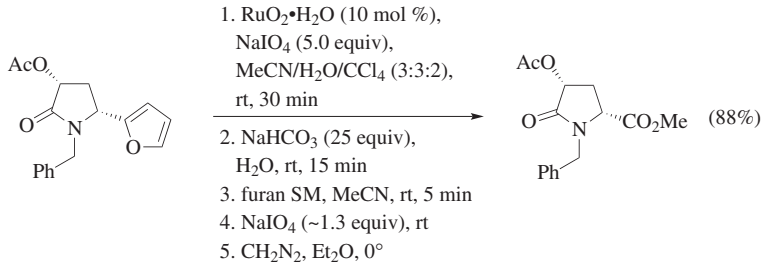
(2*S*,4a*R*,6a*R*,7*R*,9*S*,10a*S*,10b*R*)-9-(Acetyloxy)-2-(2,5-dimethoxy-2,5-dihydrofuran-3-yl)-dodecahydro-6a,10b-dimethyl-4,10-dioxo-2*H*-naphtho-[2,1-*c*]pyran-7-carboxylic Acid, Methyl Ester [Oxidation of a Furan to a 2,5-Dihydrofuran with Bromine].[233] A solution of bromine (0.075 mL, 1.46 mmol) in MeOH (1 mL) was added dropwise to a solution of methyl (1*R*,3*S*,4a*R*,4b*S*,6*R*,8a*R*,10a*R*)-3-acetoxy-6-(furan-3-yl)-4b,10a-dimethyl-4,8-dioxo-tetradecahydrophenanthrene-1-carboxylate (0.25 g, 0.59 mmol) in a mixture of CH_2Cl_2 (50 mL) and MeOH (2 mL) at −30°. The mixture was stirred at −30° for 1 h and was quenched by the addition of saturated aq $NaHCO_3$ solution (100 mL). The layers were separated, and the organic layers washed with saturated aq $NaHCO_3$ (50 mL) and H_2O (70 mL), and dried (Na_2SO_4). Removal of the solvent under reduced pressure afforded a white foam. The foam was purified by flash column chromatography (hexane/EtOAc, 3:2) to afford the title compound (0.27 g, 93%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.85 (m, 2H), 5.59 (m, 1H), 5.14 (m, 2H), 3.73 (s, 3H), 3.44 (m, 3H), 3.39 (dd, J = 1.4, 2.0 Hz, 3H), 2.75 (dd, J = 5.6, 10.9 Hz, 1H), 2.47 (m, 1H), 2.30 (m, 2H), 2.17 (s, 3H), 2.17 (s, 1H), 2.13 (m, 1H), 2.03 (dd, J = 2.7, 11.4 Hz, 1H), 1.78 (dd, J = 2.7, 9.9 Hz, 1H), 1.68 (dd, J = 2.7, 12.6 Hz, 1H), 1.56 (m, 2H), 1.40 (s, 3H), 1.10 (s, 3H); HRMS (*m*/*z*): $[M + Na]^+$ calcd for $C_{25}H_{34}O_{12}$, 551.2104; found, 551.2080.



2,5-Diacetoxy-2,5-dihydrofuran [Oxidation of a Furan to a 2,5-Dihydrofuran with Lead Tetraacetate].[622] To a solution of $Pb(OAc)_4$, (5.0 g, 11.3 mmol) in acetic acid (10 mL) at 60° was added furan (0.85 mL, 11.4 mmol). After 1 h the mixture was allowed to cool to rt. The acetic acid was removed under vacuum until a thick paste remained. To this material was added ether (30 mL), and the vessel was vigorously shaken until the lead salts formed a precipitate. Filtration through Celite, followed by evaporation of the solvent, afforded the crude product. Bulb to bulb vacuum distillation (90°, 0.1 mm Hg) provided 2,5-diacetoxy-2,5-dihydrofuran (1.98 g, 10.6 mmol, 94%) as a 2:1 (by NMR) mixture of isomers: IR

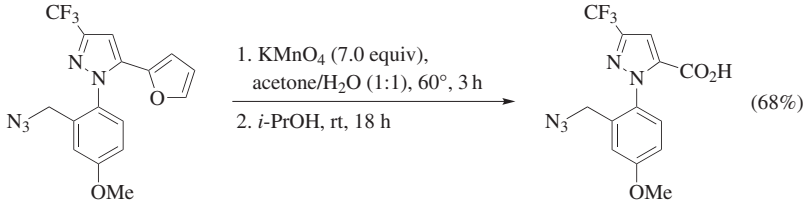
(neat) 1757 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.96 (s, 1H), 6.73 (s, 1H), 6.21 (s, 1H), 6.19 (s, 1H), 2.08 (s, 3H), 2.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 169.9, 169.7, 131.3, 130.9, 101.5, 100.0, 21.1, 20.9; MS (*m*/*z*): 127 (3), 84 (5), 68 (3), 43 (100).

Selective crystallization of the major isomer was effected by taking up the mixture of isomers in an equal volume of ether and cooling the solution to its freezing point followed by warming to rt, and recooling. This procedure was repeated four times, at which stage the crystals no longer dissolved at rt. The mother liquors were removed from the solid material, which was then washed with cold diethyl ether. Removal of the residual solvent under vacuum afforded 637 mg of the crystalline, major isomer (mp 50–51°). Vacuum removal of the solvent from the mother liquors afforded 1.34 g of a 1:1 isomeric mixture of 2,5-diacetoxy-2,5-dihydrofurans.

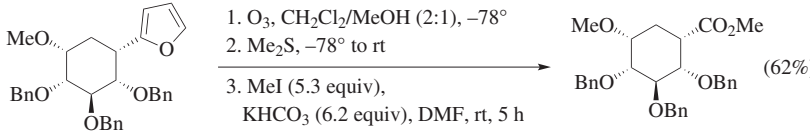


(3*R*,5*R*)-3-Acetoxy-1-benzyl-5-(methoxycarbonyl)pyrrolidin-2-one [Oxidation of a Furan to a Carboxylic Ester with Ruthenium Tetroxide].[382] To a well-stirred mixture of MeCN, (9.5 mL), CCl_4 (6.3 mL), and H_2O (9.5 mL) were added sequentially $NaIO_4$ (0.98 g, 4.6 mmol) and $RuO_2•H_2O$ (12.2 mg, 0.092 mmol). After 30 min at rt, $NaHCO_3$ (1.9 g, 23 mmol) was added in one portion followed by H_2O (4.6 mL). After 15 min, the resulting mixture was treated with a solution of (3*R*,5*R*)-3-acetoxy-1-benzyl-5-(2-furyl)pyrrolidin-2-one (0.275 g, 0.92 mmol) in MeCN (0.7 mL). The solution turned black, and after 5 min enough $NaIO_4$ (~0.250 g, 1.2 mmol) was added in small portions to turn the color light green. The mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 15 mL). The aqueous layer was acidified with 1 N HCl to pH 2–3 and reextracted with EtOAc (3 x 20 mL). The combined organic extracts were washed sequentially with 20% aq $NaHSO_3$ until colorless and then with brine and dried ($MgSO_4$). The solvent was evaporated under reduced pressure. The crude acid was dissolved in Et_2O (20 mL), and the solution was cooled to 0° and treated with an ethereal solution of diazomethane until a slight yellow color persisted. The excess diazomethane was destroyed with acetic acid. The resulting solution was concentrated under reduced pressure, and the crude ester was purified by column chromatography on silica gel (hexane/Et_2O, 50:50) to afford (3*R*,5*R*)-3-acetoxy-1-benzyl-5-(methoxycarbonyl)pyrrolidin-2-one (0.236 g, 88%) as an oil: $[\alpha]_D$ – 16.2 (c 0.55, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.10–7.30 (m, 5H), 5.29 (dd, J = 6.4, 8.5 Hz, 1H), 5.13 (d, J = 14.9 Hz, 1H), 4.13 (d, J = 14.9 Hz,

1H), 3.92 (dd, J = 6.4, 8.5 Hz, 1H), 3.65 (s, 3H), 2.77 (dt, J = 8.5, 13.9 Hz, 1H), 2.07 (s, 3H), 2.00 (dt, J = 6.4, 13.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 170.8, 170.1, 170.0, 134.8, 128.7, 128.4, 128.0, 69.5, 55.4, 52.5, 45.8, 29.9, 20.6. Anal. Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.93; H, 6.01; N, 4.72.

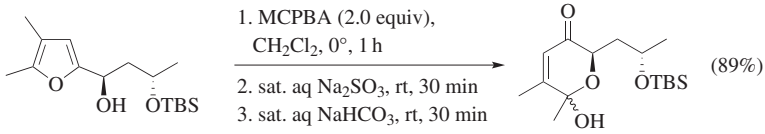


1-(2-Azidomethyl-4-methoxyphenyl)-3-trifluoromethyl-1*H*-pyrazole-5-carboxylic Acid [Oxidation of a Furan to a Carboxylic Acid with Potassium Permanganate].[391] To 1-(2-azidomethyl-4-methoxyphenyl)-3-trifluoromethyl-5-(furan-2-yl)-1*H*-pyrazole (1.43 g, 3.9 mmol) in acetone (60 mL) was added a solution of $KMnO_4$ (5.0 g, 27.5 mmol) in water (60 mL). The reaction mixture was heated at 60° for 3 h, then was cooled to ambient temperature, and isopropyl alcohol (60 mL) was added. This mixture was stirred for 18 h and then filtered through a Celite pad and washed with copious amounts of isopropyl alcohol. The combined filtrates were evaporated, the residue was dissolved in 1 N NaOH (50 mL) and the solution was washed with Et_2O (2 × 50 mL). The basic layer was acidified with 1 N HCl (75 mL) and solid NaCl was added. The suspension was extracted with EtOAc (3 × 100 mL), and the extracts were dried and evaporated to give 3-trifluoromethyl-1-(2-azidomethyl-4-methoxyphenyl)-1*H*-pyrazole-5-carboxylic acid (0.91 g, 68%): ^{1}H NMR ($CDCl_3$) δ 7.3 (s, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.1–7.0 (br s, 1H), 7.05 (d, J = 1.0 Hz, 1H), 6.95 (dd, J = 8.0, 1.0 Hz, 1H), 4.05 (br s, 2H), 3.9 (s, 3H); EIMS (70 eV) (m/z): 340.

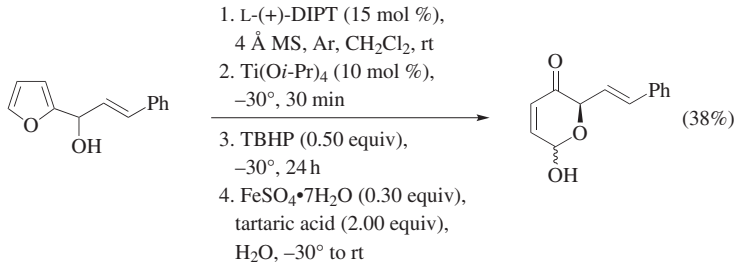


(1*S*,2*S*,3*R*,4*R*,5*R*)-Methyl 2,3,4-tris(Benzyloxy)-5-methoxycyclohexanecarboxylate [Oxidation of a Furan to a Carboxylic Ester with Ozone].[396] Ozone gas was bubbled through a solution of 2-((1*S*,2*S*,3*R*,4*R*,5*R*)-2,3,4-tris(benzyloxy)-5-methoxycyclohexyl)furan (92 mg, 0.18 mmol) in MeOH (3 mL) and CH_2Cl_2 (6 mL) at −78° until the solution remained blue in color. Oxygen was then bubbled through the solution for 1 min and then dimethyl sulfide (50 μL) was added. The solution was allowed to warm to rt, and the solvent was removed under vacuum. The residue

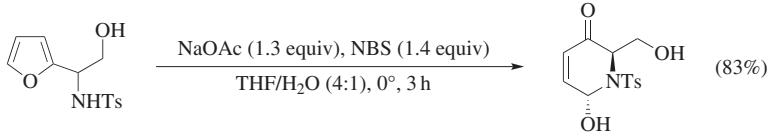
was dissolved in DMF (3 mL), and MeI (59 μL, 0.95 mmol) and $KHCO_3$ (111 mg, 1.11 mmol) were added. After stirring for 5 h at rt, TLC (cyclohexane/EtOAc, 7:3) indicated completion of the reaction. The solvent was removed under vacuum and the residue was partitioned between CH_2Cl_2 (5 mL) and water (5 mL). The organic layer was dried ($MgSO_4$), and the solvent was removed under vacuum. The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 85:15), to afford (1*S*,2*S*,3*R*,4*R*,5*R*)-methyl 2,3,4-tris(benzyloxy)-5-methoxycyclohexanecarboxylate (56 mg, 62%), as a colorless oil: $[\alpha]_D^{20}$ − 14 (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.40–7.26 (m, 15H), 4.73 (d, *J* = 12.3 Hz, 1H), 4.63 (d, *J* = 12.3 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.58 (d, *J* = 11.7 Hz, 1H), 4.55 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 3.99 (br s, 1H), 3.88 (br s, 1H), 3.74 (br s, 1H), 3.69 (s, 3H), 3.50 (dt, 1H, *J* = 10.3, 3.3 Hz, 1H), 3.37 (s, 3H), 2.84 (dt, *J* = 10.8, 3.8 Hz, 1H), 2.49 (td, *J* = 12.3 Hz, 1H), 1.94–1.86 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 173.0, 138.8, 138.4, 138.0 (3C), 128.4–127.3 (15C), 77.6, 76.3, 73.1, 72.8, 72.3 (3C), 56.6, 51.6 (2C), 42.5, 26.9; EIMS (70 eV) (*m/z*): $[M + H]^+$ 491. Anal. Calcd for $C_{30}H_{34}O_6$: C, 77.08; H, 6.87. Found: C, 77.03; H, 6.92.



(2*R*,6*RS*,2′*S*)-2-(2′-*tert*-Butyldimethylsilyloxypropyl)-6-hydroxy-5,6-dimethyl-2*H*-pyran-3-one [Achmatowicz Reaction Using *m*-Chloroperoxybenzoic Acid].[453] *m*-CPBA (70%, 8.60 g, 34.9 mmol) was added to a stirred solution of (1*R*,3*S*)-3-(*tert*-butyldimethylsilyloxy)-1-(4,5-dimethylfuran-2-yl)butan-1-ol (5.20 g, 17.4 mmol) in dry CH_2Cl_2 (100 mL) at 0°. The mixture was stirred for 1 h, poured into a saturated aq Na_2SO_3 solution, stirred for 30 min, then poured into saturated aq $NaHCO_3$ solution and stirred for an additional 30 min. The mixture was then extracted with Et_2O. The organic layers were washed with saturated aq Na_2SO_3 solution and brine, dried (Na_2SO_4) and concentrated under vacuum. The residue was purified by chromatography over silica gel (100 g, *n*-hexane/EtOAc, 5:1) yielding (2*R*,6*RS*,2′*S*)-2-(2′-*tert*-butyldimethylsilyloxypropyl)-6-hydroxy-5,6-dimethyl-2*H*-pyran-3-one (4.59 g, 89%) as a colorless solid (4:1 diastereomeric mixture). This material was further purified by crystallization from *n*-pentane to give the pure product mixture as colorless needles: mp 68–74°; $[\alpha]_D^{24}$ + 19.9 (c 1.08, $CHCl_3$); IR (nujol): 3430, 1660, 1255, 1140, 1025, 835, 780 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.85 (br s, 1H), 4.13–4.00 (m, 1H), 2.59 (br s, 1H), 2.16 (ddd, *J* = 14.3, 9.8, 2.7 Hz, 0.8H), 2.08 (ddd, *J* = 14.3, 9.8, 2.7 Hz, 0.2H), 2.02 (br s, 3H), 1.68 (ddd, *J* = 14.3, 10.5, 2.9 Hz, 0.2H), 1.60 (s, 2.4H), 1.59 (s, 0.6H), 1.50 (ddd, *J* = 14.3, 10.5, 2.9 Hz, 0.8H), 1.15 (d, *J* = 6.1 Hz, 3H), 0.87 (s, 9H), 0.07 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 197.4, 158.7, 124.3, 94.9, 71.3, 64.2, 39.7, 27.1, 25.8, 24.4, 19.4, 18.0, −4.1, −4.6. Anal. Cald for $C_{16}H_{30}O_4Si$: C 61.11, H 9.61. Found C 60.60, H 9.91.



(2*S*)-6-Hydroxy-2-[(*E*)-styryl]-6*H*-pyran-3(2*H*)-one [Achmatowicz Reaction Using *tert*-Butyl Hydroperoxide].[524] To a stirred solution of (*E*)-1-(furan-2-yl)-3-phenylprop-2-en-1-ol (11.0 g, 0.055 mol) and L-(+)-DIPT (1.93 g, 8.25 mmol) in anhydrous CH_2Cl_2 (120 mL) was added activated 4 Å molecular sieves (1.84 g) at rt under argon. The stirred mixture was cooled to −30°, treated with Ti(O*i*-Pr)$_4$ (1.57 g, 5.5 mmol), and stirring was continued for 30 min at −30°. The reaction mixture was treated with TBHP (5.0–6.0 M, nonane solution, 5.5 mL, 27.5 mmol) and was then stirred for 24 h at the same temperature. A freshly prepared solution of $FeSO_4$•$7H_2O$ (4.62 g, 16.6 mmol) and tartaric acid (16.6 g, 110 mmol) in deionized water (30 mL) was added to the reaction mixture at −30°. The resulting mixture was stirred at rt until the mixture was clear. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (5 × 40 mL). The organic layer was combined and washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue, which was purified by column chromatography on silica gel (petroleum ether/EtOAc, 4:1 v/v) to afford (2*S*)-6-hydroxy-2-[(*E*)-styryl]-6*H*-pyran-3(2*H*)-one (4.51 g, 38%) as a brown oil: $[\alpha]_D^{20}$ + 126.3 (c 0.5, $CHCl_3$); IR (KBr) 3350, 1720, 1680, 1640 cm^{-1}; ^{1}H ($CDCl_3$) δ 7.45–7.25 (m, 5H), 6.98 (dd, *J* = 10.3, 1.9 Hz, 0.2H), 6.95 (dd, *J* = 10.3, 3.3 Hz, 0.8H), 6.75 (dd, *J* = 15.8, 1.9 Hz, 1H), 6.48 (dd, *J* = 15.8, 6.3 Hz, 0.2H), 6.39 (dd, *J* = 15.8, 5.7 Hz, 0.8H), 6.18 (dd, *J* = 10.3, 1.5 Hz, 1H), 5.77 (br s, 1H), 5.26 (dd, *J* = 5.7, 1.5 Hz, 0.8H), 4.80 (d, *J* = 5.9 Hz, 0.2H), 4.2–3.8 (br s, 1H); ^{13}C ($CDCl_3$) δ 190.2, 133.6, 131.2, 129.5, 128.5 (2C), 127.4, 126.9, 126.5, 125.8 (2C), 91.8, 86.3. EIMS (*m/z*): M^+ 216 (6), 198 (8), 131 (16), 115 (29), 84 (84), 77 (19). Anal Calcd for $C_{13}H_{12}O_3$: C, 72.2; H, 5.56. Found: C, 72.4; H, 5.57.



6-Hydroxy-2-(hydroxymethyl)-1-[(4-methylphenyl)sulfonyl]-1,6-dihydropyridin-3(2*H*)-one [Aza-Achmatowicz Reaction Using *N*-Bromosuccinimide].[558] The furan derivative (5.00 g, 17.8 mmol) and sodium acetate (1.86 g,

22.7 mmol) were dissolved in THF/H_2O (80 mL, 4:1), cooled to −5°, and then treated portionwise with *N*-bromosuccinimide (4.37 g, 24.6 mmol) such that the reaction temperature did not exceed 0°. The deep-orange solution was then stirred at 0° for 3 h. After the addition of EtOAc (200 mL), the mixture was treated sequentially with saturated aq KI (100 mL), saturated aq NaS_2O_3 (100 mL) and saturated aq $NaHCO_3$ (100 mL). The organic layer was separated, washed with saturated aq NaCl (80 mL), and dried over $MgSO_4$. Removal of the solvent and silica gel chromatography (cyclohexane/EtOAc) afforded the title compound (4.38 g, 83%): mp 132–136° (dec.); $[\alpha]_D^{20}$ + 40 (*c* 1.0, acetone); IR (neat) 3193, 3113, 3068, 2980, 2887, 1691, 1597, 1453, 1388, 1340, 1310, 1230, 1153, 1060, 970, 917, 850, 811, 730 cm^{-1}; ^1H NMR (400 MHz, [d^6]acetone) δ 7.42 (m, 4H), 7.05 (dd, *J* = 4.7, 10.2 Hz, 1H), 6.06 (dd, *J* = 4.7, 8.6 Hz, 1H), 6.01 (d, *J* = 10.2 Hz, 1H), 5.92 (d, *J* = 9.4 Hz, 1H), 5.03 (s, 1H), 4.39 (m, 1H), 3.93 (m, 1H), 3.65 (d, *J* = 11.1 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, [d^6]acetone) δ 194.3, 147.7, 145.5, 139.4, 131.4, 128.9, 128.7, 73.7, 64.9, 64.3, 22.1.

TABULAR SURVEY

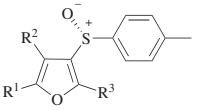
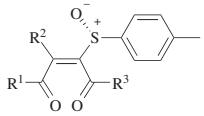
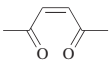
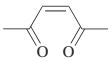
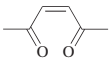
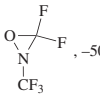
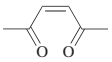
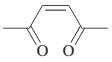
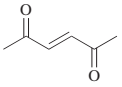
The furan oxidation to give 1,4-diketoalkenes, 4-oxoalkenals, 4-oxoalkenoic acids and esters, and 4-hydroxybutenolides are grouped in Tables 1–4. Reactions yielding the complete oxidation of furan derivatives to give carboxylic acids and esters are collected in Table 5 and transformations of furans into 2,5-dialkoxy-2,5-dihydrofurans are compiled in Table 6. The Achmatowicz reaction and the aza version of the process are grouped in Tables 7 and 8. Within each table entries are listed by increasing numbers of carbon atoms, using the *Chemical Abstracts* convention, and excluding chiral auxiliaries, protecting groups, and simple alkyl groups on heteroatoms. Yields, in parentheses, are based on isolated products. Em-dashes (—) indicate that no yield was reported. Numbers not in parentheses are product ratios. The literature has been reviewed to mid-2014.

The following abbreviations (not included in "*The Journal of Organic Chemistry* Standard Abbreviations and Acronymns") are used in the Tabular Survey:

Ad	adamantyl
BOM	benzyloxymethyl
DET	diethyltartrate
DIPT	diisopropyltartrate
DMP	Dess–Martin periodinane
HMIM	1-hexyl-3-methylimidazolium
MCPBA	meta-chloroperoxybenzoic acid
MMPP	magnesium monoperoxyphthalate
PMP	*p*-methoxyphenyl
PTSA	*p*-toluenesulfonic acid

TBDPS	*tert*-butyldiphenlsilyl
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxy
TPP	*meso*-tetraphenylporphyrin
Tr	trace

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-6} 	O_2, methylene blue, hν, solvent, –40°, 20 min; then Me_2S, –40° to rt, 3 h	 R^1 R^2 R^3 Solvent H H H CH_2Cl_2 (84) Me H Me MeOH (88) Me Br Me MeOH (94)	297
C_6 	MMPP (0.5 eq), $EtOH/H_2O$ (2:1), rt, 10 min	 (99)	139, 623
	H_2O_2 (35 wt %, 1.25 eq), titanium silicalite (10 g/mol), MeCN, rt, 3 h	 (—)	48
	O_2, methylene blue, hν, –78°, $CFCl_3$; then Me_2S, –78° to rt	 (—)	624
	 , –50°, 0.25 h	 (—)	39
	m-CPBA (0.9 eq), CH_2Cl_2, –10° to rt, 2 h	 (—)	35, 625
	1. O_2, methylene blue, hν, $CFCl_3$ 2. PPh_3 (1.5 eq), benzene, 0°, 1 h	 (93)	624,79

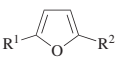
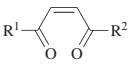
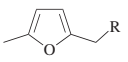
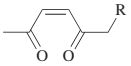
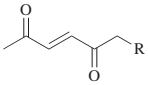
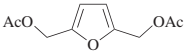
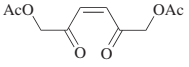
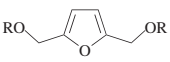
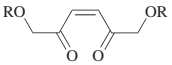
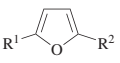
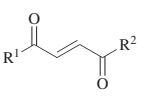
C_{6-18} 	$NaClO_2$ (3 eq), NaH_2PO_4 (1.5 eq), *t*-BuOH/H_2O (5:1), rt, 1 h	 R^1 R^2 Me Me (93) Me (*E*)-*n*-C_4H_9CH=CH (78) $CHO(CH_2)_7$ (*E*)-*n*-C_4H_9CH=CH (76)	211
C_{6-15} 	cumyl hydroperoxide (1.0 eq), $Mo(CO)_6$ (0.1 eq), Na_2CO_3 (1.0 eq), $CHCl_3$, 50°	 R Time (h) H 24 (93) *n*-Bu 20 (65) *n*-C_7H_{15} 16 (67) *n*-C_9H_{19} 20 (63)	41
	cumyl hydroperoxide (1.0 eq), $Mo(CO)_6$ (0.1 eq), $CHCl_3$, 50°	 R Time (h) H 12 (53) *n*-Bu 20 (64) *n*-C_7H_{15} 20 (61) *n*-C_9H_{19} 24 (63)	41
C_6 	O_2, methylene blue, hν, CH_2Cl_2, –40°, 5 h; then Me_2S (1.2 eq), –40° to rt	 (88)	161
	*m*-CPBA (1.9 eq), CH_2Cl_2, rt, 18 h	 R Ac (90) Bn (70)	161
C_{6-7} 	O_2, rose bengal, hν, MeOH, –40°, 2 h; then Me_2S, –40° to rt	 R^1 R^2 H $(EtO)_2PO(CH_2)_2$ (92) H $(EtO)_2PO(CH_2)_3$ (94) Me $(EtO)_2PO(CH_2)_2$ (96) Me $(EtO)_2POCH$=CH (76)	249

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

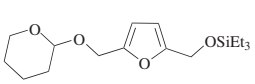
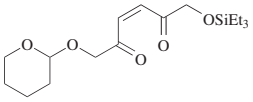
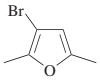
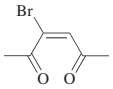
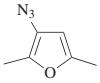
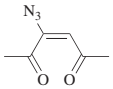
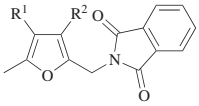
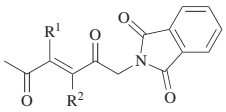
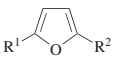
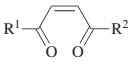
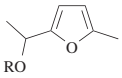
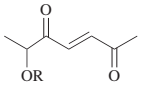
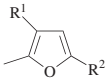
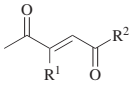
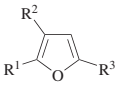
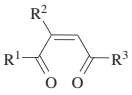
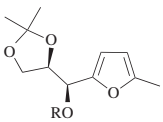
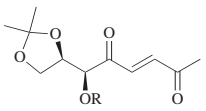
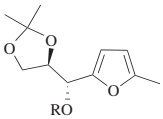
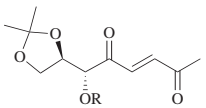
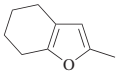
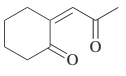
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	*m*-CPBA (1.5 eq), CH_2Cl_2, rt, 3 h	 (51)	625a
	*m*-CPBA (1.5 eq), CH_2Cl_2, –10°, 2 h	 (—)	626
	Br_2 (1.05 eq), py, acetone, H_2O, rt to –20°, 0.5 h	 (—)	627
C_{6-8}			
	1. Br_2 (1.05 eq), CH_2Cl_2, MeOH, –40 to –50°, 35 min 2. 2 N HCl, CH_2Cl_2, rt, 4 h		226
		R^1 R^2 H H (—) H Me (—) Me H (78) Et H (65)	
C_{7-10}			
	350 U laccase (*T. versicolor*), 4-OH-TEMPO (10 mol %), pH 4.5, *n*-octane, rt		174
		R^1 R^2 Time (h) Me Et 72 (52) Me *n*-Pr 72 (59) Et Et 72 (65) Me *n*-Bu 96 (33) *n*-Pr *n*-Pr 72 (22)	
C_7			
	Py (4.0 eq), acetone/H_2O (85:15), Br_2 (1.0 eq)		97, 118
		R MOM (85) TBS (80) Bn (89) Bz (88) TBDPS (91)	97, 118 118 118 118
C_{7-12}			
	*m*-CPBA (0.9 eq), CH_2Cl_2, –10° to rt, 2 h		35
		R^1 R^2 Me Me (—) Me Me_2C=CH (75) H (*E*)-CH_2=CH-CH=CH$(CH_2)_2$ (61) Me (*E*)-CH_2=CH-CH=CH$(CH_2)_2$ (87)	180 35 180
C_{7-13}			
	Peracid (1.13 eq), CH_2Cl_2, 0–7°, 1 h		45
		R^1 R^2 R^3 Peracid Me TMS Et $MeCO_3H$ (70) *n*-Pr TMS Et $MeCO_3H$ (79) *n*-Pr TMS *i*-Pr $MeCO_3H$ (78) Me H *n*-C_6H_{13} *m*-CPBA (86) Me H *n*-C_6H_{13} $MeCO_3H$ (58) *n*-Bu H *n*-Bu *m*-CPBA (87) *n*-Pr TMS Ph $MeCO_3H$ (91)	
C_8			
	Py (4.0 eq), MeCN/H_2O (85:15), Br_2 (1.0 eq), –20° to rt, 2 h		21, 143
		R $PhCH_2OCH_2$ (90) TBDPS (82)	
	Py (4.0 eq), MeCN/H_2O (85:15), Br_2 (1.0 eq), –20° to rt, 2 h		21
		R BOM (80) TBDPS (85)	
C_9			
	*m*-CPBA (1.0 eq), CH_2Cl_2, rt, 3 h	 (77)	44

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

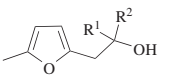
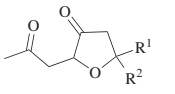
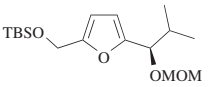
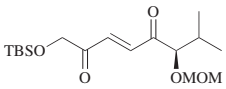
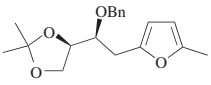
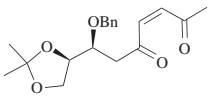
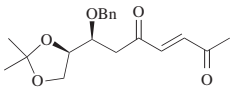
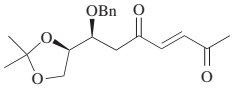
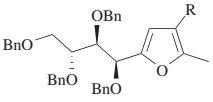
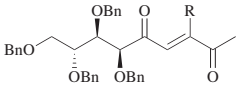
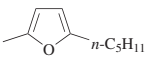
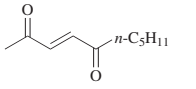
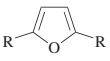
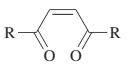
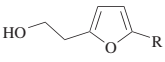
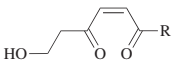
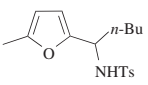
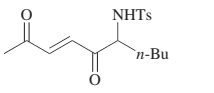
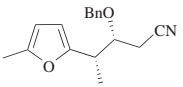
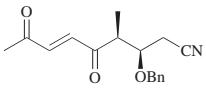
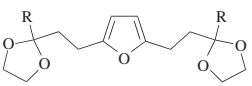
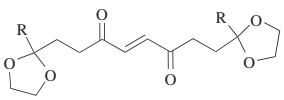
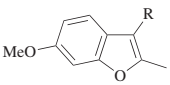
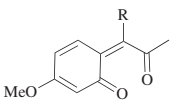
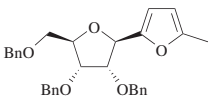
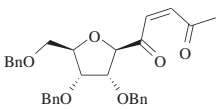
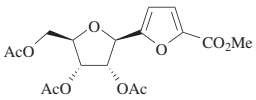
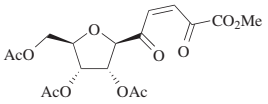
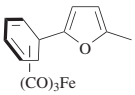
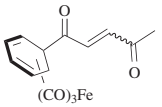
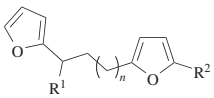
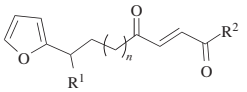
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{9–13}$ 	1. O_2, rose bengal (cat.), hν, MeOH, 0°, 2 min 2. Me_2S (10 eq), CH_2Cl_2, rt, 18 h; then 4-TsOH, rt, 0.5–6 h		309
C_9 	NBS; then py	 (92)	152
	*m*-CPBA (1.1 eq), CH_2Cl_2, –10°, 36 h	 (80)	162
	PCC (5.0 eq), CH_2Cl_2, rt, 24 h; then reflux, 9 h	 (75)	162
	Py (4.0 eq), acetone, H_2O, Br_2	 (82)	162
$C_{9–10}$ 	CAN (5.0 eq), MeCN/H_2O (9:1), rt, 75 min		161
		R: TBDPSO (24)	161
		$HOCH_2$ (50)	161
		EtO_2C (35)	161, 131
C_{10} 	DDQ, CH_2Cl_2, rt, 15–28 h	 (57)	628
$C_{10–12}$ 	*m*-CPBA (0.9 eq), CH_2Cl_2, –10° to rt, 2 h	 R: *i*-Pr (—); *t*-Bu (—)	625
$C_{10–14}$ 	MMPP (1.0 eq), EtOH, H_2O, rt, 2 h	 R: *n*-Bu (95); Ph (88); CH_2=$CH(CH_2)_2CH(Me)(CH_2)_2$ (64)	138
C_{10} 	NBS, NaOAc, THF, H_2O	 (95)	154
	Br_2 (1.3 eq), MeCN/H_2O (6:1), –10°, 15 min; then–10° to rt, 2 h	 (85)	142
$C_{10–12}$ 	*m*-CPBA (0.9 eq), $CHCl_3$, 50°, 12 h	 R: H (71); Me (52)	629
$C_{10–15}$ 	Dimethyldioxirane (2.5 eq), acetone, CH_2Cl_2, –78 to 20°	 R: Me (66); Ph (100)	46 38, 630

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	O_2, methylene blue, hv, CH_2Cl_2, –20°, 30 min; then Et_2S (1.2 eq), –20° to rt, 1 h	 (—)	293
	O_2, methylene blue, hv, CH_2Cl_2, –20°; then Et_2S (1.2 eq), Et_2O, –20° to rt, overnight	 (68)	86
C_{11}			
	O_2, hv, MeOH, 0°, 2 h; then PPh_3, Et_2O, 20°	 (65)	631
C_{11-13}			
	O_2, rose bengal, hv, MeOH, 0°, 2 h; then PPh_3, Et_2O, 20°		97

n	R^1	R^2	
0	MeO	Me	(75)
1	H	TMS	(58)
1	H	Me	(75)
1	MeO	Me	(80)
2	MeO	Me	(75)

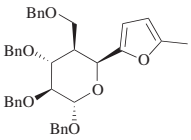
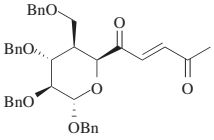
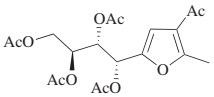
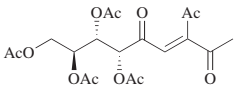
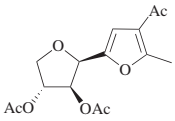
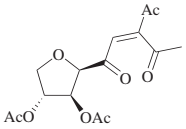
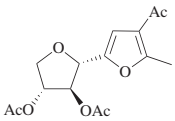
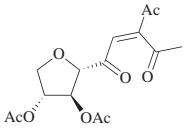
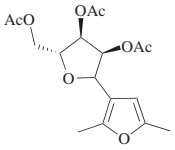
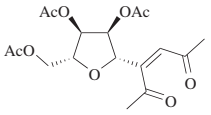
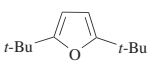
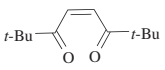
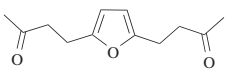
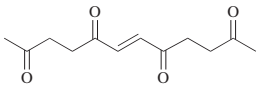
C_{11}			
	1. O_2, methylene blue, hv, CH_2Cl_2, –20° 2. Et_2S, CCl_4, –20° to rt, 1 h 3. SiO_2	 (70)	94
	O_2, methylene blue, hv, acetone, rt, 45 min; then Me_2S (10 eq)	 (—)	289
	O_2, hv, acetone, rt, 40 min; then Me_2S (10 eq)	 (—)	292
	O_2, hv, acetone, rt, 40 min; then Me_2S (10 eq)	 (—)	292
	1. O_2, methylene blue, hv, CH_2Cl_2, –20°, 1.5 h 2. Et_2S (1.2 eq), Et_2O, –20° to rt, 2 h	 (90)	93, 293
C_{12}			
	$Ca(OCl)_2$, HCl	 (—)	632
	*m*-CPBA, $CHCl_3$	 (51)	629

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

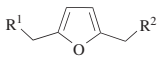
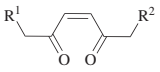
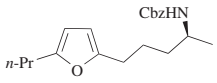
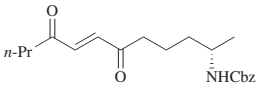
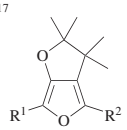
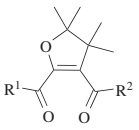
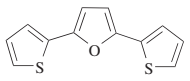
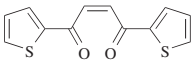
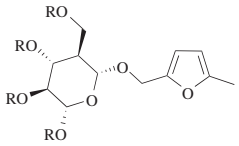
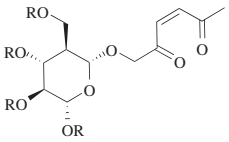
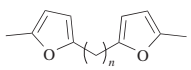
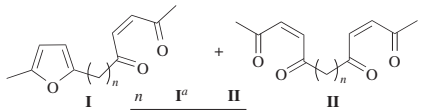
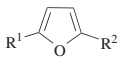
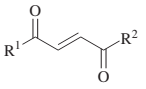
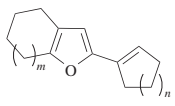
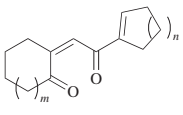
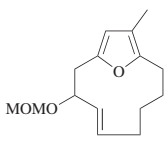
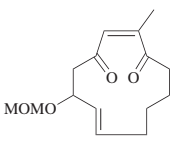
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12-13} 	*m*-CPBA (0.9 eq), CH_2Cl_2, rt, 15 h	 R^1 R^2 H Ph (88) H 3-ClC_6H_4 (83) H 3-$MeOC_6H_4$ (91) Me Ph (79) Me 4-FC_6H_4 (85)	156
C_{12} 	MMPP (0.68 eq), EtOH/H_2O (1:1), rt, 3 h	 (62)	141
C_{12-17} 	O_2, SiO_2	 R^1 R^2 Me Me (—) Me Ph (—) Ph Me (—)	633
C_{12} 	*m*-CPBA (1.5 eq), CH_2Cl_2, rt, 5 min	 (68)	163
	*m*-CPBA (1.9 eq), CH_2Cl_2, rt, 18 h	 R Ac (93) Bn (90)	161
C_{12-14} 	*m*-CPBA (0.5 eq), CH_2Cl_2, –10°	 **I** **II** *n* **I**[a] **II** 2 (55) (4) 3 (74) (4) 4 (63) (12)	164
C_{13-17} 	PCC (5.0 eq), CH_2Cl_2, reflux, 24 h	 R^1 R^2 Me *n*-C_8H_{17} (90) Me *n*-$C_{10}H_{21}$ (90) H *n*-$C_{12}H_{25}$ (60) Me *n*-$C_{12}H_{25}$ (90)	135 618 135 135
C_{13-15} 	Dimethyldioxirane (2.0 eq), acetone, CH_2Cl_2, –20°	 *m* *n* 1 1 (100) 1 2 (100) 2 2 (100)	148
C_{13} 	O_2, EtOAc, rt, 7 d	 (47)	173

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

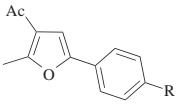
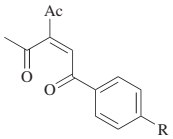
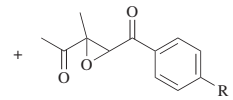
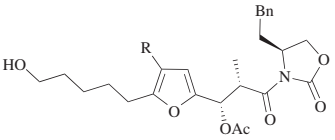
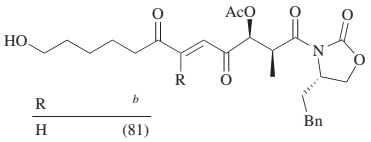
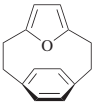
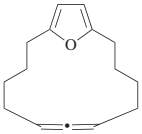
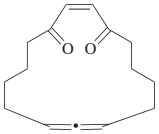
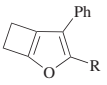
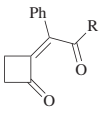
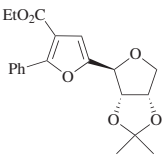
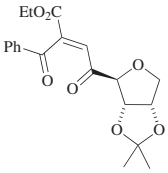
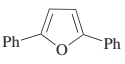
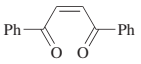
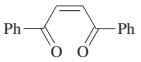
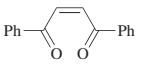
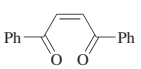
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{13–14}$ 	O_2, rose bengal, hv, MeCN, 0°, 5 min; then rt, 12 h	 **I** +  **II** R **I** **II** H (68) (6) F (62) (10) Cl (68) (8) MeO (67) (10) Me (69) (11)	300, 298
$C_{13–20}$ 	NBS, PPTS, CH_2Cl_2, 40–45°, 20 h	 R [b] H (81) 3-MeC_6H_4 (72)	175, 153
C_{14} 	H_2SO_4, KOAc	 (—)	634
C_{15} 	Dimethyldioxirane (1.5 eq), acetone, CH_2Cl_2, −45°, 2 h	 (83)	147
$C_{15–19}$ 	DMP (2.5 eq), CH_2Cl_2, rt, 5 h	 R *n*-Pr (62) *i*-Pr (53) *n*-Bu (66) Bn (64)	635
C_{15} 	O_2, hv, acetone, rt, 20 min; then Me_2S (10 eq), rt, 30 min	 (67)	292
C_{16} 	CAN, MeCN, H_2O	 (77)	636
	$Pb(OAc)_4$ (2 eq), $CHCl_3$, 20–30°, 5 h	 (59)	129
	m-CPBA (1.5 eq), CH_2Cl_2, rt, 5 min	 (92)	163
	$K_2S_2O_8$ (1 eq), MeCN, H_2O, rt, 15 min	 Atm Temp Time (h) O_2 rt 48 (57) O_2 rt 72 (62) O_2 rt 192 (74) O_2 70° 0.5 (97) O_2 70° 1 (97) Ar 70° 0.5 (97) Ar 70° 1 (87)	308

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

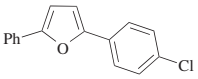
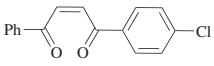
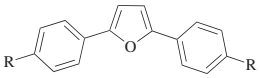
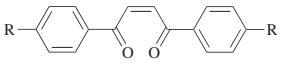
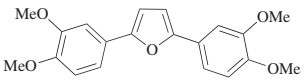
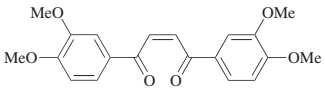
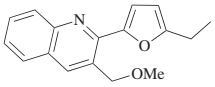
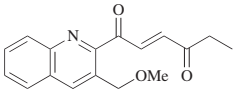
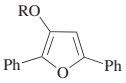
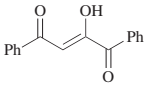
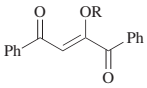
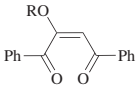
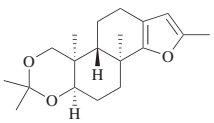
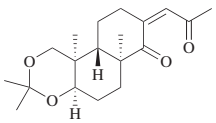
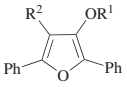
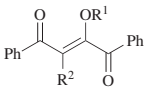
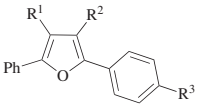
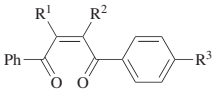
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}			
	*m*-CPBA (1.5 eq), CH_2Cl_2, rt, 5 min	 (89)	163
	Selectfluor (2 eq), THF, H_2O, 60–70°, 3 h	 R: H (100); Br (69)	177
	$K_2Cr_2O_7$, AcOH, H_2O	 (17)	637
	1. NBS (1.1 eq), $NaHCO_3$ (2 eq), py (3.75 eq), H_2O 2. HCl (1 N)	 (87)	150
	$PhNMe_3{\bullet}Br_3$ (1 eq), *t*-BuOH, rt, 15 h	 R: Me (80); Et (83); *n*-Pr (92); *i*-Pr (80); *n*-Bu (90); *i*-Bu (83)	176
	$PhNMe_3{\bullet}Br_3$ (1 eq), rt, 20 h	 R: Me, THF/DMSO (2:1), 22 h, (80); Et, DMSO, 24 h, (88); Et, THF/DMSO (2:1), 24 h, (89); *n*-Pr, THF/DMSO (2:1), 21 h, (82); *i*-Pr, THF/DMSO (2:1), 22 h, (95); *n*-Bu, DMSO, 21 h, (96); *n*-Bu, THF/DMSO (2:1), 17 h, (95); *i*-Bu, DMSO, 22 h, (96); *i*-Bu, THF/DMSO (2:1), 31 h, (96)	175
	DDQ (1 eq), CH_2Cl_2, rt, 15–28 h	 R: Me (98); Et (98); *n*-Pr (98); *i*-Pr (80); *n*-Bu (87); *i*-Bu (90)	628
	*m*-CPBA (1 eq), CH_2Cl_2, 0°, 1 h; then rt, 7 h	 (97)	159, 158

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

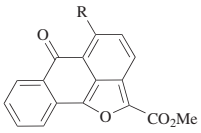
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16-22} 	DDQ (1 eq), *t*-BuOH, rt, 21 h		176

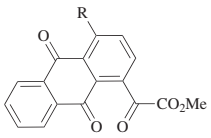
R^1	R^2		
Me	H	(95)	
Et	H	(93)	
n-Pr	H	(92)	
i-Pr	H	(94)	
n-Bu	H	(91)	
i-Bu	H	(90)	
Et	Ph	(92)	
n-Pr	Ph	(84)	
i-Pr	Ph	(90)	
n-Bu	Ph	(85)	
i-Bu	Ph	(90)	

C_{16-28} 

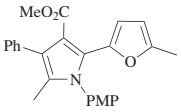
NH_4NO_3 (1.25 eq), AcOH, H_2O, reflux, 1.5 h 

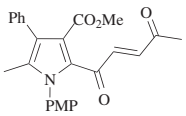
R^1	R^2	R^3		
H	H	H	(70)	126
Ph	H	H	(72)	126
Ph	Cl	H	(78)	126
Ph	Br	H	(74)	126, 127
Ph	Br	Br	(74)	126
Ph	Br	Cl	(75)	126
Ph	Br	MeO	(73)	126
Ph	Br	Me	(73)	126
Ph	Br	*c*-C_6H_{11}	(72)	126

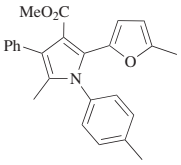
C_{16} 

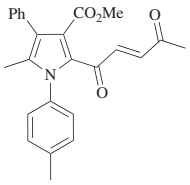
Br_2, AcOH 

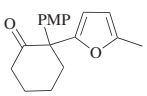
R		
H	(—)	638
Cl	(—)	

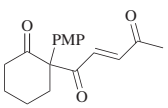
C_{17} 

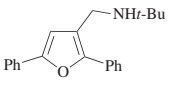
CAN (2.3 eq), MeCN, H_2O, –20°  (45) 134



CAN (2.3 eq), MeCN, H_2O, –20°, 0.5 h  (45) 134



m-CPBA (1.1 eq), CF_3CO_2H, CH_2Cl_2, rt  (70) 639



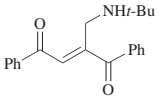
m-CPBA (1.0 eq), CH_2Cl_2  (46) 640

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

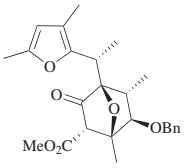
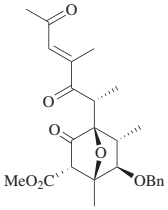
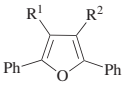
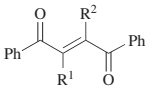
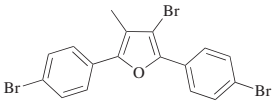
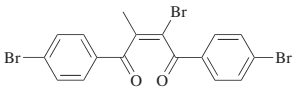
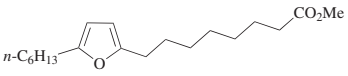
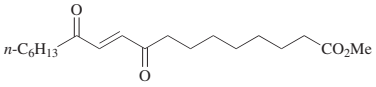
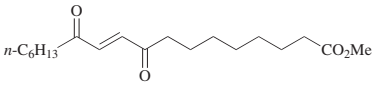
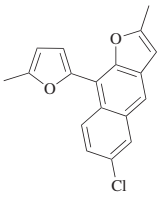
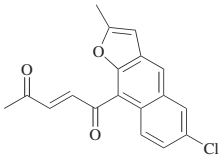
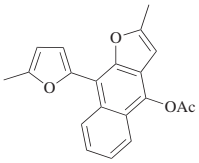
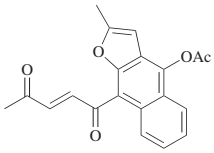
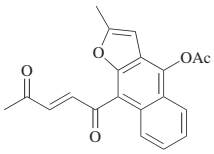
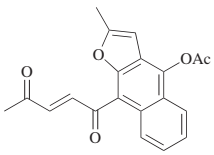
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17} 	MMPP (0.5 eq), DMF	 (61)	641
C_{17-21} 	$EtCO_2H$, HNO_3, –5°, 15 min		125
		R^1 = H, R^2 = $HOCH_2$ (70)	125
		R^1 = H, R^2 = $ClCH_2$ (—)	122
		R^1 = H, R^2 = Et (74)	642
		R^1 = Me, R^2 = 1-morpholinyl (95)	
C_{17} 	HNO_3, AcOH, 50°, 1 h	 (91)	123
C_{18} 	PCC, CH_2Cl_2	 (95)	643
	MMPP, EtOH, H_2O	 (93)	643
	PCC (2.0 eq), CH_2Cl_2, rt, 60 h	 (35)	136
	KNO_3 (1.5 eq), AcOH, 50°, 1 h	 (50)	136
	PCC (2.0 eq), CH_2Cl_2, rt, 60 h	 (50)	136
	MMPP (10 eq), benzene, reflux, 5 h	 (34)	136

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

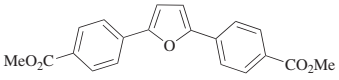
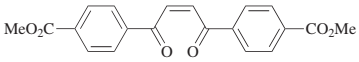
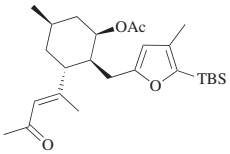
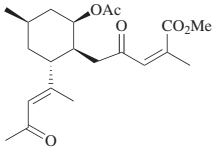
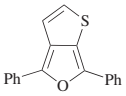
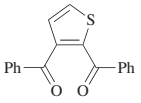
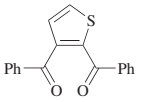
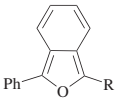
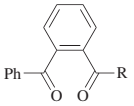
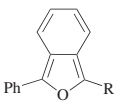
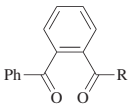
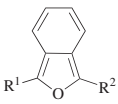
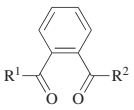
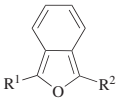
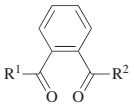
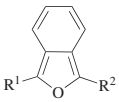
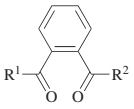
Furan	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{18}				
	Dimethyldioxirane, acetone, $CHCl_3$, rt		(100)	644
	1. O_2, rose bengal, hv, CH_2Cl_2, 0°, 12 h 2. TBAF (1.5 eq), MeI (2.0 eq), THF, rt, 1 h		(97)	322
	$Pb(OAc)_4$ (2.0 eq), Et_2O		(89)	645
	H_2SO_4, $K_2Cr_2O_7$, Et_2O		(71)	645
C_{18-34}				
	*m*-CPBA (1.5 eq), CH_2Cl_2, rt, 5 min		R 2-thienyl (88) 4-$MeOC_6H_4$ (93) 4-$Ph_2NC_6H_4$ (81) 9-*n*-hexyl-9*H*-carbazole-3-yl (80) 9-(2-ethylhexyl)-9*H*-carbazole-3-yl (83)	163
C_{18-39}				
	$Pb(OAc)_4$ (1.0 eq), THF, 50°, 0.5 h		R 2-thienyl (84) 4-$MeOC_6H_4$ (87) 4-MeC_6H_4 (87) 3,4-$Me_2C_6H_3$ (90) 3-benzothienyl (85) 1-naphthyl (85) 2-MeO-1-naphthyl (88) 4-Me-1-naphthyl (87) 4-PhC_6H_4 (85) dibenzo[*b*,*d*]thiophene-2-yl (81) 9-(2-ethylhexyl)-9*H*-carbazole-3-yl (83) 9,9-dihexyl-9*H*-fluorene-2-yl (71)	646 646, 163 646 646 646 646 646 646 646 646 646 646
C_{18-43}				
	*m*-CPBA (1.5 eq), CH_2Cl_2, rt, 5 min		R^1 / R^2 2-thienyl / 4-$Ph_2NC_6H_4$ (77) 2-thienyl / 2,2'-bithiophene-5-yl (86) 4-$MeOC_6H_4$ / 4-$MeOC_6H_4$ (94) 4-$MeOC_6H_4$ / 4-$Ph_2NC_6H_4$ (83) 4-BnC_6H_4 / 4-MeC_6H_4 (91) 4-MeC_6H_4 / 2,2'-bithiophene-5-yl (88) 4-hexyl-2-thienyl / 4-$Ph_2NC_6H_4$ (79) 1-naphthyl / 4-MeC_6H_4 (91) 1-naphthyl / 2,2'-bithiophene-5-yl (85) 5-hexyl-2-thienyl / 5-hexyl-2-thienyl (87) 1-naphthyl / 1-naphthyl (90) 2-thienyl / 9-hexyl-9*H*-carbazole-5-yl (78)	163

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

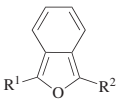
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{18–43}$ 	*m*-CPBA (1.5 eq), CH_2Cl_2, rt, 5 min		163

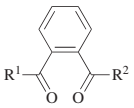
R^1	R^2	
5-hexyl-2-thienyl	dibenzo[*b*,*d*]furan-2-yl	(80)
1-naphthyl	dibenzo[*b*,*d*]furan-2-yl	(83)
4-MeC_6H_4	pyrene-1-yl	(94)
4-$MeOC_6H_4$	9-hexyl-9*H*-carbazole-3-yl	(82)
4-MeC_6H_4	9-hexyl-9*H*-carbazole-3-yl	(82)
1-naphthyl	9-hexyl-9*H*-carbazole-3-yl	(81)
2-thienyl	9,9-dihexyl-9*H*-fluorene-2-yl	(78)
4-$MeOC_6H_4$	9,9-dihexyl-9*H*-fluorene-2-yl	(81)
4-MeC_6H_4	9,9-dihexyl-9*H*-fluorene-2-yl	(83)
1-naphthyl	9,9-dihexyl-9*H*-fluorene-2-yl	(80)

$C_{18–30}$ 

$Pb(OAc)_4$ (1.0 eq), THF, 50°, 0.5 h  646

R^1	R^2	
2-thienyl	4-ClC_6H_4	(72)
2-thienyl	4-$MeOC_6H_4$	(91)
2-thienyl	3,4-$(MeO)_2C_6H_3$	(89)
2-thienyl	2,4-$Me_2C_6H_3$	(91)
2-thienyl	3,4-$Me_2C_6H_3$	(85)
2-thienyl	3-benzothienyl	(88)
2-thienyl	2-Me-3-benzothienyl	(92)
2-thienyl	1-naphthyl	(—)
2-thienyl	2-MeO-1-naphthyl	(93)
2-thienyl	4-Me-1-naphthyl	(83)
1-naphthyl	3,4-$(MeO)_2C_6H_3$	(87)
2-thienyl	4-PhC_6H_4	(85)
2-thienyl	dibenzo[*b*,*d*]thiophene-2-yl	(92)
5-hexyl-2-thienyl	dibenzo[*b*,*d*]furan-2-yl	(89)
1-naphthyl	2-MeO-1-naphthyl	(89)
1-naphthyl	4-Me-1-naphthyl	(85)
1-naphthyl	dibenzo[*b*,*d*]thiophene-2-yl	(87)

$C_{19–40}$ 

$Pb(OAc)_4$ (1.0 eq), THF, 50°, 0.5 h 

R^1	R^2		
2-MeC_6H_4	2-thienyl	(88)	646
4-MeC_6H_4	2-thienyl	(89)	646
4-$MeOC_6H_4$	4-$Ph_2NC_6H_4$	(24)	163
4-MeC_6H_4	3,4-$(MeO)_2C_6H_3$	(90)	646
4-MeC_6H_4	4-MeC_6H_4	(86)	646
4-$MeOC_6H_4$	3,4-$Me_2C_6H_3$	(96)	646
4-$MeOC_6H_4$	3-benzothienyl	(92)	646
4-MeC_6H_4	3-benzothienyl	(85)	646
4-MeC_6H_4	2,2'-bithiophene-5-yl	(88)	646
4-MeC_6H_4	2-Me-3-benzothienyl	(91)	646
4-$MeOC_6H_4$	4-Me-1-naphthyl	(88)	646
2-MeC_6H_4	2-MeO-1-naphthyl	(89)	646
4-MeC_6H_4	1-naphthyl	(85)	163, 646
4-MeC_6H_4	2-MeO-1-naphthyl	(96)	646
4-$MeOC_6H_4$	dibenzo[*b*,*d*]thiophene-2-yl	(89)	646

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

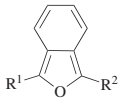
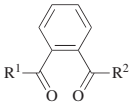
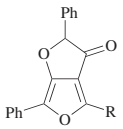
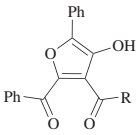
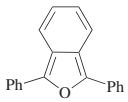
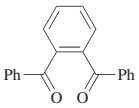
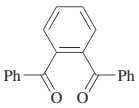
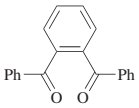
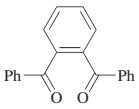
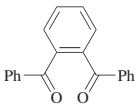
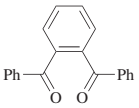
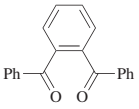
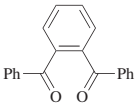
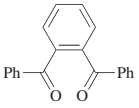
Furan	Conditions	Product(s) and Yield(s) (%)			Refs.
$C_{19–40}$					
	$Pb(OAc)_4$ (1.0 eq), THF, 50°, 0.5 h				
		R^1	R^2		
		4-MeC_6H_4	4-Me-1-naphthyl	(82)	646
		2,4-$Me_2C_6H_3$	1-naphthyl	(89)	646
		2-MeC_6H_4	dibenzo[*b*,*d*]thiophene-2-yl	(82)	646
		4-MeC_6H_4	4-PhC_6H_4	(96)	646
		4-MeC_6H_4	dibenzo[*b*,*d*]thiophene-2-yl	(90)	646
		4-MeC_6H_4	4-$Ph_2NC_6H_4$	(25)	163
		4-MeC_6H_4	9,9-dihexyl-9*H*-fluorene-2-yl	(88)	646
$C_{19–24}$					
	*m*-CPBA, dichloroethane, rt, 2 h				
		R			
		Me	(86)		647
		Ph	(83)		
C_{20}					
	H_2O_2, Na_2MoO_4•$2H_2O$, NaOH, THF, 30°, 280 min			(96)[c]	77
	H_2O_2, Na_2MoO_4•$2H_2O$, sodium dodecyl sulfate, BuOH, H_2O, rt			(91)[c]	50
	$PhI(O_2CCF_3)_2$ (2.5 eq), H_2O_2 (6.0 eq), CH_2Cl_2, 10°, 2–3 h			(80)	76
	CaO_2•$2H_2O_2$ (8.0 eq), MeOH, 50°, 3 h			(88)	648
	O_3, $P(OPh)_3$, CH_2Cl_2			(88)	649
	O_2, hν, CH_2Cl_2, –78°, 4 h			(40)	171
	O_2, benzene, reflux, 34 h			(86)	168
	m-CPBA (1.5 eq), CH_2Cl_2, rt, 5 min			(92)	163
	$^1O_2$, *t*-BuOK, Ac_2O, MeCN, rt, 5 min			(31)	78

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

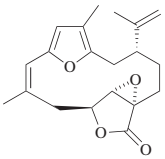
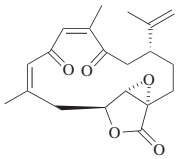
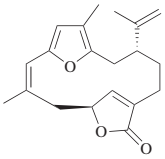
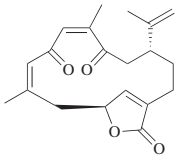
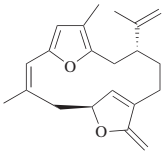
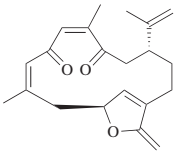
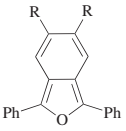
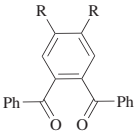
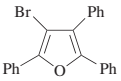
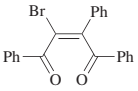
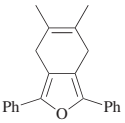
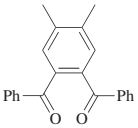
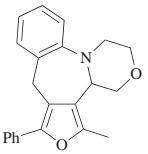
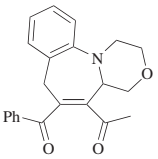
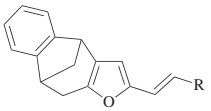
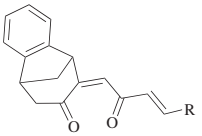
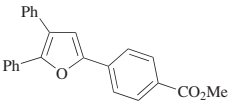
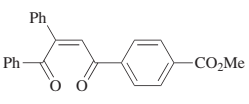
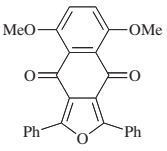
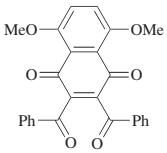
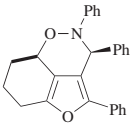
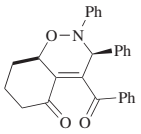
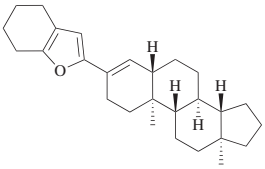
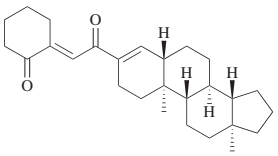
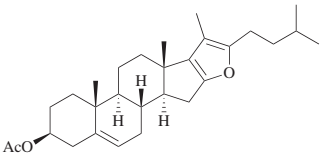
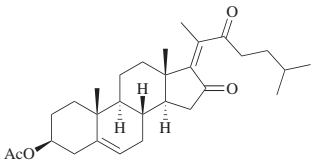
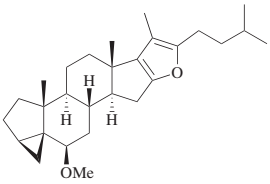
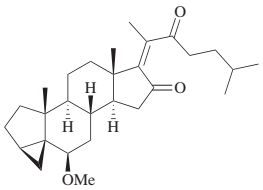
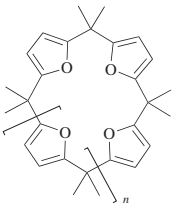
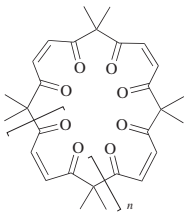
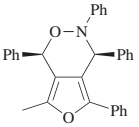
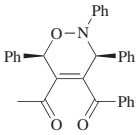
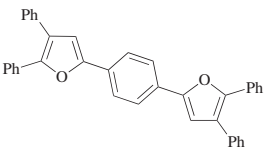
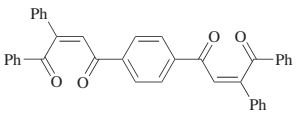
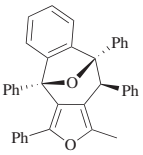
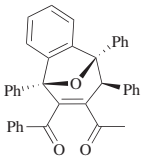
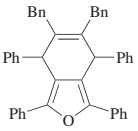
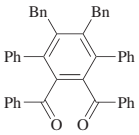
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{20}			
	*m*-CPBA (1.0 eq), CH_2Cl_2, 0°	 (73)	650
	*m*-CPBA (1.0 eq), CH_2Cl_2, 0°	 (73)	180
C_{21}			
	*m*-CPBA (1.0 eq), CH_2Cl_2, 0°	 (88)	310
	hv, CH_2Cl_2, air, rt, 48 h	 R: NC– (99); EtO_2C (99)	301
C_{22}			
	KNO_3 (1.25 eq), AcOH, H_2O, reflux, 10 min	 (80)	126
	Br_2, NaOAc, AcOH, H_2O, reflux, 5 min	 (90)	128
	*m*-CPBA (0.9 eq), CH_2Cl_2, 0°	 (81)	651
C_{22-24}			
	*m*-CPBA (1.0 eq), CH_2Cl_2, –10°; then rt, 2.5 h	 R: Ph (88); 2-MeC_6H_4 (83); 2-$(CH_2{=}CH)C_6H_4$ (71)	652
C_{23}			
	e^- (Ag/Ag^+), Bu_4NPF_6, THF	 (91)	69

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{24}			
	CAN (2.2 eq), MeCN, H_2O	 (64)	653
C_{27}			
	CAN (2.2 eq), MeCN/H_2O (10:1), rt, 30 min	 (62)	133
	Dimethyldioxirane (1.0 eq), acetone, CH_2Cl_2, –20°	 (100)	148
	*m*-CPBA (1.0 eq), CH_2Cl_2, rt, 1 h	 (84)	654
	air	 (100)	172
$C_{28–42}$			
	*m*-CPBA (1.1 eq), $CHCl_3$, rt		144, 165, 166
C_{31}			
	CAN (2.2 eq), MeCN/H_2O (1:1), rt	 (66)	133
C_{38}			
	e^- (Ag/Ag^+), Bu_4NPF_6, THF	 (92)	69

n		
1	(78)	144
2	(56)	165
3	(85)	144, 166

TABLE 1. SYNTHESIS OF 1,4-DIKETOALKENES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{38} 	*m*-CPBA (1.1 eq), CH_2Cl_2, 0°, 3 h		(91)	655
C_{46} 	Br_2, MeOH		(70)	656

[a] The yield is based on recovered starting material.

[b] The yield was determined by LCMS.

[c] The yield was determined by GC.

TABLE 2. SYNTHESIS OF 4-OXOALKENALS

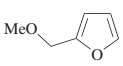
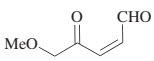
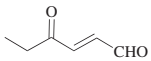
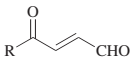
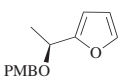
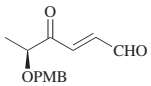
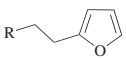
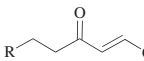
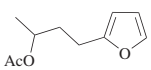
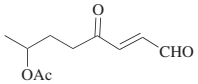
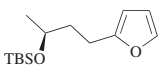
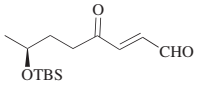
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	O_2, rose bengal, 18-crown-6 (0.01 eq), CH_2Cl_2, –60°; then $CHCl_3$, –10°	 (96)	304
C_6 	NBS, py, acetone/H_2O, rt, 2 h	 (—)	657
C_{6-9} 	NBS (1.1 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 0.5 h	 R: Et (44); *n*-Pr (64); *n*-Bu (46); *n*-C_5H_{11} (44)	188
C_6 	NBS (1.1 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 0.5 h; then py (2.1 eq), rt, 6 h	 (74)	185, 569
C_{7-9} 	NBS (1.5 eq), py (1.33 eq), THF/acetone/H_2O (5:4:1), –20°, 1 h; then rt, 3 h	 R: EtO_2C, Time 3 h (60); *n*-Pr, Time 6 h (44)	658, 659
C_8 	PCC (5.3 eq), CH_2Cl_2, rt, 12 h; then reflux, 36 h	 (60)	179
	NBS (1.3 eq), py (4.0 eq), THF/acetone/H_2O (5:4:1), –20°, 1 h; then rt, 5 h	 (64)	182

TABLE 2. SYNTHESIS OF 4-OXOALKENALS (*Continued*)

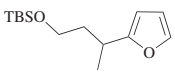
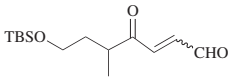
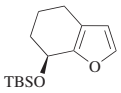
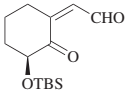
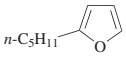
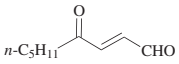
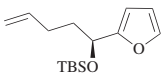
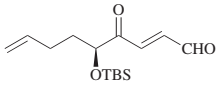
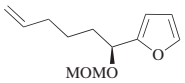
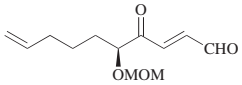
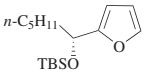
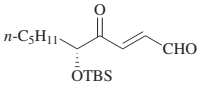
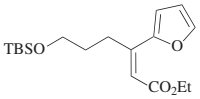
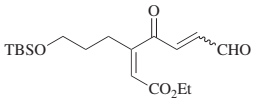
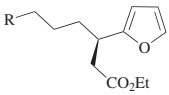
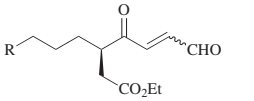
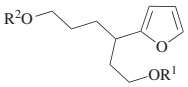
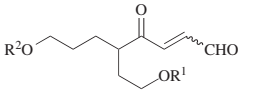
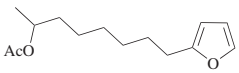
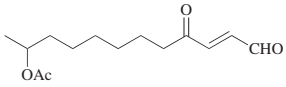
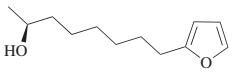
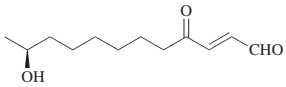
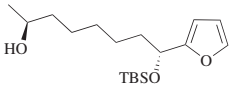
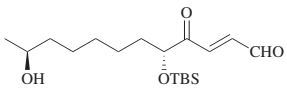
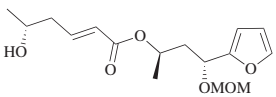
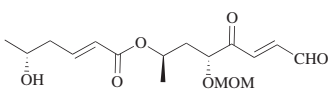
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	NBS (1.1 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 1 h; then py (1.5 eq), rt, 1 h	 (72)	187
	*m*-CPBA, CH_2Cl_2	 (50)	660
C_9			
	PCC (5.2 eq), CH_2Cl_2, rt, 12 h	 (70)	178
	NBS (1.2 eq), acetone/H_2O (10:1), $NaHCO_3$ (2.0 eq), –15°, 2 h; then py (1.0 eq), rt, 4 h	 (55)	661
C_{10}			
	NBS (1.3 eq), $NaHCO_3$ (2.0 eq), py (4.0 eq), THF/acetone/H_2O (5:4:1), –20°, 1 h	 (55)	186
	NBS (1.1 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 1 h; then py (1.5 eq), rt, 1 h	 (—)	662
	NBS (1.1 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 1 h; then py (1.5 eq), rt, 1 h	 (62)	187
	NBS (1.1 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 1 h; then py (1.5 eq), rt, 1 h	 R: BocHN (56); TBSO (67)	187
	NBS (1.1 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 1 h; then py (1.5 eq), rt, 1 h	 R^1 R^2: Ac TBS (89); TBS MOM (81)	187
C_{12}			
	Br_2 (0.1 eq), py (5.0 eq), acetone/H_2O (4:1), –20°; then rt, 12 h	 (85)	181
	NBS (1.3 eq), py (4.0 eq), THF/acetone/H_2O (5:4:2), –20°, 1 h; then rt, 4 h	 (73)	182
	NBS, H_2O, $NaHCO_3$, acetone, –15°, 30 min; then py, rt, 5 h	 (76)	663
C_{14}			
	NBS (1.2 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 2.5 h; then py (1.0 eq), rt, 21 h	 (—)	184

TABLE 2. SYNTHESIS OF 4-OXOALKENALS (*Continued*)

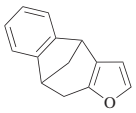
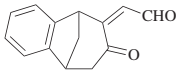
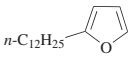
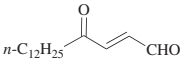
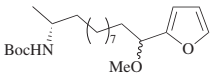
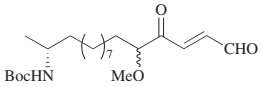
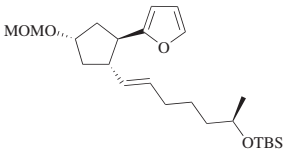
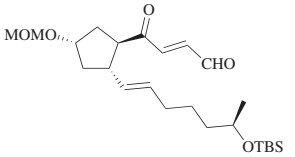
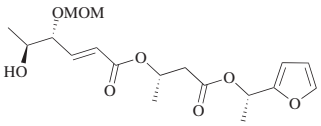
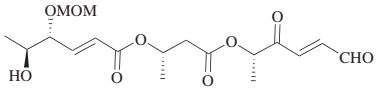
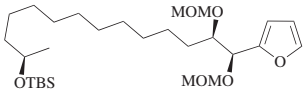
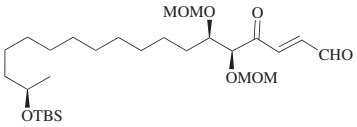
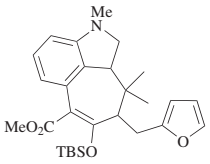
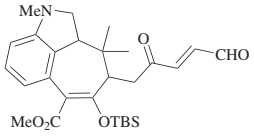
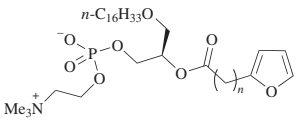
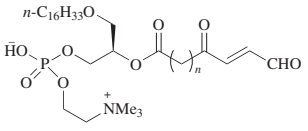
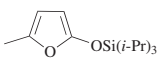
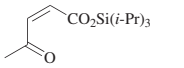
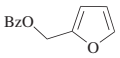
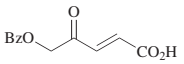
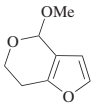
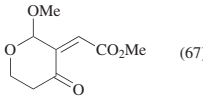
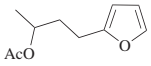
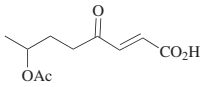
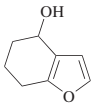
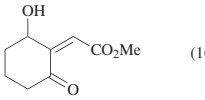
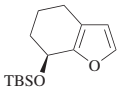
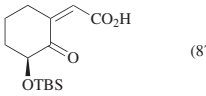
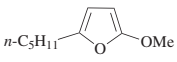
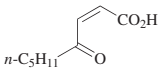
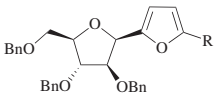
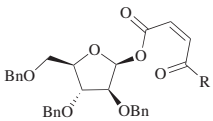
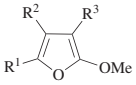
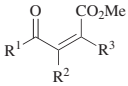
	Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}		*m*-CPBA (1.0 eq), CH_2Cl_2, –10°, 2.5 h	 (77)	652
C_{16}		NBS (1.2 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 1 h; then py (2.0 eq), rt, 2 h	 (60)	199
		NBS, H_2O, $NaHCO_3$, acetone, –15°, 30 min; then py, rt	 (66)	664
		NBS, THF/acetone/H_2O, –20°, 0.5 h; then rt, 4 h	 (71)	183
		NBS (1.1 eq), $NaHCO_3$ (2.0 eq), acetone/H_2O (10:1), –15°, 0.5 h; then py (2.1 eq), rt, 6 h	 (—)	185, 569
C_{18}		NBS (1.3 eq), THF/acetone/H_2O (5:4:2), –20°, 1 h; then py (4.0 eq), rt, 4 h	 (71)	182, 198
C_{20}		NBS (1.0 eq), py (4.0 eq), DMF/H_2O (85:15), 0°, 2 h	 (34)	665, 666
$C_{28–33}$		NBS (1.5 eq), py (1.33 eq), THF/acetone/H_2O (5:4:1), –20°, 1 h; then rt, 6 h	 *n*: 2 (79); 3 (68); 7 (70)	189, 193, 192, 190

TABLE 3. SYNTHESIS OF 4-OXOALKENOIC ACIDS AND ESTERS

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	Dimethyldioxirane (1.1 eq), acetone, –78°, 1 h	 (100)	203
	O_2, methylene blue, hv, solvent, 10°, 2 d	 Solvent: EtOH (14); acetone (17)	92
C_7			
	1. *m*-CPBA (2.0 eq), CH_2Cl_2, darkness, rt, 2 h 2. CH_2N_2, Et_2O	 (67)	197
C_8			
	1. PCC (1.43 eq), acetone, rt, 2.5 h 2. 2-Mercaptobenzimidazole (0.03 eq), rt, 6 h	 (—)	195
	1. *m*-CPBA (2.0 eq), CH_2Cl_2, darkness, rt, 2 h 2. CH_2N_2, Et_2O	 (16)	197
	$MeCO_3H$, NaOAc, CH_2Cl_2, rt, 6.5 h	 (87)	667
C_9			
	TPP, Me_2S, CCl_4, –20°; then O_2, hv, –20° to rt, 40 min	 (99)	668
$C_{9–10}$			
	O_2, methylene blue, hv, CH_2Cl_2, –20°; then heat	 R: H (90); Me (90)	293
$C_{9–17}$			
	1. O_2, methylene blue, hv, MeOH 2. Et_2S (2.0 eq)		296

R^1	R^2	R^3	Time (h)	
MeO_2C	Et	Et	180	(77)
H	MeO_2C	Ph	15	(98)
H	MeO_2C	4-BrC_6H_4	15	(98)
H	MeO_2C	3-$MeOC_6H_4$	15	(92)
MeO_2C	H	Ph	30	(85)
MeO_2C	H	4-BrC_6H_4	30	(80)
MeO_2C	H	3-$MeOC_6H_4$	30	(94)
MeO_2C	H	4-$MeOC_6H_4$	30	(88)
H	Ac	Ph	15	(76)
H	MeO_2C	4-MeC_6H_4	15	(92)
Ac	H	Ph	10	(90)
MeO_2C	H	4-MeC_6H_4	15	(89)
MeO_2C	Me	Ph	60	(75)
MeO_2C	MeO_2C	Ph	15	(92)
MeO_2C	Me	Bn	30	(83)
MeO_2C	MeO_2C	Bn	720	(90)
EtO_2C	Ph	Ph	30	(84)

TABLE 3. SYNTHESIS OF 4-OXOALKENOIC ACIDS AND ESTERS (*Continued*)

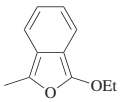
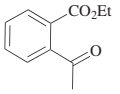
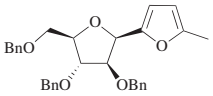
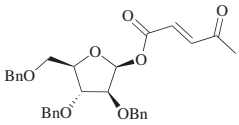
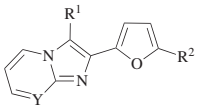
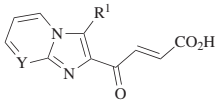
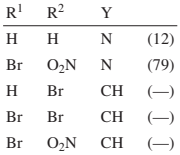
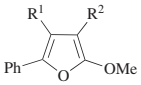
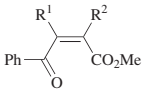
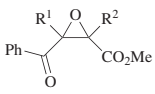
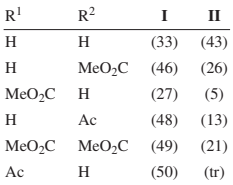
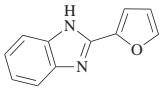
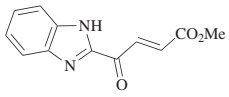
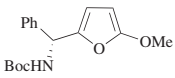
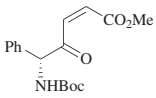
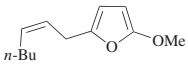
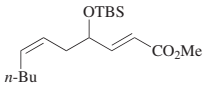
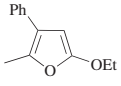
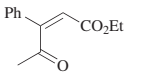
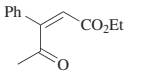
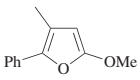
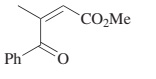
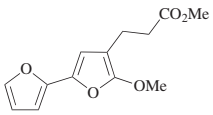
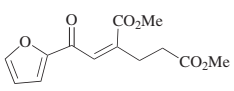
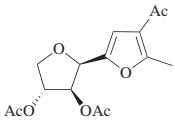
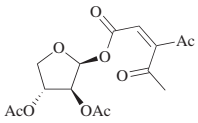
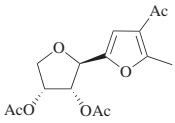
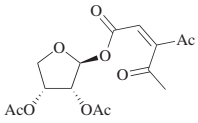
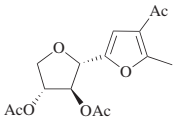
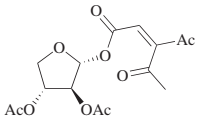
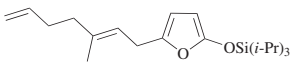
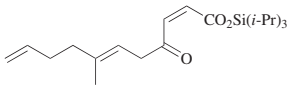
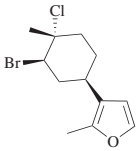
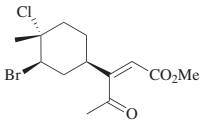
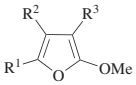
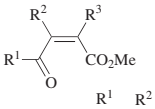
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	air	 (—)	669
C_{10}			
	O_2, methylene blue, hν, CH_2Cl_2, –20°, 1–1.5 h; then 40°, SiO_2	 (70)	94
C_{10-11}			
	93% HNO_3, H_2SO_4, 15 min		670
			670
			196
			196
			196
C_{10-12}			
	O_2, methylene blue, hν, nitromethane, –25°, 2 h	 **I** +  **II**	88
			
C_{11}			
	O_2, methylene blue, hν, MeOH, 18 h; then SiO_2	 (12)	307
	NBS (1.0 eq), $NaHCO_3$, Et_2O/H_2O, 0°, 15 min	 (90)	202
	1. PCC (5.0 eq), CH_2Cl_2, rt, 2.5 h 2. I_2 (0.15 eq), Et_2O, rt, 4 h 3. $NaBH_4$ (1.0 eq), MeOH, 0°, 0.25 h 4. TBSCl (1.1 eq), imidazole (2.2 eq), DMF, 50°, 2.5 h	 (42)	200
	Pb(OAc)$_4$, benzene, 60°	 (70)	671
	O_2, hexane, 15–20°	 (100)	671
	O_2, rt, 10 d	 (100)	672
	10% HCl, MeOH, H_2O, rt, 4 h	 (93)	673

TABLE 3. SYNTHESIS OF 4-OXOALKENOIC ACIDS AND ESTERS (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
	1. O_2, methylene blue, hv, acetone, –20°, 30 min 2. Petroleum ether, –20°, 48 h 3. Acetone, rt, 50 h	 (—)	292
	O_2, methylene blue (0.01 mol %), hv, acetone, –20°, 40 min; then rt, 24 h	 (47)	292
	1. O_2, methylene blue, hv, acetone, –20°, 25 min 2. Acetone, rt, 10 h	 (78)	292
C_{12}			
	Dimethyldioxirane (1.1 eq), acetone, –78°, 1 h	 (98)	203
	1. *m*-CPBA, CH_2Cl_2 2. CH_2N_2, Et_2O	 (—)	216
C_{12-13}			
	1. O_2, methylene blue, hv, MeOH 2. HCl (2 N), acetone, rt, 0.5 h		674

R^1	R^2	R^3	Temp (°)	Time (h)	
Ph	Ac	H	–40	3	(—)
Ph	MeO_2C	MeO_2C	–20	5	(—)
Bn	MeO_2C	MeO_2C	–20	2	(90)

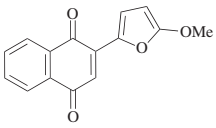
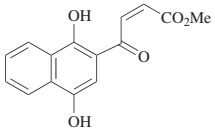
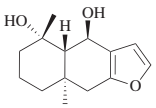
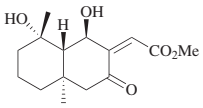
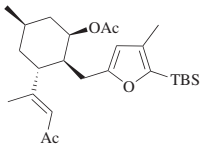
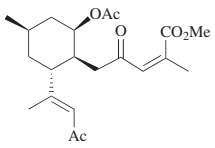
C_{14}			
	H_2SO_4, MeOH, H_2O, 0°, 1 h	 (89)	675
	1. *m*-CPBA (1.0 eq), CH_2Cl_2, rt, 43 h 2. CH_2N_2, Et_2O	 (100)	191, 676
C_{18}			
	1. O_2, rose bengal, CH_2Cl_2, 0°, 12 h 2. MeI, Bu_4NF, THF, rt, 1 h	 (97)	677, 305

TABLE 4. SYNTHESIS OF 4-HYDROXYBUTENOLIDES

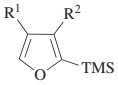
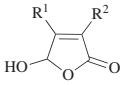
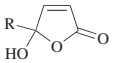
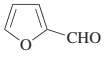
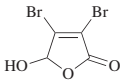
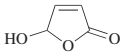
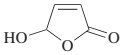
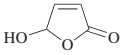
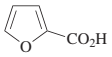
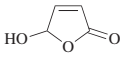
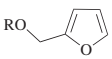
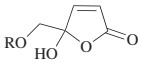
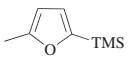
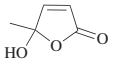
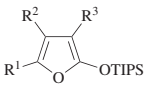
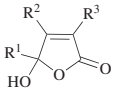
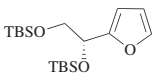
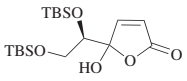
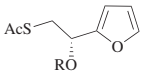
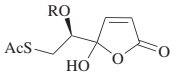
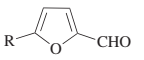
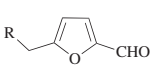
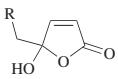
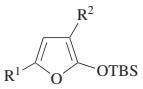
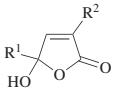
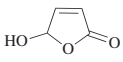
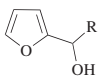
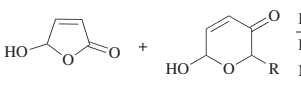
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4			
	O_2, TPP, hν, CH_2Cl_2, –78°, 5 min		R^1 = H, R^2 = $TBSCH_2O$ (94); R^1 = $TBSCH_2O$, R^2 = H (91)	316
$C_{5–9}$			
	$NaClO_2$ (3.0 eq), NaH_2PO_4 (1.5 eq), *t*-BuOH/H_2O (5:1), rt, 1 h		R = Me, 0.5 h (96); $TsO(CH_2)_4$, 4 h (90); $THPO(CH_2)_4$, 2 h (78); $TBSO(CH_2)_4$, 2 h (77); $Me(TBSO)CH(CH_2)_2$, 2 h (75); n-C_5H_{11}, 1.5 h (95)	211
C_5			
	Br_2, H_2O		(73)	678
	O_2, methylene blue, hν, MeOH, rt, 23 h		(96)	679
	O_2, rose bengal, hν, 2-BuOH, rt, 1 h		(95)	680
	O_2, rose bengal wool, hν, $CHCl_3$, rt, 8 h		(72)	82
	O_2, sensitizer, hν, solvent, rt, 6 h		Sensitizer / Solvent: rose bengal disodium salt / MeOH (79); rose bengal-polystyrene 1% cross-linking / MeOH (70); rose bengal-resin 20% cross-linking / MeOH (68); rose bengal-resin 80% cross-linking / MeOH (71); rose bengal disodium salt / CH_2Cl_2 (100); rose bengal-polystyrene 1% cross-linking / CH_2Cl_2 (65); rose bengal-resin 20% cross-linking / CH_2Cl_2 (67); rose bengal-resin 80% cross-linking / CH_2Cl_2 (100)	679
	O_2, methylene blue, hν, EtOH, 10–15°, 2 d		R = Ac (46); Bz (32)	92
	O_2, TPP, hν, CCl_4, 0°		(100)	91
$C_{5–14}$			
	1. Dimethyldioxirane (1.1 eq), acetone, –78°, 0.5–1 h 2. Amberlyst-15, H_2O, rt, 1–12 h		R^1 = H, R^2 = H, R^3 = Me (87); R^1 = H, R^2 = Me, R^3 = H (81); R^1 = H, R^2 = $ClCH_2$, R^3 = H (94); R^1 = H, R^2 = $BnOCH_2$, R^3 = H (89); R^1 = Me, R^2 = H, R^3 = H (77); R^1 = H, R^2 = *i*-Pr, R^3 = Bn (87)	203

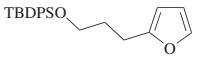
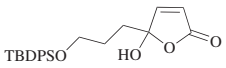
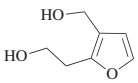
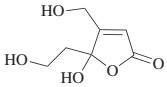
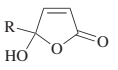
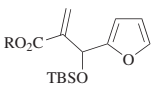
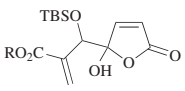
TABLE 4. SYNTHESIS OF 4-HYDROXYBUTENOLIDES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	O_2, rose bengal, hv, EtN(*i*-Pr)$_2$, MeOH	 (88)	327
	O_2, rose bengal, hv, EtN(*i*-Pr)$_2$, MeOH, CH_2Cl_2, –78°	 R: TBS (71); TBDPS (69)	225
	O_2, rose bengal, hv, Sephadex A-25, EtOH, 20°	 **I** + **II**	681

R	**I**	**II**
Me	(20)	(80)
$HOCH_2$	(73)	(11)
$MeOCH_2$	(77)	(0)
$HO(CH_2)_2OCH_2$	(72)	(0)

C_6 	O_2, rose bengal, hv, EtOH, 20°, 4 h; then rt, 12 h	 R: AcO (90); BnO (80); AcHN (58); BzHN (61); phthalimide (71)	324
C_{6-8} 	*m*-CPBA (1.0 eq), CH_2Cl_2, rt, 0.5 h	 R^1, R^2: Et H (50); Me *i*-Pr (53)	221
C_7 	O_2, rose bengal, MeOH, 5°, 4 min; then Me_2S (3.0 eq), CH_2Cl_2, rt, 15 h	 (—)	682
C_{7-9} 	O_2, rose bengal, MeOH, 5°, 4 min; then Me_2S (3.0 eq), CH_2Cl_2, rt, 15 h	 **I** + **II** (—)	682

R	**I/II**
EtO_2CCH_2	98:2
$Me_2C{=}CHCH_2$	100:0
n-Bu	98:2

C_7 	O_2, rose bengal (0.02 eq), hv, [HMIM]Cl, rt, 2 h	 (76)	90
	$NaOCl_2$ (3.0 eq), *t*-BuOH/H_2O, 20°, 3 h	 (86)	212
C_{8-12} 	NaOCl (3.2 eq), NaH_2PO_4•H_2O (1.6 eq), *t*-BuOH, rt, 1.5 h	 R: $TBSO(CH_2)_4$ (98); $HO_2C(CH_2)_7$ (80)	683
C_8 	O_2, rose bengal (0.001 eq), hv, EtN(*i*-Pr)$_2$ (1.2 eq), CH_2Cl_2, –78°		89

R	
Me	(88)
$ClCH_2$	(78)
Et	(91)
allyl	(82)
n-Bu	(90)
Bn	(80)
(*E*)-PhCH=$CHCH_2$	(87)
n-$C_{12}H_{25}$	(78)

TABLE 4. SYNTHESIS OF 4-HYDROXYBUTENOLIDES (*Continued*)

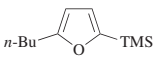
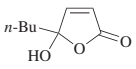
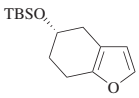
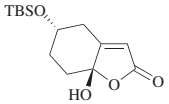
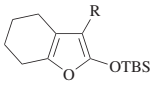
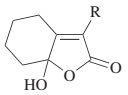
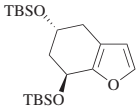
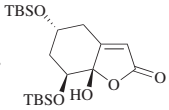
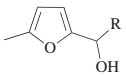
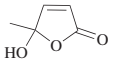
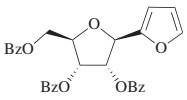
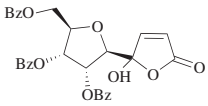
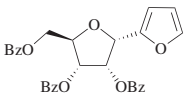
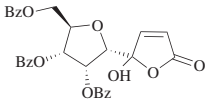
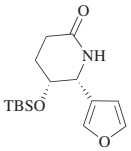
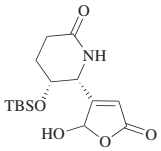
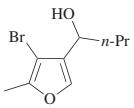
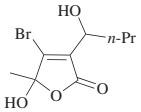
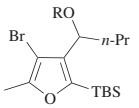
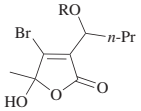
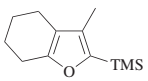
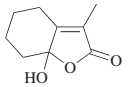
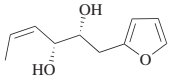
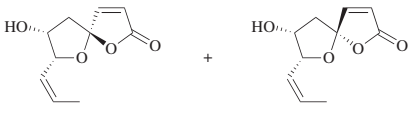
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	O_2, rose bengal, hv, MeOH, 20°, 5 min	 (90)	306
	*m*-CPBA (2.4 eq), NaOAc (2.9 eq), CH_2Cl_2, 22°, 1.25 h	 (86)	660
C_{8-9} 	*m*-CPBA (1.0 eq), CH_2Cl_2, rt, 0.5 h	 R: H (45); Me (45)	221
C_8 	*m*-CPBA (2.4 eq), NaOAc (2.9 eq), CH_2Cl_2, rt, 1.25 h	 (81)	660
C_{9-12} 	O_2, rose bengal, MeOH, 5°, 4 min; then Me_2S (3.0 eq), CH_2Cl_2, rt, 15 h	 R: $Me_2C{=}CHCH_2$ (—); Ph (—)	682
C_9 	CrO_3 (2.0 eq), H_2SO_4 (concd), acetone, 0°; then rt, 4 h	 (93)	208
	CrO_3 (2.0 eq), H_2SO_4 (concd), acetone, 0°; then rt, 4 h	 (87)	208
	O_2, rose bengal, hv, $EtN(i\text{-}Pr)_2$ (1.0 eq), CH_2Cl_2, –78°, 1 h	 (91)	684
	MMPP (1.6 eq), H_2O/*i*-PrOH (7:3), rt, 6 h	 (40)	209
	O_2, TPP, hv, –78°	 R: Ac (—); TMS (81)	317
	O_2, rose bengal, hv, MeOH, –78°, 3 h	 (99)	313, 312
C_{10} 	O_2, methylene blue, hv, CH_2Cl_2, 2.5 min; then Ac_2O, py	 **I** (—) **I/II** = 2.7:1 **II** (56)	224

TABLE 4. SYNTHESIS OF 4-HYDROXYBUTENOLIDES (*Continued*)

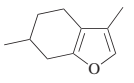
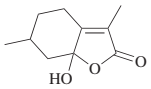
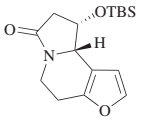
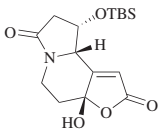
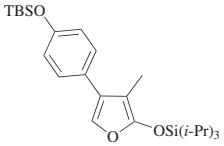
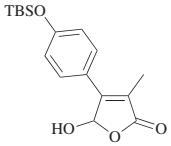
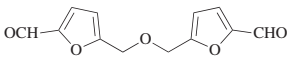
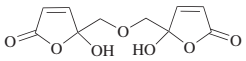
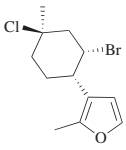
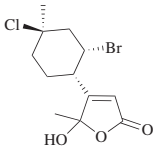
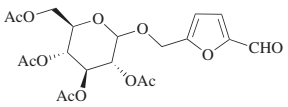
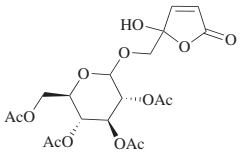
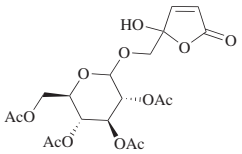
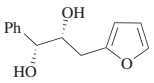
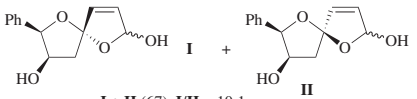
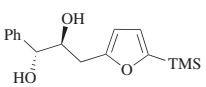
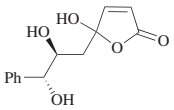
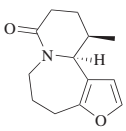
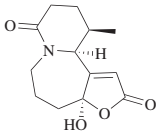
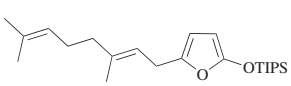
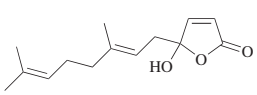
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	O_2, neat, 100°, 1 h	 (3)	313
	*m*-CPBA (3.0 eq), CH_2Cl_2, rt, 2 h	 (68)	684
C_{11}			
	Dimethyldioxirane (2.0 eq), acetone, CH_2Cl_2, –78° to rt, 1 h; then 10% HCl/THF (2:1), H_2O, rt, 18 h	 (92)	685
C_{12}			
	O_2, rose bengal, hv, EtOH, 20°, 4 h	 (68)	324
	*m*-CPBA, CH_2Cl_2	 (—)	684
	O_2, methylene blue, hv, –40°, 5 h; then Me_2S (1.25 eq), rt	 (95)	161
	m-CPBA (1.15 eq), CH_2Cl_2, 0°, 18 h	 (70)	161
C_{13}			
	*m*-CPBA (1.3 eq), CH_2Cl_2, 0°, 3 h	 **I** + **II** (67), **I/II** = 10:1	574
	O_2, methylene blue, hv, CH_2Cl_2, 1.5 min	 (—)	224
	*m*-CPBA (3.0 eq), CH_2Cl_2, rt, 3 h	 (82)	684
C_{14}			
	1. Dimethyldioxirane (1.1 eq), acetone, –78°, 0.5–1 h 2. Amberlyst-15, H_2O, rt, 1–12 h	 (100)	203

TABLE 4. SYNTHESIS OF 4-HYDROXYBUTENOLIDES (*Continued*)

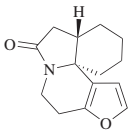
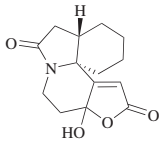
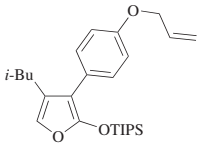
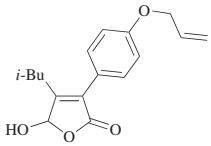
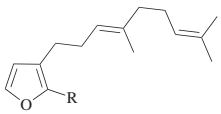
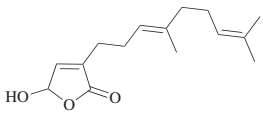
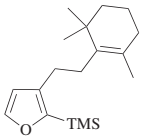
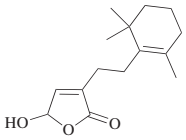
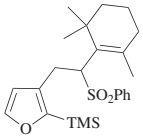
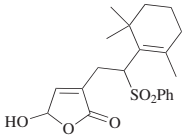
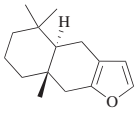
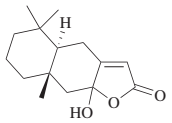
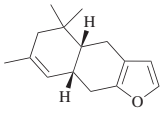
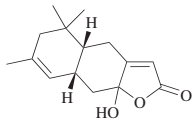
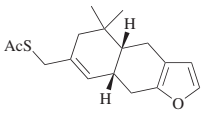
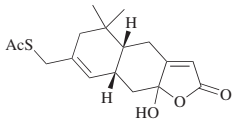
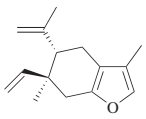
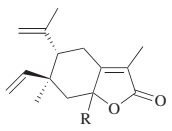
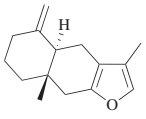
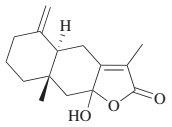
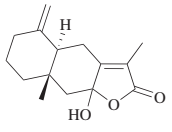
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			
	NBS (3.0 eq), dioxane, H_2O, rt, 1.5 h	 (72)	214, 213
	1. Dimethyldioxirane (2.0 eq), CH_2Cl_2, –78°, 0.5 h 2. Amberlyst-15, acetone, rt, 0.5 h	 (98)	686
C_{15}			
	O_2, rose bengal, $NaNO_2$, hv, CH_2Cl_2, –78°, 5 min	 R: H (48); TMS (93)	316
	O_2, rose bengal, $NaNO_2$, hv, CH_2Cl_2, –78°, 5 min	 (93)	316
	O_2, TPP, hv, CH_2Cl_2, –78°, 5 min	 (93)	316
	*m*-CPBA, $NaHCO_3$, $CHCl_3$, 0°	 (77)	218
	O_2, polysterene-bound rose bengal, hv, $EtN(i\text{-}Pr)_2$ (1.2 eq), CH_2Cl_2	 (50)	326
	O_2, rose bengal, hv, CH_2Cl_2, –78°, 1 h	 (—)	687
	O_2, PtO_2, benzene, rt, 10 h	 R: HO (16); HOO (8)	688
	Air, MeOH, rt, 35 d	 (35)	313
	O_2, neat, 100°, 1 h	 (16)	313

TABLE 4. SYNTHESIS OF 4-HYDROXYBUTENOLIDES (*Continued*)

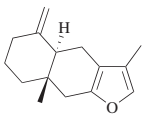
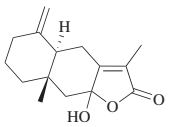
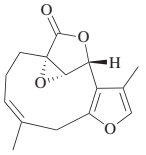
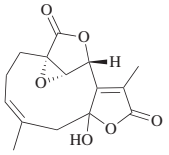
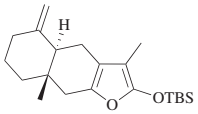
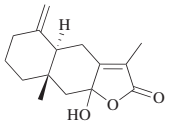
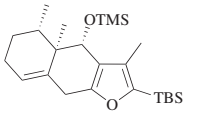
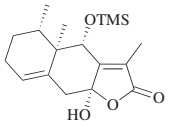
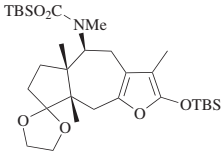
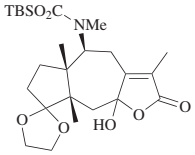
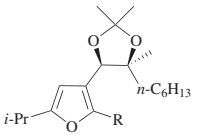
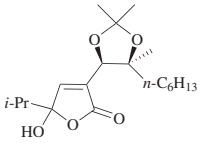
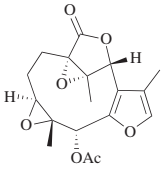
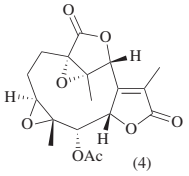
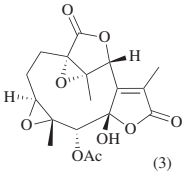
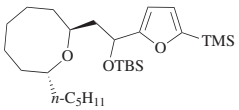
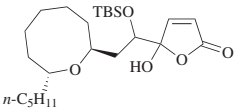
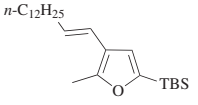
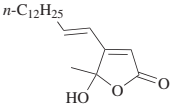
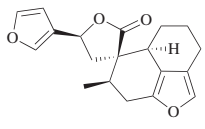
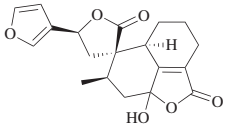
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	*Aspergillus niger*, H_2O	 (8)	689
	Air, AcOH, $CHCl_3$, rt, 15 d	 (—)	690
	*m*-CPBA (1.0 eq), CH_2Cl_2, rt, 0.5 h	 (55)	221, 313, 222
	1. O_2, rose bengal, hv, CH_2Cl_2, –78°, 30 min 2. PPTS, THF/H_2O (1:1), rt, 3 h	 (100)	573
	Dimethyldioxirane (2.0 eq), THF/acetone, –15°, 0.5 h	 (—)	691
C_{16}			
	O_2, rose bengal, hv, EtN(*i*-Pr)$_2$ (1.1 eq), CH_2Cl_2, –17°, 20 min	 R: H (60); TMS (99)	318, 311
	*m*-CPBA (1.0 eq), $CHCl_3$, rt, 14 d	 (4) +  (3)	217
C_{18}			
	O_2, methylene blue, hv, MeOH, –40°, 10 min	 (100)	319
C_{19}			
	O_2, methylene blue, 0°, 5 min; then SiO_2, H_2O	 (52)	692
	PDC, DMF, rt, 12 h	 (45)	693

TABLE 4. SYNTHESIS OF 4-HYDROXYBUTENOLIDES (*Continued*)

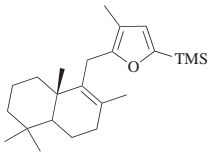
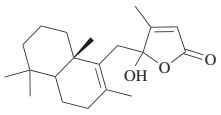
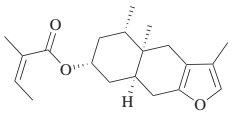
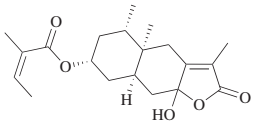
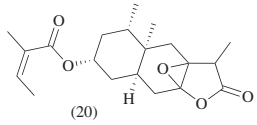
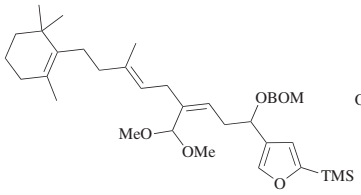
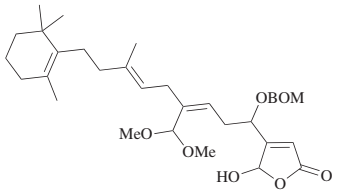
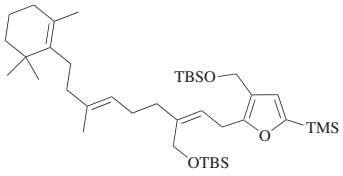
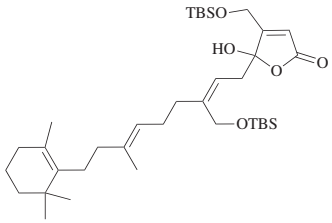
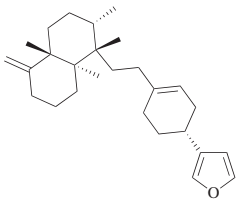
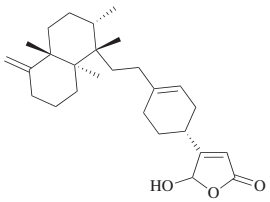
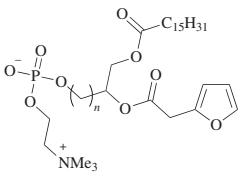
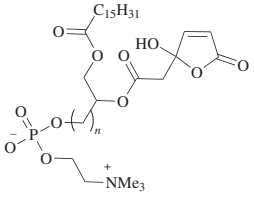
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{20} 	O_2, methylene blue, hv, $CDCl_3$, 8°, 30 s	 (—)	314
	Air, hv, benzene	 (38) +  (20)	80
C_{24} 	O_2, rose bengal, $NaNO_2$, hv, CH_2Cl_2, –78°, 5 min	 (93)	316
C_{25} 	O_2, rose bengal, $NaNO_2$, hv, CH_2Cl_2, –78°, 5 min	 (100)	315
C_{27} 	1. O_2, rose bengal, hv, $EtN(i\text{-}Pr)_2$, CH_2Cl_2, –78°, 1 h 2. $(CO_2H)_2$, H_2O, rt, 0.5 h	 (55)	694
$C_{29–33}$ 	$NaClO_2$ (3.0 eq), NaH_2PO_4 (1.5 eq), phosphate buffer (pH 3.5)/$CHCl_3$/H_2O (2:1:1), 1 h	 	211

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS

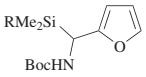
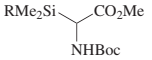
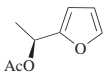
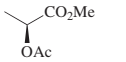
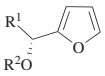
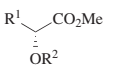
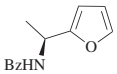
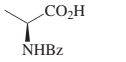
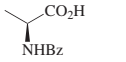
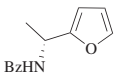
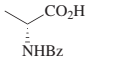
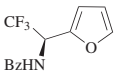
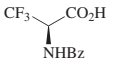
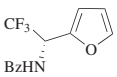
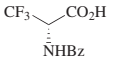
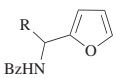
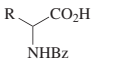
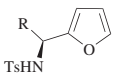
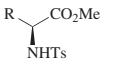
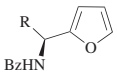
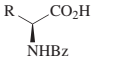
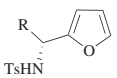
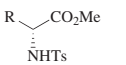
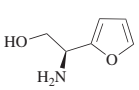
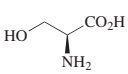
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	1. O_3, MeOH, CH_2Cl_2, 1 h, –78° 2. $TMSCHN_2$, Et_2O, 0°, 1 h	 R: Me (63); Et (66); *i*-Pr (78); *t*-Bu (80)	408
C_6 	1. RuO_4 (0.012 eq), $NaIO_4$ (15 eq), $CCl_4/MeCN/H_2O$ (2:2:3), rt, 44 h 2. CH_2N_2, EtOAc	 (31)	113
$C_{6–11}$ 	O_3, MeOH, –78°, 2 h	 R^1 / R^2: Me/TBS (95); EtO_2CCH_2/TBS (77); *i*-Pr/TBS (76); n-C_5H_{11}/Ac (89); n-C_5H_{11}/TBS (71); n-C_5H_{11}/Bn (88); Ph/TBS (79)	520
C_6 	O_3, MeOH	 Temp (°) / Time (h): — / — (95); 78 / 0.25 (91)	695, 379
	RuY (0.035 eq), $NaIO_4$ (16 eq), $CCl_4/MeCN/H_2O$ (1:1.5:1), rt, 2 h	 Y / Time (h): O_2 / — (88); Cl_3 / 0.5 (82)	380 379
	$RuCl_3$ (0.035 eq), $NaIO_4$ (16 eq), $CCl_4/MeCN/H_2O$ (1:1.5:1), rt, 0.5 h	 (81)	379
	O_3, MeOH	 (93)	415
	O_3, MeOH, –78°, 30 min	 (91)	415
$C_{6–9}$ 	$KMnO_4$, trichloroacetone, H_2O, 15°, overnight	 R: Me (50); *n*-Pr (60); *n*-Bu (70)	696
$C_{6–11}$ 	O_3, CH_2Cl_2/MeOH (20:1), –70°, 5 min; then Me_2S (2.0 eq)	 R: Me (80); *n*-Pr (88); *n*-Bu (88); *i*-Bu (82); Ph (85)	566
	RuO_2 (0.035 eq), $NaIO_4$ (16 eq), $CCl_4/MeCN/H_2O$ (1.5:1:1), rt, 2.5 h	 R: Me (88); Ph (75)	380
	O_3, CH_2Cl_2/MeOH (20:1), –70°, 5 min; then Me_2S (2.0 eq)	 R: Me (82); *n*-Pr (85); *n*-Bu (89); *i*-Bu (86); Ph (88)	566
C_6 	O_3, CH_2Cl_2, –78°, 30 min	 (—)	403

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

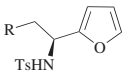
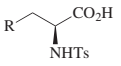
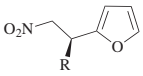
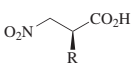
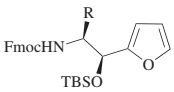
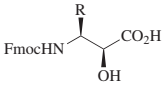
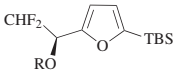
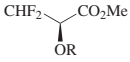
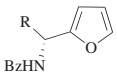
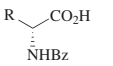
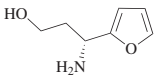
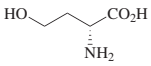
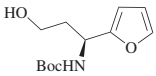
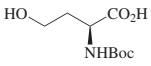
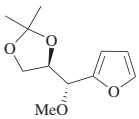
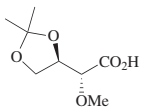
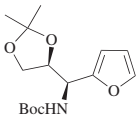
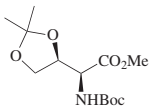
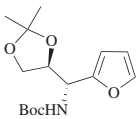
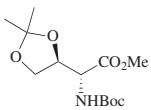
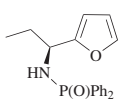
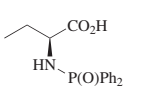
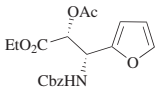
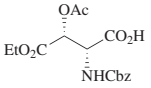
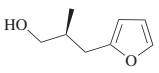
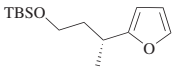
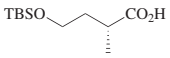
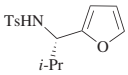
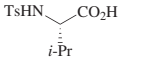
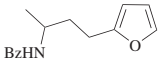
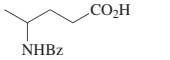
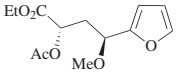
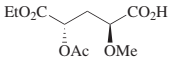
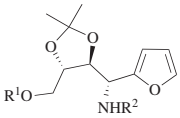
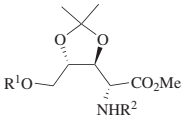
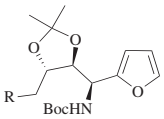
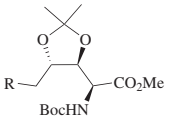
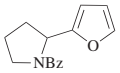
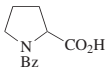
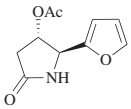
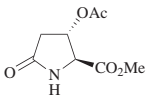
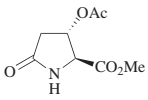
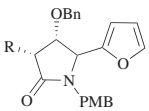
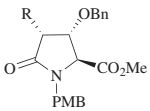
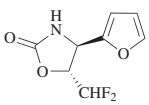
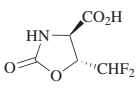
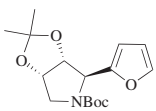
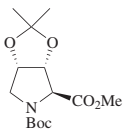
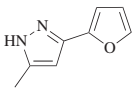
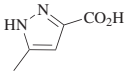
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-13} 	RuO_2 (0.05 eq), $NaIO_4$ (14.67 eq), $MeCN/CCl_4/H_2O$ (3:2:2), rt, 1 h	 R: BnO (61); Et (71); *n*-Pr (66); *t*-Bu (68); Bn (68)	377
C_6 	$RuCl_3$ (0.02 eq), $NaIO_4$ (5.0 eq), $NaHCO_3$ (3.0 eq), $MeCN/CCl_4/H_2O$ (3:2:2), 0°, 0.25 h	 R: BocHN (72); CbzHN (65)	697
C_{6-13} 	1. O_3, MeOH, CH_2Cl_2, –70°; then –70° to rt 2. THF/MeCN/H_2O (3:1:1), 40°, 2 h	 R: H (80); Me (61); *i*-Pr (52); *i*-Bu (61); Ph (69); Bn (52)	412, 411
C_6 	O_3, MeOH; then CH_2N_2, Et_2O	 R: Ac (100); Bn (100)	420
C_{7-12} 	$RuCl_3$ (0.05 eq), $NaIO_4$(6.0 eq), $MeCN/H_2O/CCl_4$ (3:3:2), 20°, 1 h	 R: Et (75); *i*-Pr (88); *i*-Bu (98); *n*-C_5H_{11} (77); Bn (90)	698
C_7 	O_3, MeOH, –78°	 (30)	405
	1. O_3, MeOH, –78°, 10 min; then –78° to rt 2. Me_2S, rt, 12 h	 (62)	699
	RuO_2 (0.2 eq), $NaIO_4$ (6 eq), $NaHCO_3$ (50 eq), $MeCN/H_2O/CCl_4$ (3:3:2), rt	 (91)	372
	1. $RuCl_3$ (1.2 eq), $NaIO_4$ (6.0 eq), $NaHCO_3$ (0.1 eq), $MeCN/CH_2Cl_2/H_2O$ (3:2:2), rt, 2 min 2. CH_2N_2, Et_2O	 (78)	374
	1. $RuCl_3$ (1.2 eq), $NaIO_4$ (6.0 eq), $NaHCO_3$ (0.1 eq), $MeCN/CH_2Cl_2/H_2O$ (3:2:2), rt, 2 min 2. CH_2N_2, Et_2O	 (72)	374
	$RuCl_3$ (0.03 eq), $NaIO_4$ (4.0 eq), $H_2O/MeCN/CH_2Cl_2$ (3:2:2), rt, 2.5 h	 (60)	343
	1. O_3, CH_2Cl_2, MeOH, 0°, 15 min 2. Me_2S (1.0 eq), rt, 1 h	 (74)	548

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	O_3, CH_2Cl_2, –60°; then HCO_2H, –10°, 1 h; then H_2O_2 (0.5 eq), H_2O, 90°	 (—)	395
	$RuCl_3$ (cat.), $NaIO_4$ (15.0 eq), H_2O/MeCN/CCl_4, rt, 1 h	 (82)	700
	$RuCl_3$ (0.012 eq), $NaIO_4$ (15 eq), H_2O/MeCN/CCl_4 (3:2:2), rt, 44 h	 (—)	515
	$KMnO_4$, H_2O	 (50)	696
	$RuCl_3$ (cat.), $NaIO_4$ (15 eq), H_2O/MeCN/CCl_4 (3:2:2), rt, 40 min	 (90)	337
	1. $RuCl_3$ (1.2 eq), $NaIO_4$ (6 eq), $NaHCO_3$ (0.1 eq), MeCN/CH_2Cl_2/H_2O (3:2:2), rt, 2 min 2. CH_2N_2, Et_2O		374
	1. $RuCl_3$ (1.2 eq), $NaIO_4$ (6 eq), $NaHCO_3$ (0.1 eq), MeCN/CH_2Cl_2/H_2O (3:2:2), rt, 2 min 2. CH_2N_2, Et_2O		373, 346 374
	$KMnO_4$, HCl, acetone	 (62)	701

R^1	R^2	
TBS	Ac	(72)
Bn	Boc	(40)

R	
H_2NCO_2	(87)
BnO	(56)

	O_3, MeOH, –78°, 2hr; Then rt, 30 min; then CH_2N_2, 0°	 (83)	362
	1. O_3, MeOH, –78° 2. CH_2N_2	 (—)	414
C_{8-9}			
	1. $RuCl_3$ (0.05 eq), $NaIO_4$ (9 eq), MeCN/H_2O/CCl_4 (3:3:2), 0°, 20 min 2. CH_2N_2, Et_2O, rt		338 338, 702
C_8			
	O_3, MeOH, –78°	 (72)	413
	1. $RuCl_3$•H_2O (0.1 eq), $NaIO_4$ (5 eq), MeCN/H_2O/CCl_4 (3:3:2), rt, 5 min 2. CH_2N_2, AcOH	 (82)	383
	$KMnO_4$, H_2O, acetone	 (69)	703

R		
H	(78)	338
Me	(75)	338, 702

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

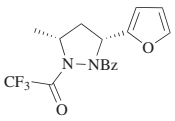
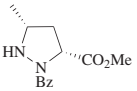
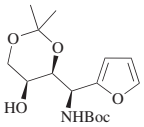
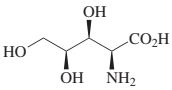
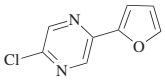
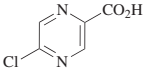
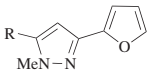
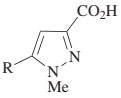
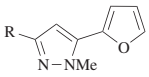
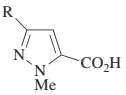
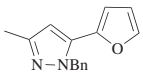
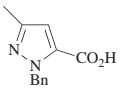
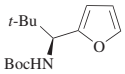
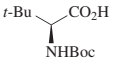
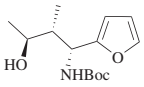
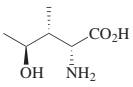
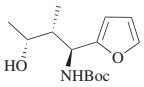
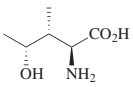
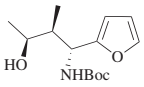
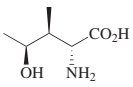
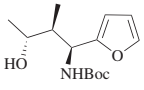
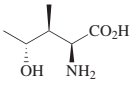
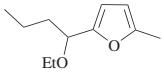
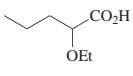
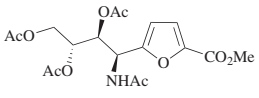
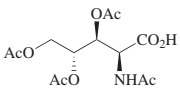
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	1. $RuCl_3$ (1.7 eq), $NaIO_4$ (15 eq), $MeCN/CH_2Cl_2$ (1:1), rt, 2 h 2. $SOCl_2$, MeOH, reflux, 20 min	 (33)	352
	1. O_3, MeOH, –78°, 5 min 2. Me_2S (1.0 eq), –78° to rt, overnight 3. TFA/H_2O (9:1), thiophenol (6 eq), 0° to rt, overnight	 (60)	407
	$KMnO_4$	 (76)	704
C_{8-9}			
	$RuCl_3•3H_2O$ (50 eq), $NaIO_4$ (10 eq), $MeCN/CCl_4/H_2O$ (3:2:2), rt, 5 min		350
		R: CF_3 (90); CF_3CF_2 (88); CH_3CF_2 (76)	
	$RuCl_3•3H_2O$ (50 eq), $NaIO_4$ (10 eq), $MeCN/CCl_4/H_2O$ (3:2:2), rt, 5 min		350
		R: CF_3 (85); EtO_2C (90); CH_3CHF (77); CF_3CHF (93); CF_3CH_2 (60); CHF_2CH_2 (65); CH_2FCH_2 (75); CF_3CF_2 (75); CH_3CF_2 (85)	351; 351; 351; 351; 351; 351; 351; 350; 350
	$KMnO_4$, H_2O, benzene, acetone	 (81)	703
C_9			
	$KMnO_4$, $Bu_4N•HSO_4$, CH_2Cl_2, H_2O	 (61)	705
	1. O_3, 10 min, –78°; then –78° to rt; then Me_2S, rt, 12 h 2. HCl (6 M), 1,4-dioxane, 0°; then 0° to rt	 (62)	402
	1. O_3, 10 min, –78°; then –78° to rt; then Me_2S, rt, 12 h 2. HCl (6 M), 1,4-dioxane, 0°; then 0° to rt	 (65)	402
	1. O_3, 10 min, –78°; then –78° to rt; then Me_2S, rt, 12 h 2. HCl (6 M), 1,4-dioxane, 0°, then 0° to rt	 (63)	402
	1. O_3, 10 min, –78°; then –78° to rt; then Me_2S, rt, 12 h 2. HCl (6 M), 1,4-dioxane, 0°, then 0° to rt	 (60)	402
	$KMnO_4$, acetone, H_2O	 (60)	706
	$RuCl_3$ (0.022 eq), $NaIO_4$ (1.0 eq), $H_2O/CH_2Cl_2/MeCN$ (3:2:2)	 (87)	707

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

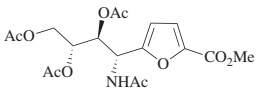
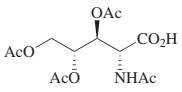
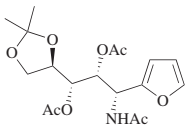
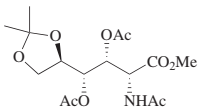
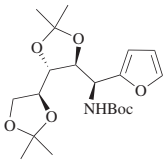
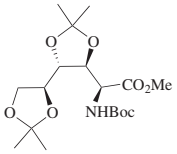
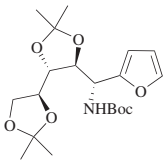
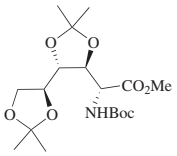
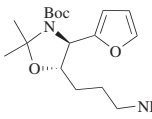
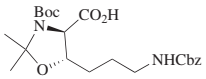
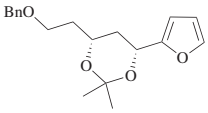
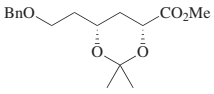
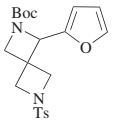
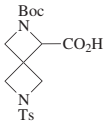
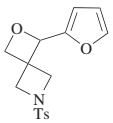
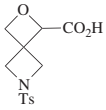
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	$RuCl_3$ (0.022 eq), $NaIO_4$ (1.0 eq), $H_2O/CH_2Cl_2/MeCN$ (3:2:2)	 (86)	707
	1. RuO_2, $NaIO_4$, $CCl_4/MeCN/H_2O$ 2. CH_2N_2	 (—)	708
	1. $RuCl_3$ (1.2 eq), $NaIO_4$ (6 eq), $NaHCO_3$ (0.1 eq), $CCl_4/MeCN/H_2O$ (3:2:2), rt, 2 min 2. CH_2N_2, Et_2O	 (82)	374
	1. $RuCl_3$ (1.2 eq), $NaIO_4$ (6 eq), $NaHCO_3$ (0.1 eq), $CCl_4/MeCN/H_2O$ (3:2:2), rt, 2 min 2. CH_2N_2, Et_2O	 (74)	374
	$RuCl_3$ (cat.), $NaIO_4$, $H_2O/CH_2Cl_2/MeCN$ (3:2:2)	 (59)	348
	1. O_3, $CH_2Cl_2/MeOH$ (1:1) 2. Ph_3P (1.5 eq) 3. CH_2N_2, Et_2O	 (66)	400
	$RuCl_3$ (0.05 eq), $NaIO_4$ (1.0 eq), $H_2O/MeCN/CCl_4$ (3:2:2), rt, 40 min	 (83)	709
	$RuCl_3$ (0.05 eq), $NaIO_4$ (1.0 eq), $H_2O/MeCN/CCl_4$ (3:2:2), rt, 40 min	 (68)	709

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TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

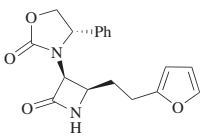
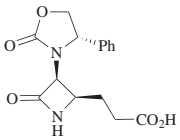
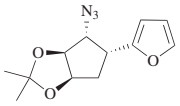
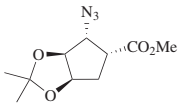
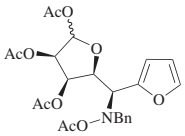
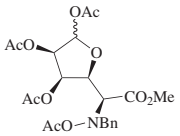
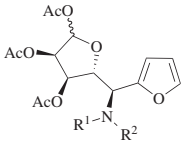
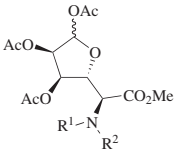
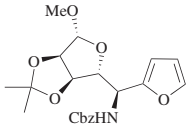
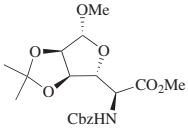
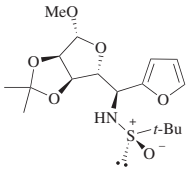
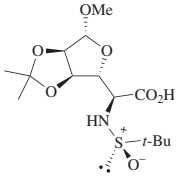
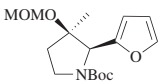
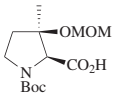
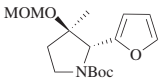
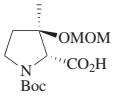
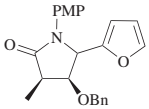
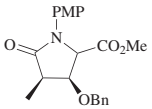
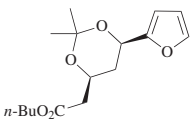
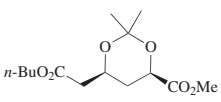
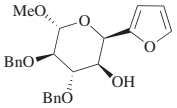
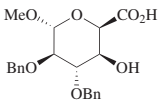
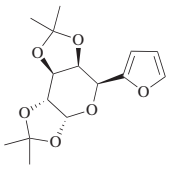
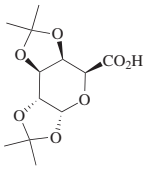
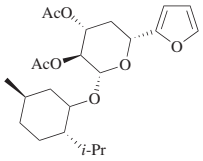
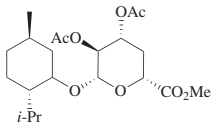
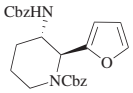
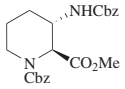
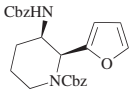
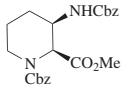
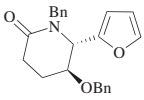
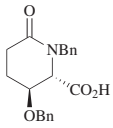
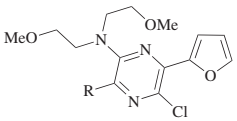
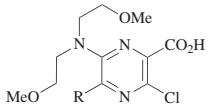
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	O_3, CH_2Cl_2, MeOH; then H_2O_2	 (77)	417
	1. $RuCl_3 \cdot 3H_2O$ (cat.), $NaIO_4$ (10 eq), $H_2O/CCl_4/MeCN$ (3:2:2), 0°, 1 h 2. CH_2N_2, Et_2O, 0°, 75 h	 (80)	340
	RuO_2 (cat.), $NaIO_4$ (4 eq), $CCl_4/MeCN/H_2O$ (2:3:2); then CH_2N_2, Et_2O, 0°, 5 min	 (46)	381
	1. $RuCl_3$ (0.05 eq), $NaIO_4$ (6 eq), $NaHCO_3$, $MeCN/CCl_4/H_2O$ (3:2:3) 2. CH_2N_2, Et_2O, rt, 5 min		346 346 341, 346
	1. $RuCl_3$ (0.05 eq), $NaIO_4$ (6 eq), $NaHCO_3$, $MeCN/CCl_4/H_2O$ (3:2:3) 2. CH_2N_2, Et_2O, rt, 5 min	 (72)	346
	$RuCl_3$, $NaIO_4$, $MeCN/CH_2Cl_2/H_2O$ (17.5:1:25), rt, 1 h; then CH_2N_2, Et_2O, 0°, 1 h	 (72)	358
	RuO_2 (0.2 eq), $NaIO_4$ (5.9 eq), $CCl_4/MeCN/H_2O$ (2:3:3), rt, 5 min	 (72)	371
	RuO_2 (0.2 eq), $NaIO_4$ (5.9 eq), $CCl_4/MeOH/H_2O$ (2:3:3), rt, 5 min	 (72)	371
	$RuCl_3$, $NaIO_4$, $CCl_4/MeCN/H_2O$; then CH_2N_2, Et_2O	 (56)	702
	1. O_3 2. $TMSCHN_2$	 (86)	406
	1. O_3, MeOH, CH_2Cl_2, –78°, 40 min 2. Me_2S, –78° to rt, 2 h	 (73)	111

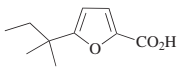
TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

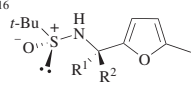
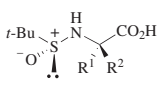
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	O_3, CH_2Cl_2, MeOH, –78°	 (50)	397
	1. O_3, CH_2Cl_2, MeOH, –78°, 2 min 2. CH_2N_2, Et_2O, rt, 10 min	 (80)	399
	1. $RuCl_3$ (0.02 eq), $NaIO_4$ (6.9 eq), MeCN/EtOAc/H_2O (3:2:2), 0°, 15 min 2. $TMSCH_2N_2$, benzene, 0°, 3 h	 (62)	710
	1. $RuCl_3$ (0.02 eq), $NaIO_4$ (6.9 eq), MeCN/EtOAc/H_2O (3:2:2), 0°, 15 min 2. $TMSCH_2N_2$, benzene, 0°, 3 h	 (—)	710
	$RuCl_3$ (0.05 eq), $NaIO_4$ (10 eq), MeCN/EtOAc/H_2O (3:2:2), rt, 10 min	 (70)	359

$C_{9–15}$  RuO_2, $NaIO_4$, CCl_4/MeCN/H_2O, rt, 0.5 h 

R		
NC–	(54)	
4-CbzNHC$_6$H$_4$	(—)	

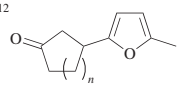
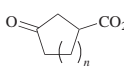
711

C_{10}  $KMnO_4$, KOH (aq), rt  (79) 712

$C_{10–16}$  $RuCl_3$, $NaIO_4$, CH_2Cl_2/MeCN/H_2O 

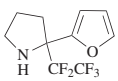
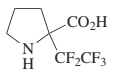
R^1	R^2	
Me	*i*-Pr	(63)
Me	*i*-Bu	(69)
i-Pr	*n*-Bu	(69)
Ph	Me	(62)
Ph	*n*-Bu	(67)

342

$C_{10–12}$  O_3, MeOH, –78°, 0.5 h; then –78° to rt, 10 min 

n	
1	(85)
2	(87)
3	(83)

713

C_{10}  O_3, MeOH, –78°  (84) 714

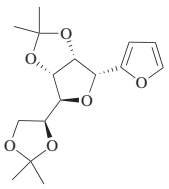
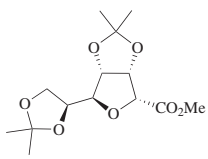
 1. O_3, CH_2Cl_2, MeOH
2. CH_2N_2, Et_2O  (60) 398

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

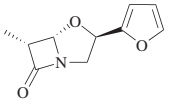
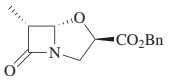
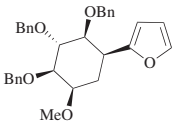
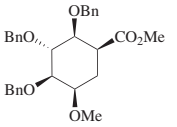
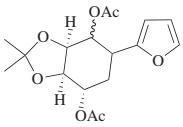
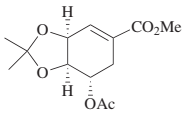
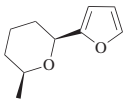
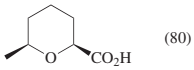
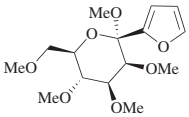
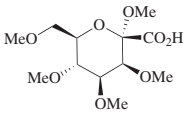
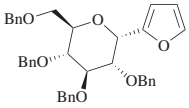
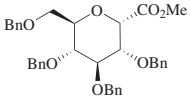
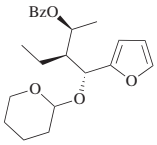
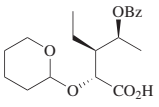
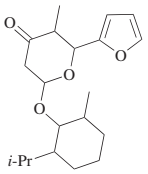
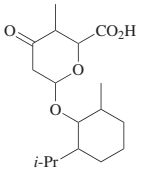
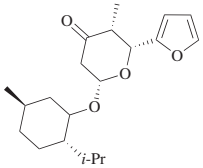
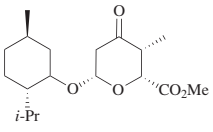
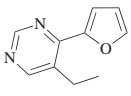
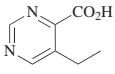
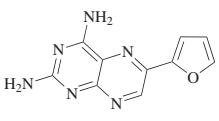
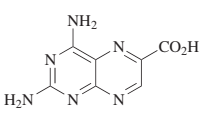
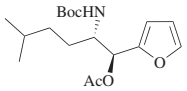
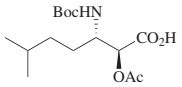
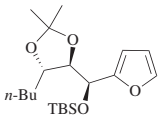
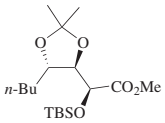
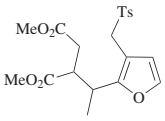
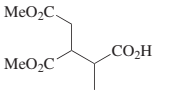
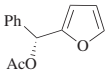
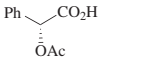
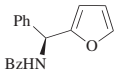
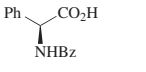
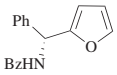
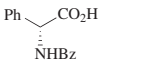
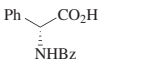
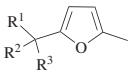
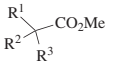
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	1. $RuCl_3$, $NaIO_4$, CCl_4/MeCN/H_2O, rt, 40 min 2. BnBr, Bu_4NBr, K_2CO_3, 50°	 (59)	715
	1. O_3, CH_2Cl_2, MeOH, –78°, 1 h; then Me_2S (4.5 eq) 2. $KHCO_3$ (6.2 eq), MeI (5.3 eq), DMF, rt, 5 h	 (62)	396
	1. RuO_2 (0.012 eq), $NaIO_4$ (15 eq), CCl_4/MeCN/H_2O (2:2:3) 2. CH_2N_2, Et_2O 3. DBU, CH_2Cl_2, 20°	 (88)	716
	$RuCl_3$ (cat.), $NaIO_4$, CH_2Cl_2/MeCN/H_2O	 (80)	355
	RuO_2 (cat.), $NaIO_4$ (14.7 eq), CH_2Cl_2/MeCN/H_2O (2:2:3), rt, 2 d	 (77)	369
	1. O_3, CH_2Cl_2, MeOH, –78° 2. CH_2N_2, Et_2O	 (40)	398
	$RuCl_3$ (0.45 eq), $NaIO_4$ (200 eq), MeCN/CCl_4/H_2O (2:2:3), rt	 (82)	717
	O_3, CH_2Cl_2, MeOH	 (—)	718
	1. O_3, CH_2Cl_2, MeOH, –78°, 2 min 2. CH_2N_2, Et_2O, rt, 10 min	 (77)	399
	$KMnO_4$, H_2O, acetone, 50°, 0.25 h; then reflux, 1 h	 (—)	719, 720
	$KMnO_4$, NaOH, H_2O	 (67)	721

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	$RuCl_3$, $NaIO_4$, EtOAc/MeCN/H_2O, rt, 1.5 h	 (92)	722
	1. $RuCl_3$ (0.06 eq), $NaIO_4$ (6 eq), CH_2Cl_2/MeCN/H_2O (2:2:3) 2. CH_2N_2, Et_2O	 (70)	339
	$RuCl_3$•$6H_2O$, $NaIO_4$, EtOAc/H_2O, rt	 (84)	360
	$RuCl_3$ (0.02 eq), $NaIO_4$ (8 eq), CCl_4/MeCN/H_2O (2:2:3), rt,1 h	 (83)	520
	$RuCl_3$ (0.035 eq), $NaIO_4$ (16 eq), CCl_4/MeCN/H_2O (2:3:2), rt, 30 min		379, 380
		Y Time (h) Cl_3 0.5 (82) O_2 — (75)	
	RuY (0.035 eq), $NaIO_4$ (16 eq), CCl_4/MeCN/H_2O (2:3:2), rt, 30 min		379, 380
		Y Time (h) Cl_3 0.5 (78) O_2 — (75)	
	O_3, MeOH		379, 695
		Temp (°) Time (h) –78 0.25 (89) — — (92)	

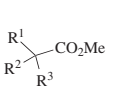
C_{11-19} 

1. $RuCl_3$ (0.05 eq), $NaIO_4$ (7 eq), CCl_4/MeCN/H_2O (2:2:3), 20°, 24 h
2. $TMSCHN_2$, benzene/MeOH



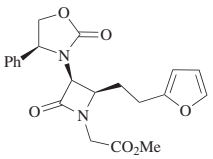
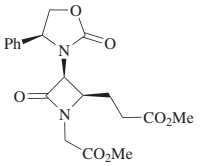
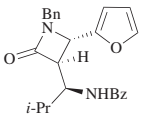
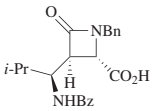
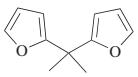
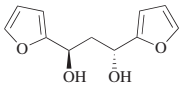
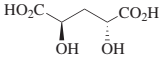
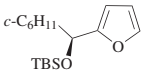
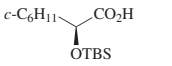
R^1	R^2	R^3		Refs.
Me	H	2-thienyl	(11)	363
Me	H	4-ClC_6H_4	(71)	
Me	H	4-$MeOC_6H_4$	(87)	
Me	H	4-$BnOC_6H_4$	(86)	
Me	H	4-$CbzHNC_6H_4$	(85)	
Me	Me	Ph	(65)	
Me	H	4-MeC_6H_4	(68)	
Me	H	1-naphthyl	(70)	
Me	H	2-MeO-1-naphthyl	(8)	
Me	H	2-naphthyl	(51)	
Me	H	6-MeO-2-naphthyl	(21)	
H	Ph	Ph	(80)	
Me	H	4-PhC_6H_4	(78)	

1. $RuCl_3$ (0.05 eq), $NaIO_4$ (7 eq), hexane/EtOAc/H_2O (*x*/*y*/*z*), 20°, 24 h
2. $TMSCHN_2$, benzene/MeOH



R^1	R^2	R^3	*x*/*y*/*z*		Refs.
Me	H	2-thienyl	0:4:4	(51)	363
Me	H	4-ClC_6H_4	2:2:4	(77)	
Me	H	4-$MeOC_6H_4$	1:3:4	(92)	
Me	H	4-$BnOC_6H_4$	1:3:4	(96)	
Me	H	4-$CbzHNC_6H_4$	1:3:4	(86)	
Me	Me	Ph	2:2:4	(88)	
Me	H	4-MeC_6H_4	1:3:4	(74)	
Me	H	1-naphthyl	2:2:4	(88)	
Me	H	2-MeO-1-naphthyl	2:2:4	(27)	
Me	H	2-naphthyl	2:2:4	(80)	
Me	H	6-MeO-2-naphthyl	1:3:4	(65)	
H	Ph	Ph	1:3:4	(87)	
Me	H	4-PhC_6H_4	1:3:4	(89)	

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
	H_2O_2, CH_2Cl_2, MeOH	 (84)	723
	$RuCl_3$ (0.02 eq), H_5IO_6 (15 eq), CCl_4/MeCN/H_2O (2:2:3), rt, 10 min	 (90)	365
	$KMnO_4$ (10 eq), H_2O, rt, 23 h	 (55)	724
	1. O_3, HCO_2H, CH_2Cl_2, MeOH 2. H_2O_2, HCO_2H 3. $Ba(OH)_2$	 (42)	419
	O_3, MeOH, –78°, 1 h	 (96)	725, 726

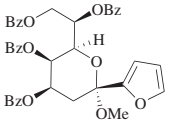
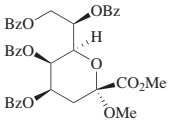
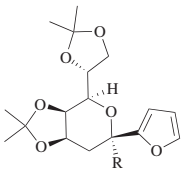
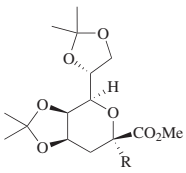
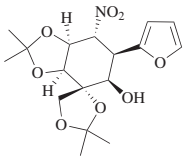
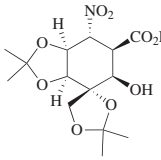
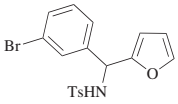
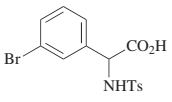
	1. $RuCl_3$ (1.0 eq), $NaIO_4$(10 eq), $NaHCO_3$ (83 eq), MeCN/CH_2Cl_2/H_2O (3:2:2) 2. CH_2N_2, Et_2O	 (94)	368
	1. RuO_2 (0.03 eq), $NaIO_4$ (14.7 eq), MeCN/CCl_4/H_2O (3:2:2) 2. CH_2N_2, Et_2O	 R: H (60), MeO (73)	370
	$RuCl_3$ (10 mol %), $NaIO_4$ (8 eq), MeCN/CCl_4/H_2O (1:1:1.25), rt, 20 min	 (52)	727
	O_3, MeOH, –78°, 0.5 h	 (82)	728

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

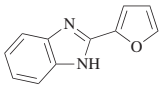
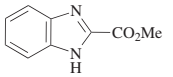
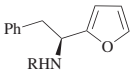
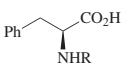
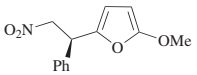
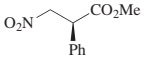
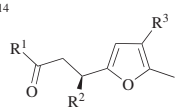
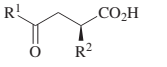
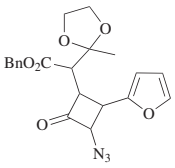
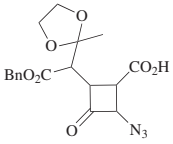
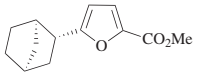
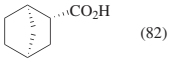
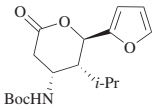
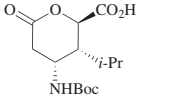
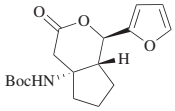
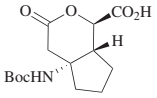
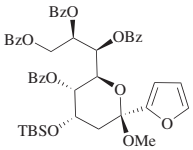
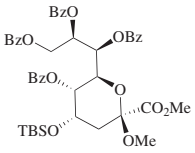
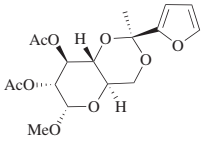
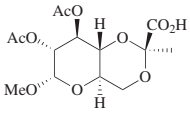
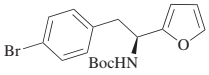
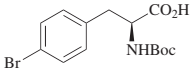
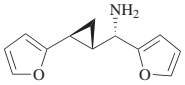
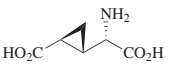
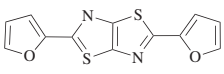
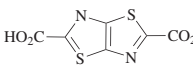
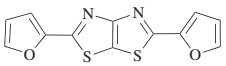
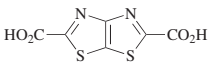
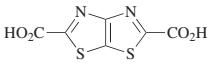
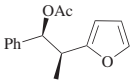
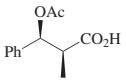
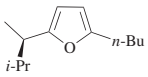
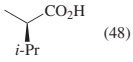
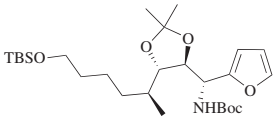
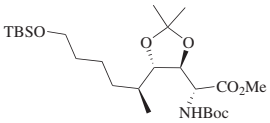
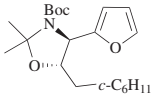
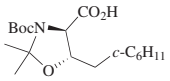
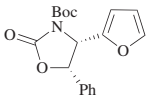
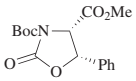
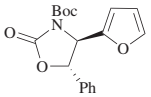
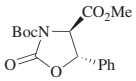
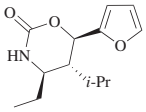
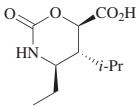
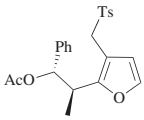
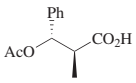
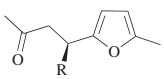
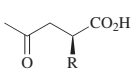
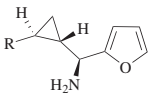
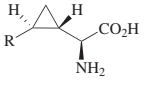
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	O_2, methylene blue, hv, MeOH, rt, 18 h	 (13)	307
C_{12} 	O_3, MeOH	 R: Bz, Temp (°) —, Time (h) —, (88); Cbz, –78, 0.5, (79)	695, 729
	$RuCl_3$ (0.06 eq), $NaIO_4$ (1.52 eq), $MeCN/CCl_4/H_2O$ (2:2:3), rt, 2 h	 (77)	364
C_{12-14} 	O_3, MeOH, –78°, 0.5 h; then –78° to rt, 10 min	 R^1: *n*-Pr, R^2: Me, R^3: H, (96); *n*-Bu, Me, H, (89); Me, *n*-Bu, Me, (85); Me, *n*-C_5H_{11}, H, (85)	730
C_{12} 	O_3, AcOH, rt, 2 h	 (64)	394
	1. O_3, CH_2Cl_2, –78°, 20 min 2. PPh_3, CH_2Cl_2, –78° to rt	 (82)	731
	$RuCl_3$ (0.03 eq), $NaIO_4$ (15 eq), $CCl_4/MeCN/H_2O$ (1:1:2.5), rt	 (89)	344
	$RuCl_3$ (0.03 eq), $NaIO_4$ (15 eq), $CCl_4/MeCN/H_2O$ (1:1:2.5), rt	 (92)	344
	1. $RuCl_3$ (1.0 eq), $NaIO_4$ (10 eq), $NaHCO_3$ (83 eq), $MeCN/CCl_4/H_2O$ (3:2:2) 2. CH_2N_2, Et_2O	 (90)	368, 732
	RuO_2, $NaIO_4$, CCl_4	 (74)	733
	$RuCl_3•3H_2O$ (0.02 eq), H_5IO_6 (5.0 eq), $CCl_4/MeCN/H_2O$ (3:3:4), rt, 20 min	 (33)	587
	O_3, MeOH, –78°, 30 min	 (91)	418
	$KMnO_4$ (10.7 eq), py/H_2O (6.3:1), 15–40°, 12 h	 (65)	734

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

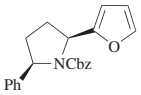
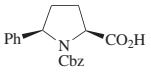
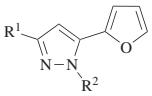
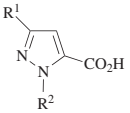
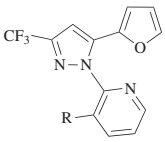
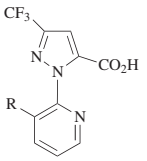
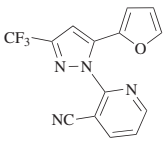
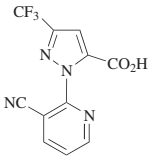
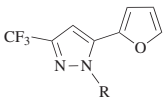
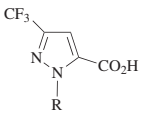
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}			
	$KMnO_4$, H_2O, rt to 40°, 12 h	 (56)	735
	$KMnO_4$, *t*-BuOH, 70°, 18 h	 (85)	736
C_{13}			
	$RuCl_3$•$6H_2O$, $NaIO_4$, H_2O, EtOAc, rt	 (68)	360
	$RuCl_3$ (0.09 eq), $NaIO_4$ (4.0 eq), CCl_4/MeCN/H_2O (1:1:1.4), rt, 15 h	 (48) + *n*-$BuCO_2H$ (71)	361
	1. RuO_2, $NaIO_4$, MeCN/CCl_4/H_2O, rt, 0.25 h 2. MeI, $KHCO_3$, rt, 12 h	 (65)	375
	$RuCl_3$, $NaIO_4$, CCl_4/MeCN/H_2O	 (80)	347
	$RuCl_3$, $NaIO_4$, CCl_4/MeOH/H_2O, rt, 1 h	 (48)	737
	$RuCl_3$, $NaIO_4$, CCl_4/MeOH/H_2O, rt, 1 h	 (92)	737
	$RuCl_3$ (0.03 eq), $NaIO_4$ (15 eq), CCl_4/MeCN/H_2O (1:1:1.25), rt	 (71)	344
C_{14}			
	$RuCl_3$, $NaIO_4$, H_2O, rt, 10 min	 (68)	360
$C_{14–15}$			
	O_3, MeOH, –78°, 0.5 h; then –78° to rt, 10 min		713

R		
n-C_5H_{11}	(85)	
Ph	(91)	

$C_{14–18}$			
	RuO_2•H_2O (0.04 eq), $NaIO_4$ (16.6 eq), CCl_4/MeCN/H_2O (1:1.5:1), rt, 2 h		385

R		
Ph	(—)	
2-ClC_6H_4	(—)	
4-$MeOC_6H_4$	(—)	
3-MeC_6H_4	(—)	
2-naphthyl	(—)	

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	$KMnO_4$ (8.0 eq), KOH (20% aq), acetone/H_2O, rt, 1 h	 (80)	389
$C_{14–15}$ 	$KMnO_4$ (7 eq), acetone/H_2O (1:1), 60°, 3 h	 R¹ = NC–, R² = 4-$MeOC_6H_4$ (71); R¹ = CF_3, R² = 2-$BocHNCH_2C_6H_4$ (71); R¹ = *t*-BuO_2C, R² = 3-NC-4-FC_6H_3 (68)	738, 739 392 391
C_{14} 	$KMnO_4$ (5 eq), acetone/H_2O (1:1), reflux, 0.5 h	 R = NC– (51); R = EtO_2C (50)	740 741
	$KMnO_4$ (5 eq), KH_2PO_4, acetone/H_2O, reflux, 1 h	 (56)	742
$C_{14–18}$ 	$KMnO_4$ (7 eq), acetone/H_2O (1:1), 60°, 3 h	 R = Ph (—); 3-$O_2NC_6H_4$ (30); 2-$MeO_2CC_6H_4$ (35); 2-N_3CH_2-4-$MeOC_6H_3$ (68); 3-F-2-naphthyl (—)	743 738 393, 391 391 390

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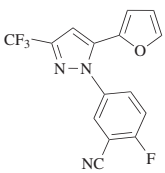
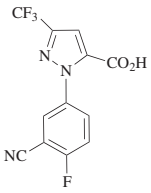
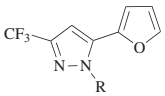
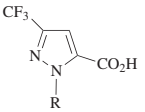
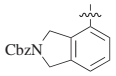
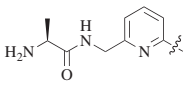
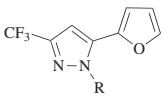
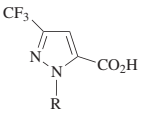
C_{14} 	$RuCl_3$ (0.15 eq), $NaIO_4$ (4.5 eq), $MeCN/CCl_4$ (1:1), rt, 12 h	 (64)	349
$C_{14–17}$ 	$RuCl_3$, $NaIO_4$, $MeCN/CH_2Cl_2/H_2O$	 R = 3-BrC_6H_4 (75);  (—);  (100)	744 425 425
$C_{14–20}$ 	$NaClO_2$, NaH_2PO_4, $MeCN/H_2O$	 R = Ph (90); 2-ClC_6H_4 (90); 3-ClC_6H_4 (90); 4-ClC_6H_4 (90); 3-F-4-BrC_6H_3 (75); 2-$NCCH_2C_6H_4$ (90); 2-$N_3CH_2C_6H_4$ (60); 3-$BocHN(CH_2)_2C_6H_4$ (—)	745 745 745 745 746 391 391 424

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TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

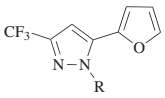
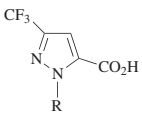
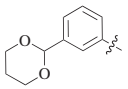
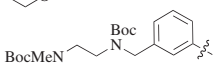
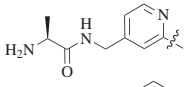
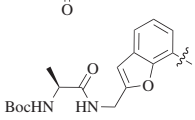
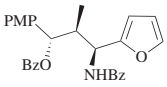
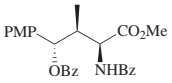
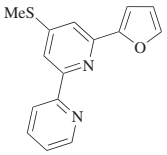
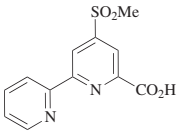
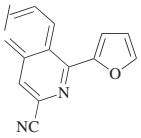
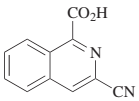
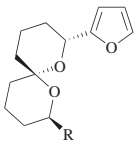
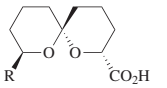
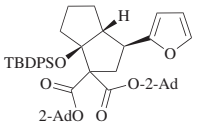
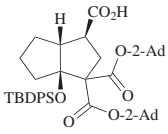
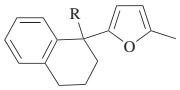
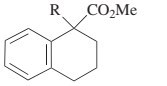
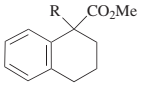
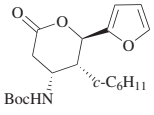
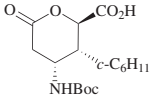
Furan	Conditions	Product(s) and Yield(s) (%)		Refs.
$C_{14–20}$ 	$NaClO_2$, NaH_2PO_4, MeCN/H_2O		R  (—)  (—)  (77)  (—)	424 424 425 425
C_{14} 	1. RuO_2 (0.44 eq), $NaIO_4$ (13 eq), EtOAc/H_2O (4:1), −6°, 2 h 2. CH_2N_2, Et_2O, 0°, 10 min	 (47)		378
	$KMnO_4$, acetone, rt, 3 d	 (66)		747
	$RuCl_3$, $NaIO_4$, MeCN/CH_2Cl_2/H_2O, rt, 2 h	 (55)		748, 749, 750, 751, 752, 753, 754, 755
$C_{14–19}$ 	$RuCl_3$, $NaIO_4$, CH_2Cl_2/MeCN/H_2O		R: Me (90); n-C_6H_{13} (94)	357, 356
C_{14} 	$RuCl_3$, $NaIO_4$, MeCN/CCl_4/H_2O, rt, 2 h		(60)	756
$C_{15–16}$ 	1. $RuCl_3$ (0.05 eq), $NaIO_4$ (7.0 eq), CCl_4/MeCN/H_2O (2:2:3), 20°, 24 h 2. $TMSCHN_2$, benzene/MeOH		R: H (73)[a]; Me (59)	363
	1. $RuCl_3$ (0.05 equiv), $NaIO_4$ (7 eq), hexane/EtOAc/H_2O (*x*/*y*/*z*), 20°, 24 h 2. $TMSCHN_2$ (1.5 eq), benzene/MeOH (2:7), rt, 5 min		R: H (*x*/*y*/*z* 1:3:4) (85)[a]; Me (2:2:4) (90)	363
C_{15} 	$RuCl_3$•H_2O (0.03 eq), $NaIO_4$ (15 eq), CCl_4/MeCN/H_2O (1:1:1.25), rt		(70)	344

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

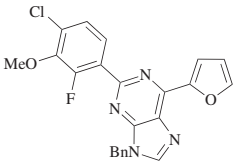
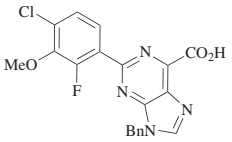
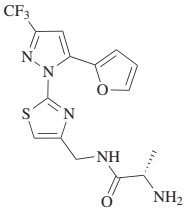
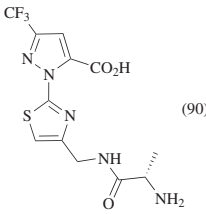
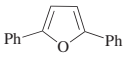
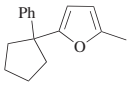
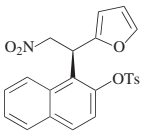
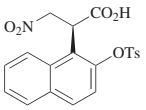
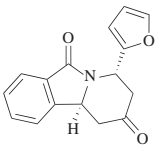
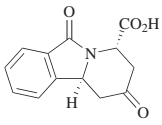
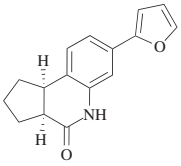
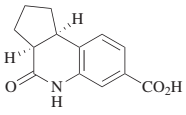
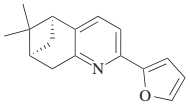
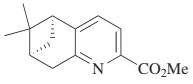
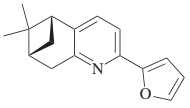
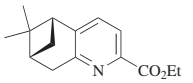
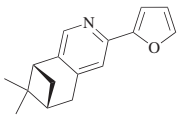
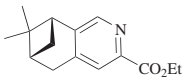
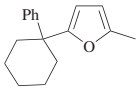
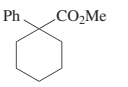
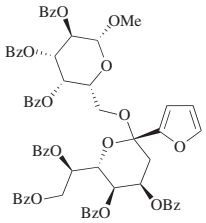
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	1. O_3, CH_2Cl_2, –78° 2. Me_2S, –78° to rt 3. rt, 4 h	 (100)	757
	$NaClO_2$, NaH_2PO_4, MeCN/H_2O	 (90)	425
C_{16}			
	1. O_3, CH_2Cl_2 2. NaOH, CH_2Cl_2, EtOH (aq)	$PhCO_2H$ (59) + $PhCO_2Et$ (39)	758
	1. O_3, CH_2Cl_2 2. $NaBH_4$, EtOH	$PhCO_2H$ (66)	759
	$RuCl_3$ (0.05 eq), $NaIO_4$ (7.0 eq), solvents (2:2:*x*)	 Solvents / *x*: hexane/EtOAc/H_2O 4 (81); CCl_4/MeCN/H_2O 3 (60)	363
	$RuCl_3$, $NaIO_4$, $NaHCO_3$, MeCN/CCl_4/H_2O, rt, 0.5 h	 (71)	760
	O_3, MeOH	 (39)	761
	RuO_2, $NaIO_4$, CCl_4/MeCN/EtOAc/H_2O	 (—)	384
	1. O_3, MeOH, CH_2Cl_2, –78° 2. CH_2N_2, MeOH, Et_2O, 0°	 (42)	416
	1. HNO_3, NH_4VO_3 (0.014 eq), H_2O, reflux, 4 h 2. H_2SO_4, H_2O, EtOH, reflux, overnight	 (47)	423

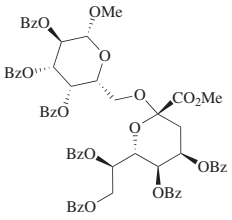
TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

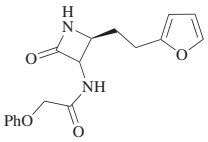
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16} 	1. HNO_3, NH_4VO_3 (0.014 eq), H_2O, reflux, 4 h 2. H_2SO_4, H_2O, EtOH, reflux, overnight	 (56)	423
C_{17} 	1. $RuCl_3$ (0.05 eq), $NaIO_4$ (7.0 eq), solvents (2:2:*x*), 20°, 24 h 2. $TMSCHN_2$, benzene/MeOH		363

Solvents	*x*	
hexane/EtOAc/H_2O	4	(81)
CCl_4/MeCN/H_2O	3	(60)

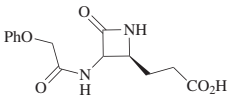


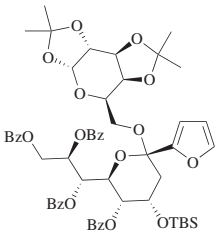
1. $RuCl_3$ (1.0 eq), $NaIO_4$ (10 eq), $NaHCO_3$ (83 eq), $MeCN/CH_2Cl_2/H_2O$ (3:2:2)
2. CH_2N_2, Et_2O

 (75) 368

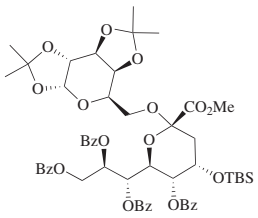


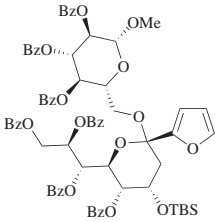
O_3, CH_2Cl_2, MeOH; then H_2O_2

 (77) 417

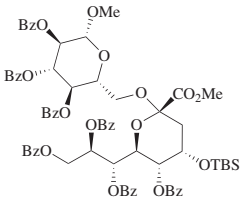
C_{18} 

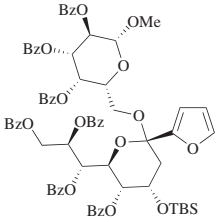
1. $RuCl_3$ (1.0 eq), $NaIO_4$ (10 eq), $NaHCO_3$ (83 eq), $MeCN/CCl_4/H_2O$ (3:2:2)
2. CH_2N_2, Et_2O

 (96) 368

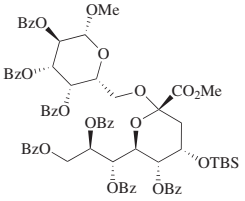


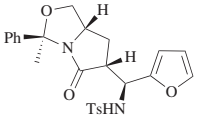
1. $RuCl_3$ (1.0 eq), $NaIO_4$ (10 eq), $NaHCO_3$ (83 eq), $MeCN/CCl_4/H_2O$ (3:2:2)
2. CH_2N_2, Et_2O

 (91) 368



1. $RuCl_3$ (1.0 eq), $NaIO_4$ (10 eq), $NaHCO_3$ (83 eq), $MeCN/CCl_4/H_2O$ (3:2:2)
2. CH_2N_2, Et_2O

 (91) 368



1. $RuCl_3$ (0.01 eq), $NaIO_4$ (10.5 eq), $CCl_4/MeCN/H_2O$ (3:3:5), rt, 4 h
2. CH_2N_2, THF/Et_2O, rt, 10 min

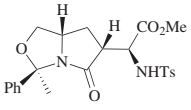
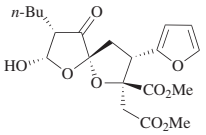
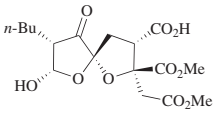
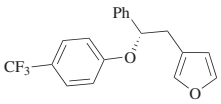
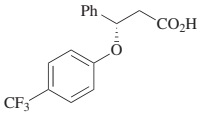
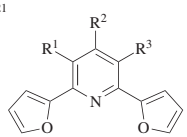
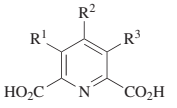
 (22) 376

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18} 	$RuCl_3•3H_2O$ (0.05 eq), $NaIO_4$ (7.0 eq), EtOAc/H_2O (1:1), rt, 5.5 h	 (68)	762
C_{19} 	$RuCl_3•H_2O$ (0.02 eq), $NaIO_4$ (7.25 eq), EtOAc/H_2O (1:1), rt, 1.75 h	 (85)	763
C_{19-21} 	$KMnO_4$ (3.0 eq), acetone, rt, 4 d; then H_2O, rt, 1 h		764

R^1	R^2	R^3		
H	Ph	H	(87)	764
H	2-$MeOC_6H_4$	H	(87)	764
H	3-$O_2NC_6H_4$	H	(76)	765
Me	Ph	H	(90)	764
Me	2-$MeOC_6H_4$	H	(90)	764
Me	3-$O_2NC_6H_4$	H	(70)	765
Me	Ph	Me	(91)	764
Et	Ph	H	(86)	764

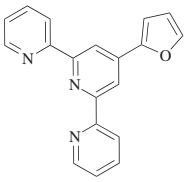
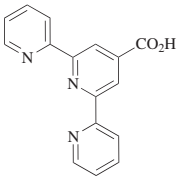
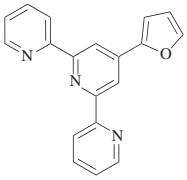
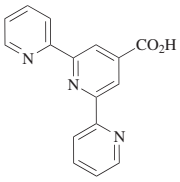
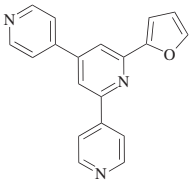
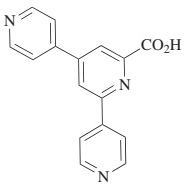
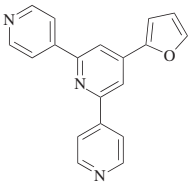
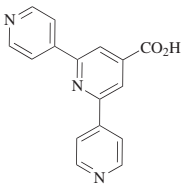
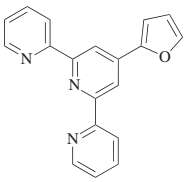
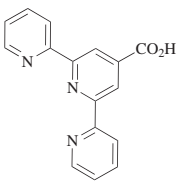
C_{19} 	$KMnO_4$ (4.0 eq), KOH, H_2O, pH 10, reflux, 2 h		(68)	766
	$KMnO_4$ (4.7 eq), py/H_2O (2:1), rt, 24 h		(78)	767
	$KMnO_4$, *t*-BuOH, H_2O		(89)	768
	$KMnO_4$, py/H_2O (2:1), 100°, 7 d		(82)	769
	$KMnO_4$ (6.4 eq), py/H_2O (2:1), rt, 48 h		(75)	770

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

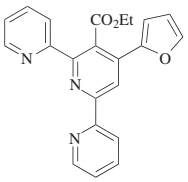
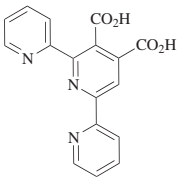
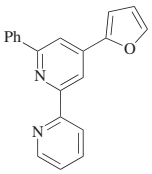
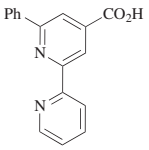
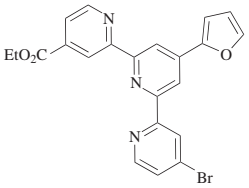
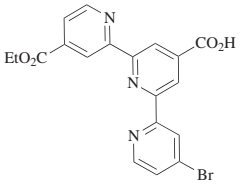
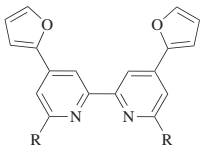
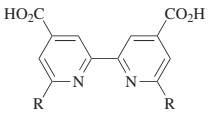
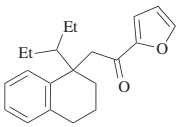
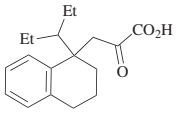
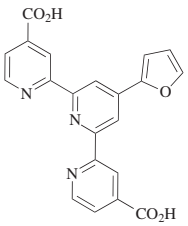
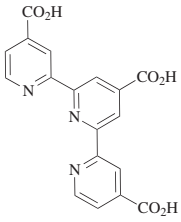
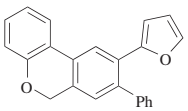
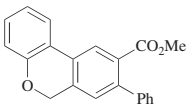
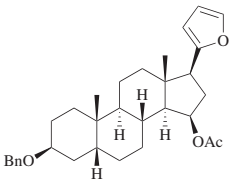
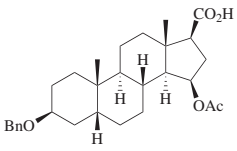
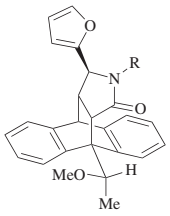
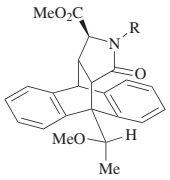
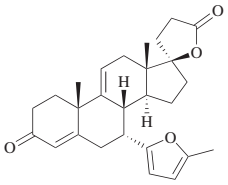
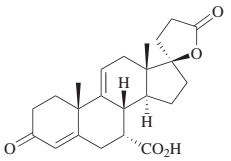
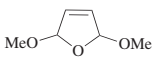
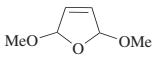
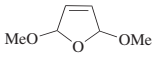
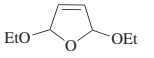
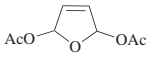
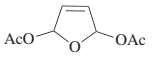
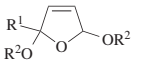
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{20}			
	$KMnO_4$ (4.7 eq), py/H_2O (2:1), rt, 24 h	 (68)	771
	$KMnO_4$ (1.2 eq), NaOH (aq), reflux, 2 h	 (40)	772
	1. $KMnO_4$ (5.5 eq), py/H_2O (2:1), rt 2. EtOH, rt	 (49)	773
C_{20-30}			
	$KMnO_4$ (13 eq), *t*-BuOH/H_2O (4.8:1), reflux, overnight	 R: Me (—); Ph (64)	774
C_{21}			
	1. O_3, MeOH, –78°, 1 h 2. Me_2S (29 eq), rt, 1 h	 (99)	421
	$KMnO_4$, NaOH (aq), rt, 24 h	 (93)	775
C_{23}			
	1. $RuCl_3$ (0.022 eq), $NaIO_4$ (4.1 eq), MeCN/CCl_4/H_2O (2:2:3), rt, 1 h 2. CH_2N_2, Et_2O	 (80)	776
	1. NBS, NaOAc, H_2O, dioxane 2. $KMnO_4$, $NaIO_4$, K_2CO_3, 18-crown-6	 (—)	387

TABLE 5. SYNTHESIS OF CARBOXYLIC ACIDS AND ESTERS (*Continued*)

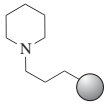
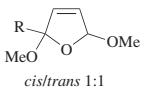
Furan	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{24} 	1. $RuCl_3$, $NaIO_4$, hexane, H_2O, rt, 10 min 2. $TMSCH_2N_2$, toluene, rt, 1 h		R Me (80) 4-$MeOC_6H_4$ (78) PMB (71)	777
C_{27} 	O_3, CH_2Cl_2, MeOH, −46°; then Me_2S (3.74 eq)		(82)	107

[a] The yield was determined by GC.

TABLE 6. SYNTHESIS OF 2,5-DIALKOXY-2,5-DIHYDROFURANS

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	Pt/Ni electrolyzer, 2 F/mol, NH_4Br (4.6 eq), MeOH, –22°, 7.5 h	 (85)	121
	–2e⁻, NH_4Br, MeOH, –22°, 16 h	 (73)	231
	Br_2 (1.0 eq), MeOH, –25°	 (77)	778
	H_2O_2 (2.0 eq), $VOSO_4$ (0.01 eq), H_2O, EtOH, rt, 6 h	 (12)	621
	Br_2, Ac_2O, KOAc, AcOH	 (83)	779
	Pt/C electrolyzer, –2e⁻, 2.5 F/mol, AcOH, NaOAc, MeCN, 7°	 (57)	279
$C_{4–5}$ 	Br_2 (1.0 eq), $CaCO_3$, R^2OH, –40°, 2 min		237

R^1	R^2	
H	Et	(79)
H	*n*-Pr	(42)
H	*n*-Pr	(65)
Me	Et	(66)
$HOCH_2$	Et	(49)
$(EtO)_2CH$	Et	(70)

$C_{4–6}$ 	 Pt–Pt, –2e⁻, 7 F/mol, MeOH	 *cis*/*trans* 1:1	616

R	
H	(78)
Me(OH)CH	(96)

TABLE 6. SYNTHESIS OF 2,5-DIALKOXY-2,5-DIHYDROFURANS (*Continued*)

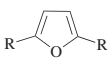
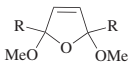
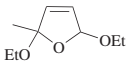
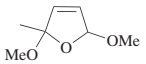
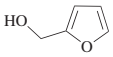
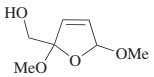
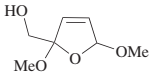
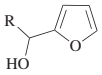
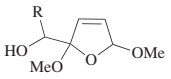
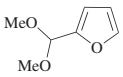
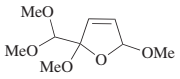
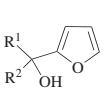
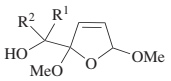
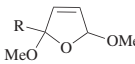
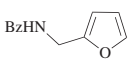
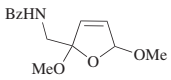
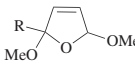
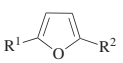
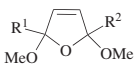
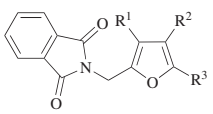
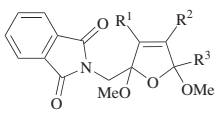
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-6} 	$PhI(OAc)_2$ (1.0 eq), $Mg(ClO_4)_2$ (2.0 eq), MeOH, rt, 2 h	 R: H (—); Me (—)	70
C_5 	Br_2, Na_2CO_3, EtOH	 (90)	780
	Anodic oxidation, 1.6 amp/h, –2e⁻, NH_4Br (0.06 eq), MeOH	 (49)	263
	Br_2 (1.09 eq), MeOH, Et_2O, –61°, 3 h	 (60)	781
	Br_2 (1.2 eq), $MeOH/Et_2O$ (3.6:1), –45°; then rt, 2 h	 (91)	244, 238, 236
C_{5-7} 	2.02 F/mol, Et_4NClO_4 (cat.), MeOH, rt, 10 min	 R: H (91); Me (95); Et (94)	782
C_5 	NBS (1.4 eq), NaOAc (2.4 eq), MeOH, 5°, 0.5 h	 (27)	256
C_{5-7} 	Br_2 (1.2 eq), MeOH/Et_2O (3.6:1), –35°, 0.5 h	 R^1 / R^2: H/H (73); H/$BnOCH_2$ (88); Me/H (92); *n*-BuO_2C/H (73); EtO_2C/EtO_2C (47); $AcOCH_2$/$AcOCH_2$ (64)	426, 427, 426, 426, 426, 426
C_5 	Pt–Ni, –2e⁻, H_2SO_4, MeOH, –15°	 R: MeO_2C (70); $PivOCH_2$ (91)	272
	Anodic oxidation, –2e⁻, NH_4Br (1.7 eq), MeOH, –12°, 7 h	 (40)	265
	Anodic oxidation, –2e⁻, 8 F/mol, NH_4Br (0.5 eq), Et_3N (0.27 eq), MeOH, 18–20°	 R: Me (82); $AcOCH_2$ (85); $AcHNCH_2$ (89)	278
C_{5-8} 	O_2, rose bengal (cat.), hν, MeOH; then V_2O_5 (0.005–0.01 eq), rt, 20 h	 R^1/R^2: H/Me (65); H/Et (50); Me/Me (72); H/$Ac(CH_2)_2$ (30)	328
	Br_2 (1.04 eq), $MeOH/CH_2Cl_2$ (1:13), –40 to –50°, 35 min; then –50 to –60°, 1 h	 R^1/R^2/R^3: H/H/H (73); H/Me/Me (80); Me/H/Me (71); H/Et/Me (98)	226, 245, 783, 226, 226

TABLE 6. SYNTHESIS OF 2,5-DIALKOXY-2,5-DIHYDROFURANS (*Continued*)

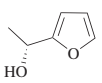
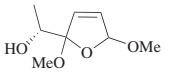
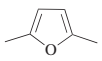
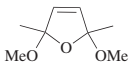
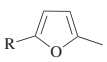
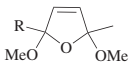
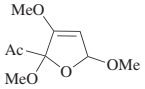
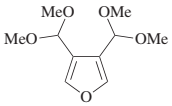
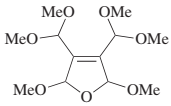
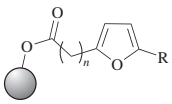
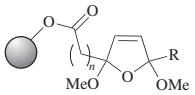
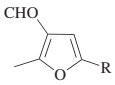
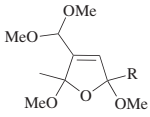
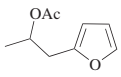
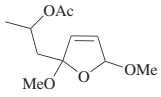
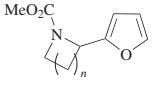
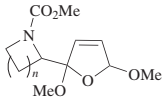
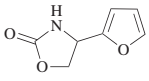
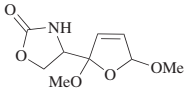
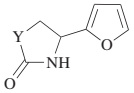
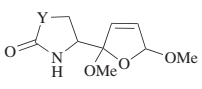
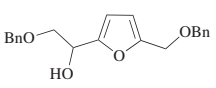
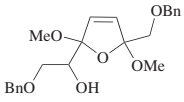
Furan	Conditions	Product(s) and Yield(s) (%)		Refs.
C_6 	Br_2 (1.03 eq), MeOH/Et_2O (2.8:1), –40°, 20 min		Temp (°) –40 (89) –35 (93)	242, 243 241
	Br_2, MeOH		(60)	140, 784
$C_{6–14}$ 	MMPP (2.0 eq), MeOH, rt, 15 h		R Me (95) n-C_6H_{13} (91) n-C_7H_{15} (93) n-C_8H_{17} (83) n-C_9H_{19} (95)	37
C_6 	Br_2 (1.1 eq), $NaHCO_3$ (2.2 eq), MeOH, –30°; then rt, 2 h		(75)	430
	Br_2 (1.0 eq), MeOH/Et_2O (2.8:1), –25°, 0.5 h; then –15°, 2 h; then rt, 20 h		(59)	253
$C_{6–8}$ 	–2e⁻, 50 F/mol, NH_4Br (0.12 eq), 1,4-dioxane, MeOH, 0°		n R 1 H (57) 1 Me (19) 2 H (100) 3 H (63)	617 617 785 617
$C_{6–7}$ 	Na, 3.74 amp/h, –2e⁻, H_2SO_4, MeOH, –30°		R H (38) MeO_2C (72)	266
C_7 	Br_2 (1.0 eq), $NaCO_3$ (2.0 eq), MeOH		(—)	248
$C_{7–8}$ 	Anodic oxidation, –2e⁻, NH_4Br (0.7 eq), MeOH		n 1 (95) 2 (83)	271
C_7 	Br_2, MeOH, Et_2O, –40°		(91)	567
$C_{7–9}$ 	Pt–Ni, –2e⁻, H_2SO_4, –15°		(85–95)	Y = O, CH_2, $(CH_2)_2$ 272
C_7 	Br_2 (1.2 eq), MeOH/Et_2O (1:1.33), –45°, 0.5 h		(94)	32

TABLE 6. SYNTHESIS OF 2,5-DIALKOXY-2,5-DIHYDROFURANS (*Continued*)

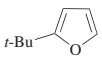
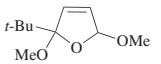
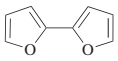
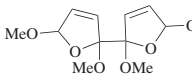
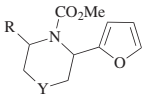
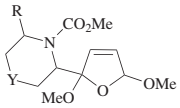
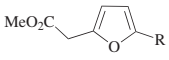
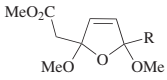
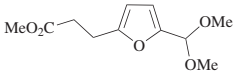
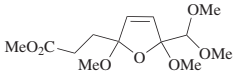
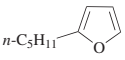
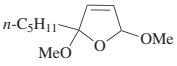
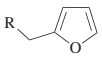
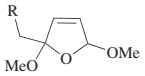
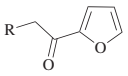
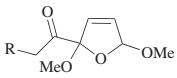
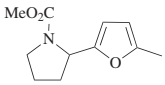
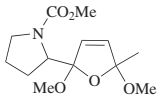
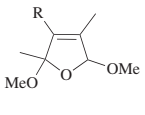
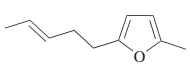
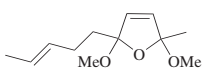
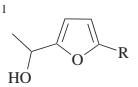
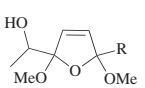
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	Anodic oxidation, –2e⁻, 4 F/mol, NH_4Br (0.4 eq), MeOH, –25°	 (76)	268
	Anodic oxidation, –2e⁻, 4 F/mol, NH_4Br (0.4 eq), MeOH, –25°	 (42)	268
$C_{8–10}$ 	Anodic oxidation, –2e⁻, NH_4Br, MeOH	 Y R (73) O H (80) CH H (87) CH Me	271
$C_{8–22}$ 	Br_2 (1.15 eq), Na_2CO_3 (4.2 eq), MeOH, rt, 1 h	 R Et (93)	252
		n-Bu (98)	252
		n-C_6H_{13} (96)	252
		n-$C_{16}H_{33}$ (84)	230, 229, 252, 251
C_8 	Br_2, $NaHCO_3$, MeOH	 (—)	250
C_9 	Br_2 (1.0 eq), Na_2CO_3 (4.0 eq), MeOH, –15°, 10 min	 (86)	228
$C_{9–11}$ 	Anodic oxidation, –2e⁻, 4 F/mol, NH_4Br (0.27 eq), MeOH, –30°	 R 2-thienyl (64) Ph (89)	270
$C_{9–23}$ 	Pt, –2e⁻, 3 F/mol, $LiClO_4$ (0.3 eq), MeOH, 45°, 0.5 h	 R *n*-C_3H_7 (81)	274
		n-C_5H_{11} (75)	
		n-C_7H_{15} (73)	
		n-C_9H_{19} (71)	
		n-$C_{11}H_{21}$ (81)	
		n-$C_{13}H_{27}$ (83)	
		n-$C_{15}H_{31}$ (80)	
		n-$C_{17}H_{35}$ (77)	
C_9 	Anodic oxidation, –2e⁻, NH_4Br, MeOH	 (96)	271
$C_{9–13}$ 	Pt, 2.78 F/mol, Et_3NClO_4 (0.25 eq), MeOH, rt, 4 h	 R allyl (93)	273
		Bn (85)	
		PMB (90)	
C_{10} 	Anodic oxidation, –2e⁻, NH_4Br, MeOH	 (71)	786
$C_{10–11}$ 	–2e⁻, NaBr, MeOH	 R *n*-C_4H_9 (—)	264
		n-C_5H_{11} (—)	

TABLE 6. SYNTHESIS OF 2,5-DIALKOXY-2,5-DIHYDROFURANS (*Continued*)

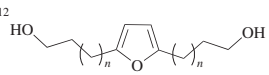
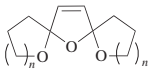
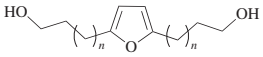
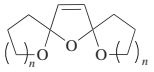
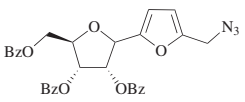
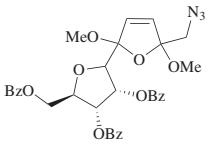
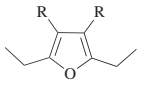
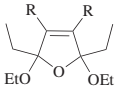
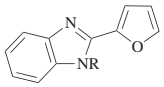
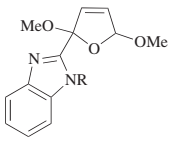
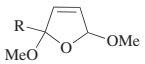
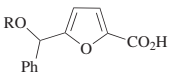
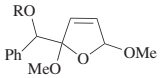
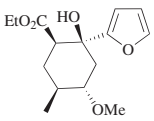
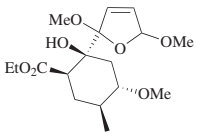
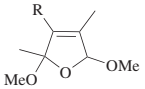
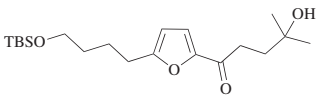
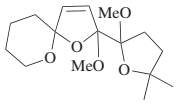
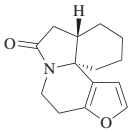
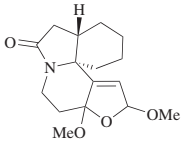
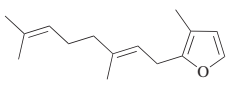
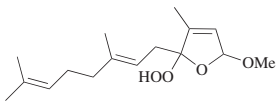
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10-12} 	O_2, methylene blue, hv, CH_2Cl_2, 0°, 2 min; then Me_2S (10 eq)	 *n* — 1 (80); 2 (77)	330
	NBS (1.2 eq), THF/H_2O (3:1), 0°, 20 min	 *n* — 1 (46); 2 (65)	120
C_{10} 	Br_2, $NaHCO_3$, MeOH	 (92)	787
C_{10-20} 	Br_2, Na_2CO_3, EtOH	 R — Me (94); Ph (73)	329
C_{11} 	Pt/Ni electrolyzer, $-2e^-$, 3–4 F/mol, NH_4Br (1.0 eq), MeOH, –15°	 R — H (70); Me (91)	269
C_{12-16} 	Br_2 (0.04 eq), Na_2CO_3 (1.8 eq), MeOH, –25°, 2 h	 R — *n*-C_8H_{17} (70); *n*-$C_{10}H_{21}$ (71); *n*-$C_{12}H_{25}$ (70)	232
C_{12} 	Br_2, Na_2CO_3, MeOH	 R — H (15); Me (73)	146
	Br_2, MeOH	 (—)	227
C_{13} 	Pt, 2.78 F/mol, Et_4NClO_4 (0.25 eq), MeOH, rt, 4 h	 R — Bn (74); PMB (77)	273
C_{14} 	Br_2, MeOH, Et_2O, –35°, 1 h	 (80)	254
	AcNHBr, MeOH, 0° to rt, 5 min	 (79)	214
C_{15} 	O_2, methylene blue, hv, MeOH, 1 min	 (—)	95

TABLE 6. SYNTHESIS OF 2,5-DIALKOXY-2,5-DIHYDROFURANS (*Continued*)

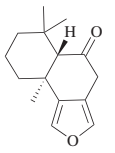
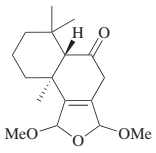
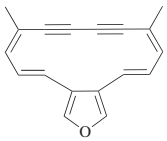
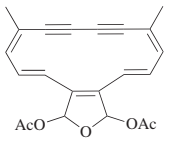
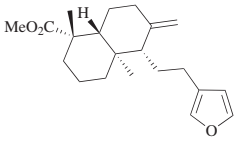
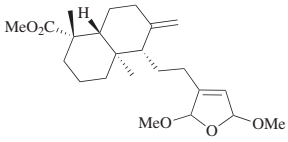
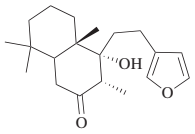
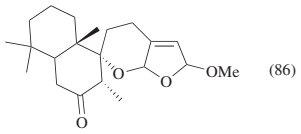
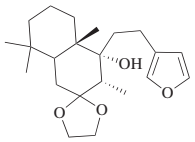
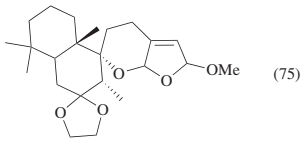
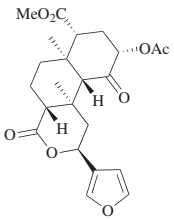
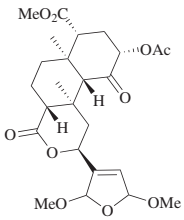
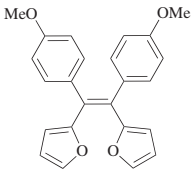
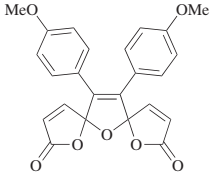
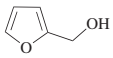
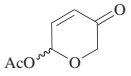
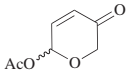
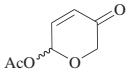
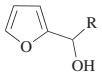
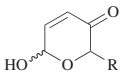
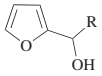
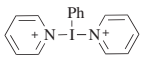
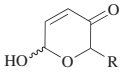
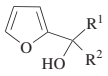
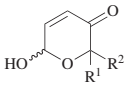
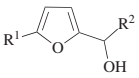
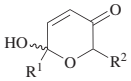
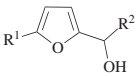
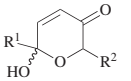
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	Br_2 (1.93 eq), Na_2CO_3 (0.67 eq), MeOH, –25 to 0°, 1 h	 (94)	276
C_{18} 	$Pb(OAc)_4$, AcOH, 20°, 0.5 h	 (—)	275
C_{20} 	NBS, MeOH, 0°, 10 min	 (85)	788
	(+)Pt–Ni(–), 2 F/mol, NH_4Br (4.6 eq), MeOH, –45°, 7 min	 (86)	121
	(+)Pt–Ni(–), 2 F/mol, NH_4Br (4.6 eq), MeOH, –22°, 7 min	 (75)	121
	Br_2, MeOH, CH_2Cl_2, –30°	 (84)	234, 235, 233
C_{22} 	O_2, rose bengal, hν, MeOH, 2 min; then silica gel	 (80)	96

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	NBS (1.05 eq), $NaHCO_3$ (2.0 eq), NaOAc (1.0 eq), THF/H_2O (4:1), 0°, 10 min; then Ac_2O (3.0 eq), 0° to rt, overnight	 (64)	614
	NBS, THF/H_2O (4:1), 0°, 0.5 h; then Ac_2O, py, DMAP, CH_2Cl_2	 (59)	460
	NBS, $NaHCO_3$, Ac_2O, MeOH, H_2O, 0° to rt, 18 h	 (55)	613
C_{5-8} 	2-$HO_2CC_6H_4CO_3H$, $CHCl_3$	 R: H (77); *i*-Pr (80)	789
C_{5-9} 	 $(TfO^-)_2$, (1.0 eq), MeCN, H_2O, pH 7, 10 min	 R: H (85); Me (85); *n*-Bu (80)	533
C_{5-7} 	Br_2 (1.0 eq), $NaHCO_3$ (2.0 eq), MeCN, H_2O, 0°, 10 min	 R^1 R^2: H H (86); H Me (82); H  (76); Me Me (78)	429
C_{5-6} 	H_2O_2 (1.25 eq), titanium silicalite, MeCN, 40°	 R^1 R^2 Time (h): H H 3.5 (99); H Me 6.5 (93); Me H 9.5 (79)	48
C_{5-16} 	O_2, TPP (cat.), hv, CH_2Cl_2, –70°, 2 h; then Ph_3P (1.0 eq), 10 min	 R^1 R^2: H H (95) —; H Me (90) 2:1; Me H (93) —; $HOCH_2$ H (85) —; $AcOCH_2$ H (90) —; $BzOCH_2$ H (90) —; H Et (90) 2:1; Me Me (89) 3:2; Et H (80) —; Et Me (70) 3:2; H Ph (65) 2:1; H *n*-$C_{11}H_{23}$ (80) 3:2	526

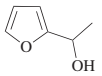
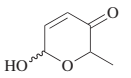
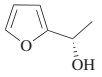
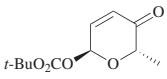
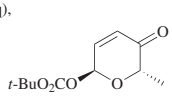
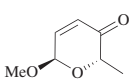
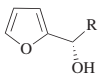
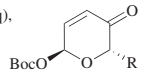
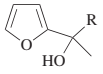
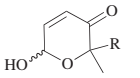
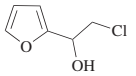
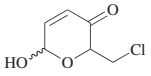
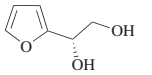
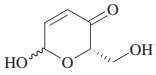
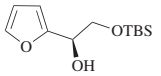
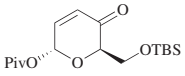
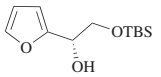
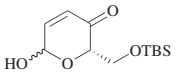
C_6 	Br_2, THF/H_2O, 5°	 (17)	526
	1. NBS, NaOAc, $NaHCO_3$, THF/H_2O, 0° 2. (*t*-BuCO)$_2$O, DMAP, CH_2Cl_2	 (54)	790
	1. NBS (1.05 eq), $NaHCO_3$ (2.0 eq), $NaOAc•3H_2O$ (1.0 eq), THF/H_2O (4:1), 0°, 1 h 2. (*t*-BuCO)$_2$O (1.5 eq), NaOAc (1.1 eq), 80°, 2 h	 (82)	499, 498
	Br_2, MeOH, Et_2O, –78°, 35 min	 (67)	791

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	1. NBS (1.05 eq), $NaHCO_3$ (2.0 eq), $NaOAc•3H_2O$ (1.0 eq), THF/H_2O (4:1), 0°, 1 h 2. $(t\text{-}BuCO)_2O$ (1.2 eq), DMAP (1.01 eq), –78°, 1 h	 R: Me (90); $TBSOCH_2$ (88); $BnOCH_2$ (48)	467, 792 467, 793 794
$C_{6–18}$ 	NBS (1.18 eq), THF/H_2O (4:1), 0°	 R: H (65); 4-$PhSC_6H_4$ (78); 4-$PhSOC_6H_4$ (67); 4-$PhSO_2C_6H_4$ (69)	435, 434
	*m*-CPBA, CH_2Cl_2, 0°, 3 h	 (70)	795
	O_2, TPP, MeOH, CH_2Cl_2; then Me_2S	 (93)	527
	1. NBS 2. PivCl, DMAP	 (57)	497
	NBS (1.0 eq), $NaOAc•3H_2O$ (1.0 eq), $NaHCO_3$ (2.0 eq), THF/H_2O (4:1), 0°, 1 h	 (95)	481, 580, 579, 793

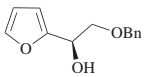
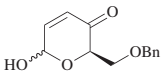
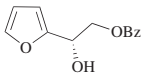
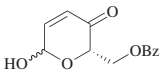
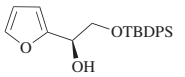
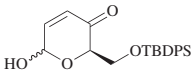
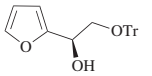
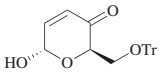
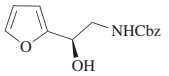
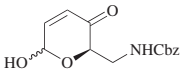
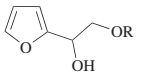
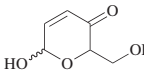
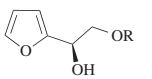
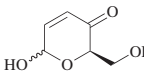
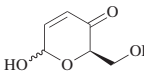
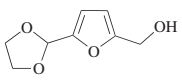
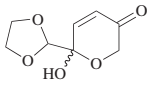
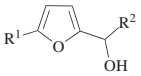
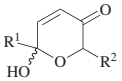
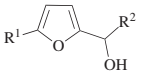
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	Br_2, $MeCN/H_2O$	 (89)	497
	Br_2, $MeCN/H_2O$	 (80)	796
	NBS, NaOAc, THF/MeOH	 (97)	797
	NBS (1.2 eq), NaOAc (1.0 eq), THF/H_2O (4:1)	 (80)	440
	NBS (1.0 eq), $NaOAc•3H_2O$ (1.0 eq), $NaHCO_3$ (2.0 eq), THF/H_2O (4:1)	 (82)	464, 611
	*m*-CPBA, CH_2Cl_2	 R: H (70); Tr (80)	440
	NBS (1.0 eq), $NaOAc•3H_2O$ (1.0 eq), $NaHCO_3$ (2.0 eq), THF/H_2O (4:1), 0°, 1 h	 R: TBS (95); Piv (95)	466
	NBS (1.0 eq), $NaOAc•3H_2O$ (1.0 eq), $NaHCO_3$ (2.0 eq), THF/H_2O (4:1), 0°, 1 h	 R: TBS (92); Bn (—)	583, 468, 798, 471, 465, 799 794

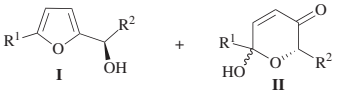
TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	*m*-CPBA, CH_2Cl_2	 (—)	800
C_{6-16} 	$PhI(OAc)_2$ (1.0 eq), $MeCN/H_2O$ (1:1), pH 7, 24 h		533

R^1	R^2	Temp	
H	Me	50°	(30)
Me	Me	rt	(50)
Me	Et	rt	(50)
H	*n*-Bu	50°	(30)
Me	*n*-Bu	rt	(50)
Me	*n*-$C_{10}H_{21}$	rt	(70)

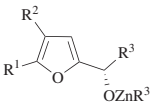
C_{6-11} 

t-BuOOH (0.6 eq), $Ti(Oi\text{-}Pr)_4$ (1.2 eq), L-(+)-DIPT (1.25 eq), –21°

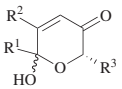


I + **II**

R^1	R^2	Time (h)	**I**	**I** er	**II**	
H	Me	24	(32)	>97.5:2.5	(53)	514
H	EtO_2CCH_2	24	(45)	>97.5:2.5	(42)	801
H	*i*-Pr	25	(39)	>97.5:2.5	(55)	514
H	*t*-Bu	40	(41)	53.0:47.0	(58)	514
H	*n*-C_5H_{11}	25	(42)	>97.5:2.5	(53)	514
H	Ph	40	(42)	>99.5:0.5	(44)	514
Me	*n*-C_5H_{11}	6	(40)	>97.5:2.5	(55)	514

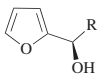
C_{6-9} 

NBS (1.1 eq), THF/H_2O (4:1) rt, 4 h

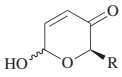


R^1	R^2	R^3	
H	H	Me	(70)
H	H	Et	(73)
Me	H	Et	(71)
Me	Me	Me	(46)
Et	H	Me	(76)
$TBSOCH_2$	H	Et	(72)
H	H	$TBSO(CH_2)_4$	(61)
Me	Me	Et	(63)
Et	H	Et	(77)

474

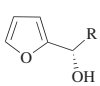
C_{7-11} 

NBS, $NaHCO_3$, THF, H_2O

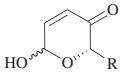


R	
Et	(42)
allyl	(52)
n-Bu	(46)
c-C_6H_{11}	(52)

513

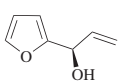
C_{7-9} 

NBS, NaOAc, $NaHCO_3$, THF, H_2O, 0°, 1 h

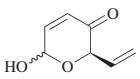


R	
Et	(88)
n-Pr	(84)
i-Pr	(87)
i-Bu	(79)

802

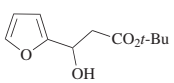
C_7 

NBS, THF/H_2O (4:1), 0°, 0.5 h

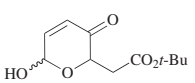


(97)

476



NBS (1.05 eq), $NaHCO_3$ (2.0 eq), $NaOAc•3H_2O$ (1.0 eq), THF/H_2O (4:1), 0°, 10 min



(97)

581, 612, 803

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

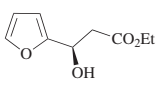
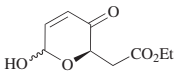
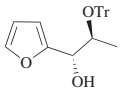
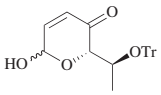
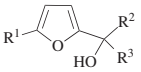
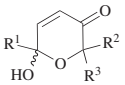
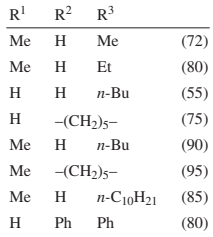
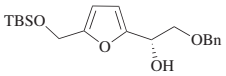
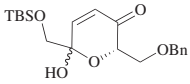
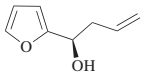
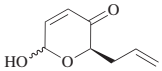
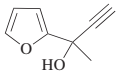
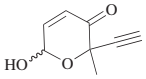
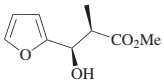
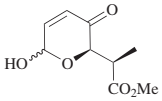
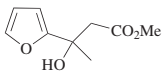
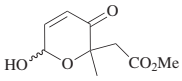
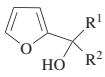
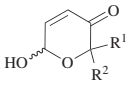
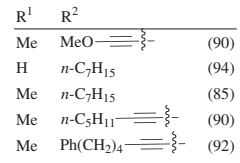
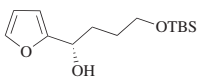
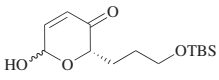
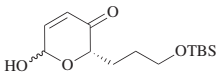
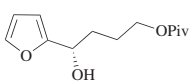
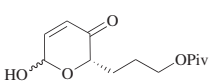
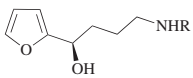
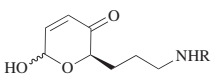
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	NBS (1.0 eq), $NaOAc•3H_2O$ (1.0 eq), $NaHCO_3$ (2.0 eq), THF/H_2O (4:1), 0°, 1 h	 (96)	804, 801
	Br_2, Na_2CO_3, MeOH	 (93)	805
$C_{7–17}$ 	$PhI(OAc)_2$ (1.0 eq), $Mg(ClO_4)_2$, $MeCN/H_2O$ (1:1), 24 h	 	70, 533
C_7 	NBS, THF/H_2O, 0°	 (—)	806
C_8 	*t*-BuOOH, $VO(acac)_2$, CH_2Cl_2, rt, 3 h	 (91)	476
	*m*-CPBA, CH_2Cl_2	 (43)	807
	Br_2 (2.1 eq), MeOH, $CHCl_3$, –78°, 1 h	 (80)	428
	*m*-CPBA, CH_2Cl_2, 6 h, 0°	 (—)	808
$C_{8–18}$ 	NBS, THF/H_2O (4:1), 0°	 	479
C_8 	NBS (1.0 eq), $NaOAc•3H_2O$ (1.0 eq), $NaHCO_3$ (2.0 eq), THF/H_2O (4:1), 0°, 30 min	 (84)	463, 469
	m-CPBA, CH_2Cl_2	 (96)	809
	NBS, NaOAc, $NaHCO_3$, THF/H_2O, 0°, 1 h; then Me_2S, 0°, 5 min	 (—)	810
	NBS (1.1 eq), THF/H_2O (1:1), rt, 4 h	 	473 473, 474, 475

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

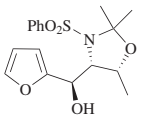
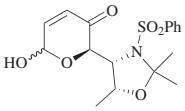
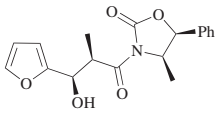
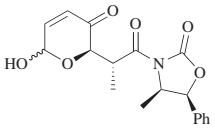
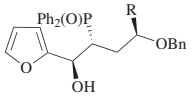
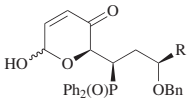
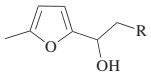
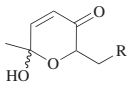
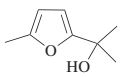
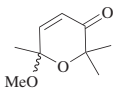
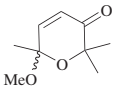
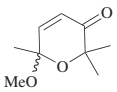
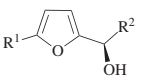
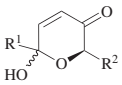
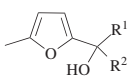
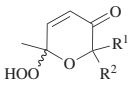
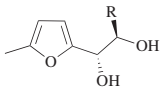
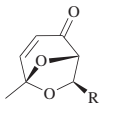
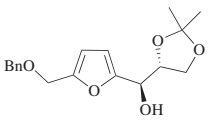
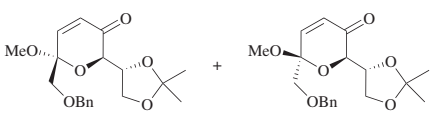
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	*m*-CPBA, CH_2Cl_2	 (98)	811
	Br_2 (1.2 eq), MeCN/H_2O (11:1), –20°, 1 h	 (95)	431
$C_{8–12}$ 	*m*-CPBA (1.0 eq), CH_2Cl_2, 0°, 2 d	 R: H (95); *n*-Bu (65)	812
$C_{8–14}$ 	O_2, rose bengal, hv, MeOH, 5°, 4 min; then Me_2S (3.0 eq), CH_2Cl_2, rt, 15 h	 R: EtO_2C (91); Bz (92)	682
C_8 	*t*-BuOOH (2.5 eq), $VO(acac)_2$ (0.015 eq), CH_2Cl_2; then $CH(OMe)_3$ (1.2 eq), BF_3•Et_2O (0.05 eq)	 (90)	521
	O_2, hv, H_2O, 5°, 0.5 h	 (71)	813
	O_2, rose bengal, hv, MeOH, 5°, 4 min; then Me_2S (3.0 eq), CH_2Cl_2, rt, 15 h	 (80)	682
$C_{8–11}$ 	*t*-BuOOH (1.5 eq), $VO(acac)_2$ (0.1 eq), CH_2Cl_2, 0°, 14 h; then Me_2S (1.5 eq), 0°, 30 min	 R^1 / R^2: H, *i*-Pr (85); H, n-C_5H_{11} (90); H, Ph (88); Me, n-C_5H_{11} (93)	520
$C_{8–15}$ 	30% H_2O_2 (1.0 eq), PTSA (0.43 eq), DME, rt	 R^1 / R^2 / Time (h): Me, Me, 7 (77); H, *i*-Pr, 16 (64); H, n-C_6H_{13}, 18 (75); H, c-C_6H_{11}, 23 (77); Et, n-C_6H_{13}, 5 (65); H, n-C_8H_{17}, 20 (65)	531
$C_{8–13}$ 	O_2, rose bengal, hv, MeOH, 5°, 4 min; then Me_2S (3.0 eq), CH_2Cl_2, rt, 15 h	 R: MeO_2C (74); Ph (60)	813, 682; 682
C_8 	1. *t*-BuOOH, $VO(acac)_2$, CH_2Cl_2, rt, 6 h 2. Ag_2O, MeI, rt, 2 h	 **I** + **II** (75), **I**/**II** = 4.5:1	488

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

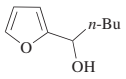
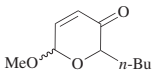
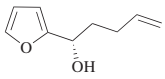
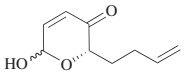
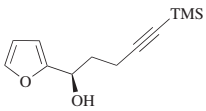
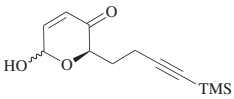
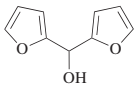
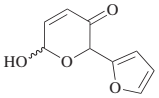
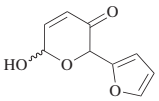
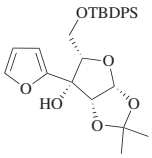
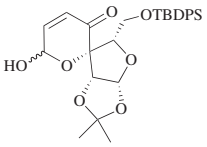
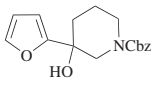
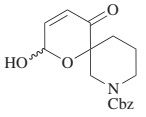
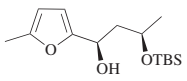
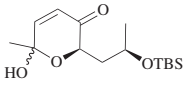
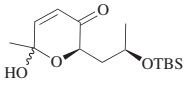
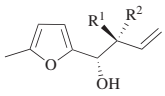
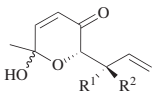
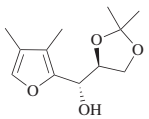
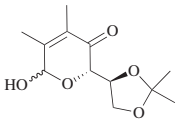
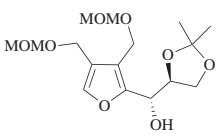
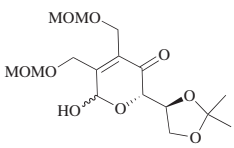
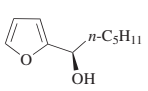
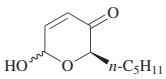
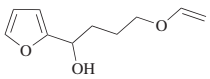
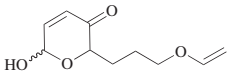
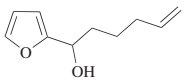
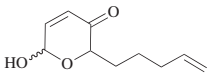
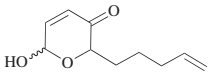
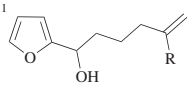
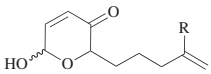
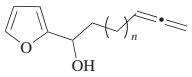
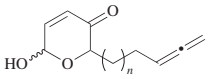
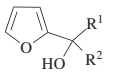
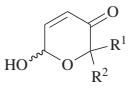
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	1. *t*-BuOOH (2.5 eq), $VO(acac)_2$ (0.015 eq) 2. $CH(OMe)_3$ (1.2 eq), BF_3•Et_2O (0.05 eq)	 (89)	521
	*t*-BuOOH (1 eq), $VO(acac)_2$ (0.01 eq), CH_2Cl_2, rt, 1 h	 (83)	506, 519, 474, 504
	NBS, NaOAc, THF/H_2O	 (98)	814, 815
	*m*-CPBA, CH_2Cl_2, 0°	 (48)	40
	NBS (1.0 eq), $NaOAc•3H_2O$ (1.0 eq), $NaHCO_3$ (2.0 eq), THF/H_2O (4:1), 0°, 3 h	 (44)	40
	NBS (1.0 eq), THF/H_2O (4:1), 0°, 5 min	 (85)	482
	*m*-CPBA, CH_2Cl_2, 0°	 (82)	316
	HCl	 (85)	445
	m-CPBA, CH_2Cl_2	 (65)	445
$C_{9–11}$ 	NBS (1.0 eq), THF/H_2O (4:1), 0°		R^1 R^2 H H (94) Me H (74) Me Me (45)	817
C_9 	NBS (1.0 eq), THF/H_2O (4:1), rt, 4 h	 (84)	818
	NBS, NaOAc, THF/H_2O, 0°, 0.5 h	 (90)	819

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	*t*-BuOOH, $VO(acac)_2$	 (78)	497
	O_2, rose bengal, hν, MeOH, CH_2Cl_2, –78°, 2 h; then Me_2S, CH_2Cl_2, 0°, 0.5 h	 (—)	820
	*m*-CPBA (1.0 eq), CH_2Cl_2, 5–10°, 30 min; then rt, 2 h	 (80)	821
	t-BuOOH (1.5 eq), $VO(acac)_2$ (0.1 eq), CH_2Cl_2, 0°, 3 h	 (—)	822
$C_{10–11}$ 	O_2, rose bengal, hν, MeOH/ CH_2Cl_2 (1:2), –60°, 8 h; then Me_2S (2.0 eq), –60° to rt	 R: H (95); Me (83)	525
	*t*-BuOOH (1.5 eq), $VO(acac)_2$ (0.1 eq), CH_2Cl_2, 0°, 1 h	 *n*: 1 (75); 2 (80)	823
$C_{10–13}$ 	*m*-CPBA (1.1 eq), CH_2Cl_2, –10° to rt, 3 h	 R^1 / R^2: –$(CH_2)_5$– (79); Me / Ph (81); Me / PMP (85); MeO_2CCH_2 / Ph (—)	437 437 437 824

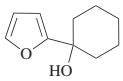
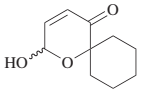
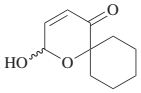
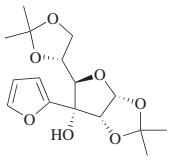
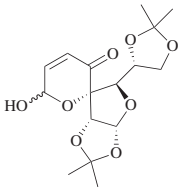
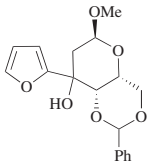
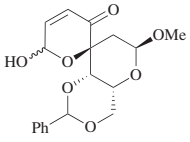
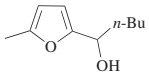
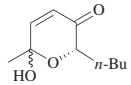
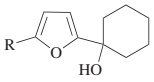
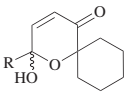
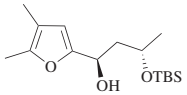
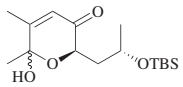
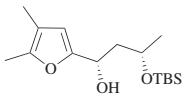
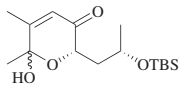
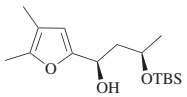
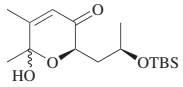
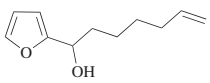
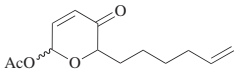
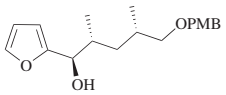
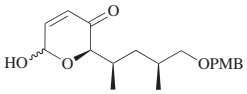
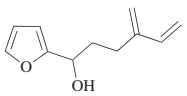
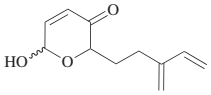
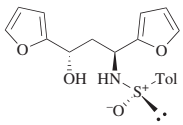
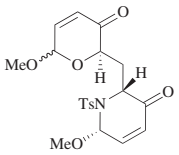
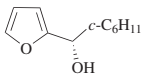
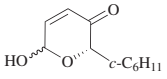
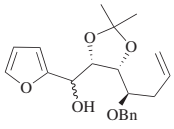
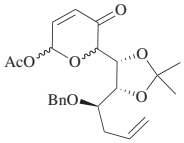
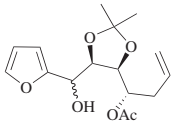
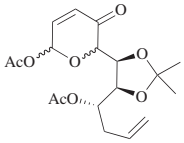
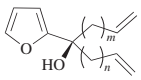
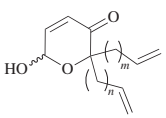
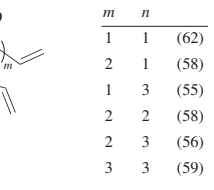
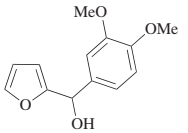
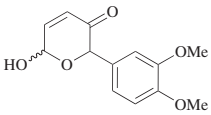
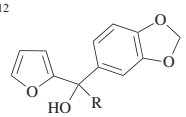
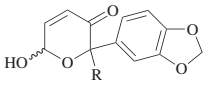
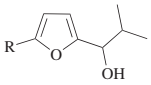
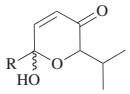
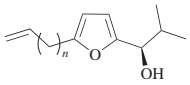
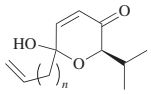
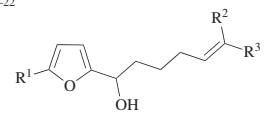
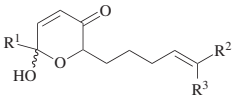
C_{10} 	*m*-CPBA (1.45 eq), CH_2Cl_2, 7–15°; then rt, 3 h	 (79)	239
	NBS (1.0 eq), THF/H_2O (4:1), 0°	 (76)	435
	NBS (1.0 eq), THF/H_2O (4:1), –5°, 5 min	 (85)	482
	*m*-CPBA, CH_2Cl_2, 0°	 (—)	454
	O_2, H_2O, 5°, 0.5 h	 (74)	813

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

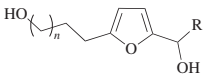
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10-11}			
	$PhI(OAc)_2$ (1.0 eq), MeCN/H_2O (1:1), pH 7, 24 h	 R = H, 50°, (40); R = Me, rt, (76)	533
C_{10}			
	*m*-CPBA (2.0 eq), CH_2Cl_2, 0°, 1 h	 (96)	453, 445
	*m*-CPBA (2.0 eq), CH_2Cl_2, 0°, 1 h	 (89)	453
	*m*-CPBA, CH_2Cl_2	 (90)	445
C_{11}			
	1. O_2, rose bengal, hν, CH_2Cl_2/MeOH (3:1), –78°, 2 h; then Me_2S, 0°, 5 h 2. Ac_2O, DMAP, py, CH_2Cl_2, 0°, 3 h	 (66)	820
	NBS (1.0 eq), $NaOAc•3H_2O$ (1.0 eq), $NaHCO_3$ (2.0 eq), THF/H_2O (4:1), 0° to rt	 (90)	825
	O_2, rose bengal, hν, MeOH, CH_2Cl_2; then Me_2S	 (82)	826, 447
	NBS (1.2 eq), $NaOAc•3H_2O$ (1.4 eq), THF/H_2O (1:1), 0°, 1 h; then $CH(OMe)_3$ (2.0 eq), $BF_3•Et_2O$ (0.05 eq)	 (29) dr 66:34	562, 563
	NBS (1.0 eq), THF/H_2O (4:1), rt, 4 h	 (94)	725, 726
	*t*-BuOOH (1.2 eq), $VO(acac)_2$ (0.6 eq), CH_2Cl_2, –20°, 5 h; then Ac_2O, DMAP (cat.), py, CH_2Cl_2, 0°, 1 h	 (88)	501, 500
	1. *t*-BuOOH, $VO(acac)_2$, CH_2Cl_2, –20°, 5 h 2. Ac_2O, py, DMAP, CH_2Cl_2, 0°, 1 h	 (—)	501
C_{11-15}			
	*m*-CPBA, CH_2Cl_2, 0°, 1.5 h	 	448

m	*n*	
1	1	(62)
2	1	(58)
1	3	(55)
2	2	(58)
2	3	(56)
3	3	(59)

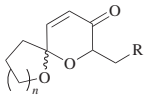
TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	*m*-CPBA, CH_2Cl_2	 (79)	827
$C_{11–12}$ 	*m*-CPBA, CH_2Cl_2	 R: H (72); Me (73)	828
	*m*-CPBA (1.1 eq), CH_2Cl_2, 0°, 1 h	 R: $TBSO(CH_2)_3$ (88); $TBSO(CH_2)_4$ (90)	441
$C_{11–14}$ 	*m*-CPBA (1.1 eq), CH_2Cl_2, 0° to rt	 *n*: 1 (81); 2 (77); 3 (96); 4 (75)	486
$C_{11–22}$ 	*t*-BuOOH (1.5 eq), $VO(acac)_2$ (0.1 eq), CH_2Cl_2, 0°, 1 h		

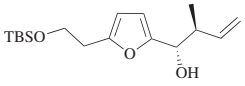
R^1	R^2	R^3		
H	H	Me	(69)	823, 822
$TBSOCH_2$	H	Me	(80)	823
Ph	Me	H	(63)	823
Ph	Me	MeO_2C	(83)	823
Ph	Ph	H	(70)	823

$C_{11–14}$ 

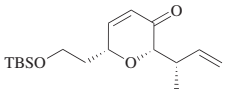
1. NBS (1.0 eq), $NaOAc•3H_2O$ (1.0 eq), $NaHCO_3$ (2.0 eq), THF/H_2O (4:1), 0°, 0.5 h
2. Amberlyst 15, CH_2Cl_2, rt, 0.5 h



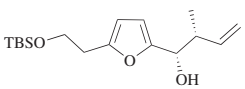
n	R		
1	*i*-Pr	(87)	829
1	allyl	(93)	
1	(*E*)-MeCH=CH	(54)	
1	$TBDPSO(CH_2)_3$	(70)	
1	Ph	(56)	
2	*i*-Pr	(84)	

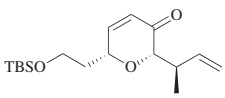
C_{11} 

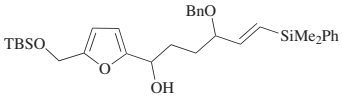
t-BuOOH (1.7 eq), $VO(acac)_2$ (0.1 eq), CH_2Cl_2, 0° to rt; then Et_3SiH (5.0 eq), TFA, CH_2Cl_2, –40°, 15 h

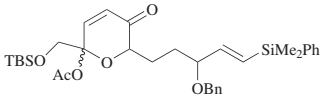
 (86) dr >20:1 505

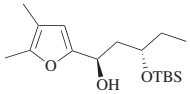
t-BuOOH (1.7 eq), $VO(acac)_2$ (0.1 eq), CH_2Cl_2, 0° to rt; then Et_3SiH (5.0 eq), TFA, CH_2Cl_2, –40°, 15 h

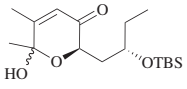


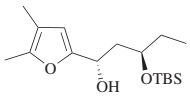
 (90) 505

 *m*-CPBA (1.0 eq), CH_2Cl_2, 0°, 1 h; then Ac_2O, $(i\text{-Pr})_2EtN$, DMAP (cat.)

 (72) 450

 *m*-CPBA (1.0 eq), CH_2Cl_2, 0°, 1 h

 (89) 830

 *m*-CPBA (1.0 eq), CH_2Cl_2, 0°, 1 h

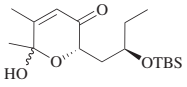
 (90) 830, 831

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

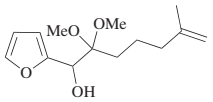
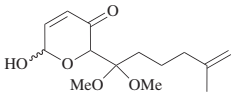
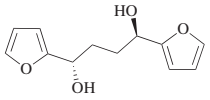
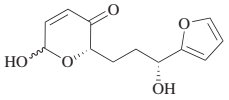
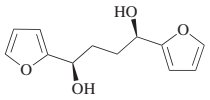
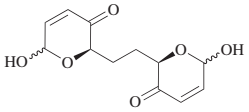
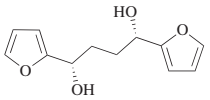
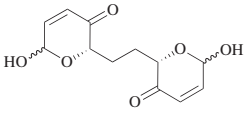
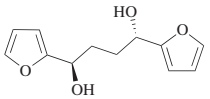
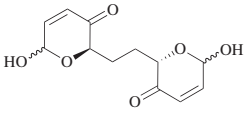
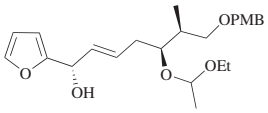
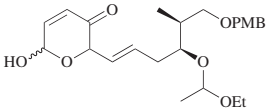
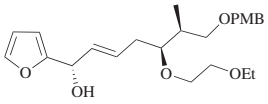
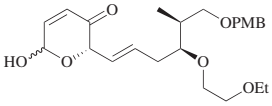
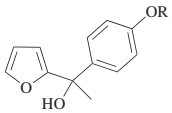
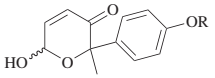
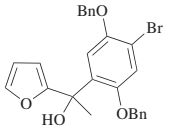
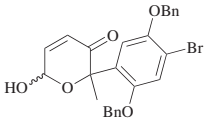
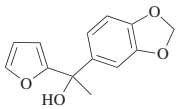
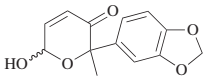
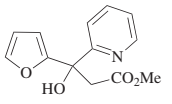
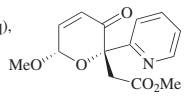
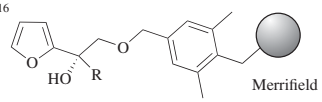
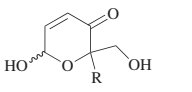
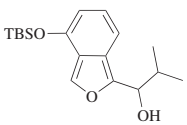
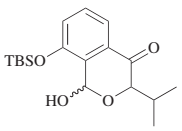
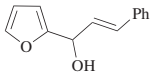
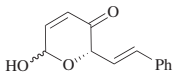
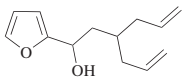
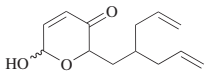
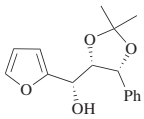
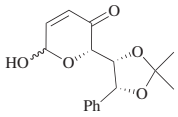
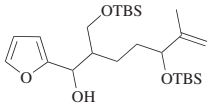
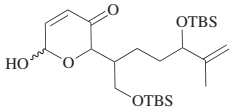
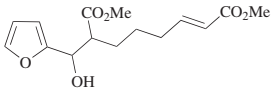
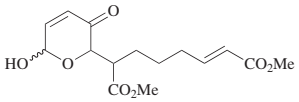
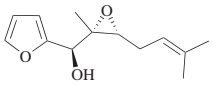
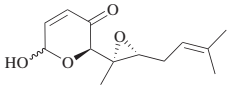
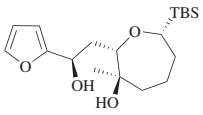
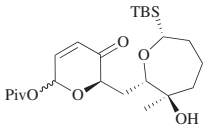
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12} 	O_2, rose bengal, hv, MeOH, CH_2Cl_2; then Me_2S	 (90)	832
	*t*-BuOOH (1.2 eq), (+)-L-DET (1.2 eq), $Ti(Oi\text{-}Pr)_4$ (1.0 eq), –40°, 2 h	 (79)	523
	*t*-BuOOH (2.5 eq), $VO(acac)_2$ (0.05 eq), CH_2Cl_2, rt, 6 h	 (95)	511, 510
	*t*-BuOOH (2.5 eq), $VO(acac)_2$ (0.015 eq), CH_2Cl_2, rt, 7 h	 (82)	40
	*t*-BuOOH (2.5 eq), $VO(acac)_2$ (0.015 eq), CH_2Cl_2, rt, 7 h	 (89)	40
	NBS, $NaHCO_3$, H_2O	 (—)	833
	NBS (1.2 eq), $NaHCO_3$ (1.9 eq), NaOAc (0.9 eq), THF/H_2O (4:1), 0°, 1 h	 (—)	834
	*m*-CPBA, CH_2Cl_2, rt, overnight	 R: Me (—), Bn (—)	835
	*m*-CPBA (1.1 eq), CH_2Cl_2, rt, overnight	 (58)	436
	NBS (1.0 eq), THF/H_2O (4:1), reflux, 5 min	 (77)	435
	1. NBS (1.35 eq), $NaHCO_3$ (2.1 eq), $NaOAc{\bullet}3H_2O$ (1.56 eq), THF/H_2O (4:1), 0°, 0.5 h 2. Ag_2O (1.0 eq), MeI (15.0 eq)	 (69)	808
C_{12-16}  Merrifield	NBS (1.2 eq), THF/H_2O (4:1), 0° to rt, 1 h	 R: Ph (95), $n\text{-}C_{10}H_{21}$ (85)	480
C_{12} 	*m*-CPBA, CH_2Cl_2, 0°, 2 h	 (—)	833

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}			
	*t*-BuOOH (0.6 eq), (+)-L-DIPT (0.3 eq), $Ti(Oi\text{-}Pr)_4$ (0.2 eq), 4 MS, CH_2Cl_2, –30°, 24 h	 (35)	836, 524
	*t*-BuOOH (1.78 eq), $VO(acac)_2$ (0.02 eq), CH_2Cl_2, 0°, 1 h	 (85)	823
	*t*-BuOOH, $VO(acac)_2$, CH_2Cl_2, 0°	 (84)	487, 578
	O_2, rose bengal, hv, MeOH, CH_2Cl_2; then Me_2S	 (—)	528
	NBS (1.1 eq), $NaHCO_3$ (2.0 eq), NaOAc (1.0 eq), THF/H_2O (4:1), 0°, 10 min	 (77)	581
	*m*-CPBA (1.1 eq), CH_2Cl_2, 0°, 22 h	 (51)	449
	NBS (1.17 eq), NaOAc (1.33 eq), THF/H_2O (1:1); then PivCl (1.5 eq), DMAP (0.17 eq), Et_3N (4.0 eq), CH_2Cl_2	 (57) dr 70:30	575

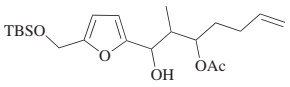
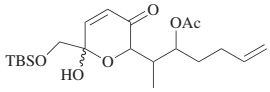
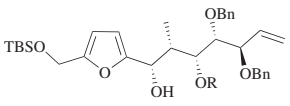
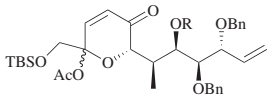
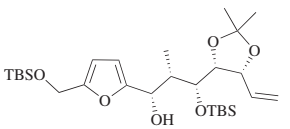
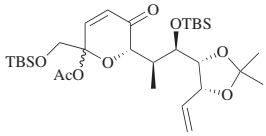
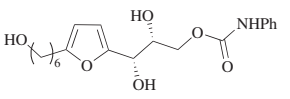
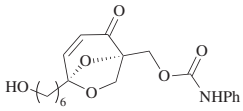
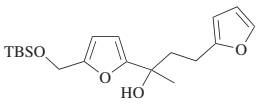
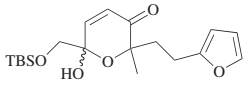
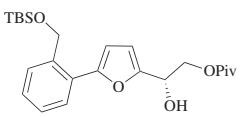
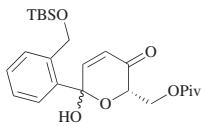
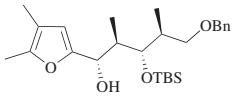
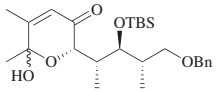
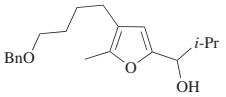
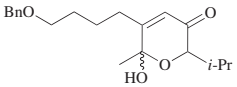
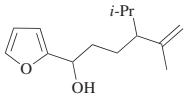
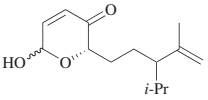
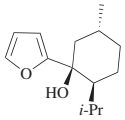
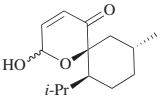
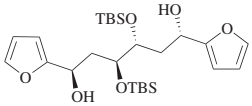
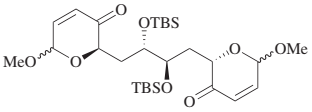
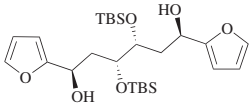
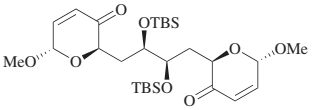
	*m*-CPBA, CH_2Cl_2	 (—)		837
	1. *t*-BuOOH (1.5 eq), $VO(acac)_2$ (0.01 eq), CH_2Cl_2, 0° to rt, 1 h 2. Ac_2O (1.0 eq), DMAP (0.5 eq), py (2.5 eq), rt, 4 h		R Ac (56) TBS (93)	496
	1. *t*-BuOOH (1.5 eq), $VO(acac)_2$ (0.01 eq), CH_2Cl_2, 0° to rt, 1 h 2. Ac_2O (1.0 eq), DMAP (0.5 eq), py (2.5 eq), rt, 4 h	 (71)		496
	NBS (34.6 eq), $NaHCO_3$ (104 eq), NaOAc (52 eq), THF/H_2O (4:1), rt, 1 h; then PPTS, CH_2Cl_2, 40–45°, 20 h	 (33)		151, 153
	*t*-BuOOH, $VO(acac)_2$, CH_2Cl_2, rt, 3 h	 (80)		838
	NBS (1.08 eq), $NaHCO_3$ (20 eq), $NaOAc \cdot 3H_2O$ (1.0 eq), THF/H_2O (4:1), 0°, 2 h	 (72)		472

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}			
	*m*-CPBA (1.0 eq), CH_2Cl_2, 0°, 30 min	 (90)	442
	*m*-CPBA (1.0 eq), CH_2Cl_2, 0° to rt, 0.5 h	 (84)	444
C_{14}			
	*t*-BuOOH, $VO(acac)_2$, CH_2Cl_2	 (71)	503
	*m*-CPBA (1.0 eq), CH_2Cl_2, 0°	 (74)	452
	1. *t*-BuOOH (3.25 eq), $VO(acac)_2$ (0.02 eq), CH_2Cl_2 2. $CH(OMe)_3$, (74 eq), BF_3•Et_2O (0.1 eq)	 (93)	523
	1. *t*-BuOOH (3.25 eq), $VO(acac)_2$ (0.02 eq), CH_2Cl_2 2. $CH(OMe)_3$, (74 eq), BF_3•Et_2O (0.1 eq)	 (52)	512

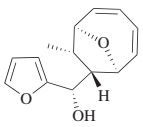
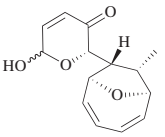
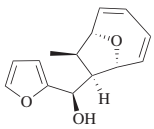
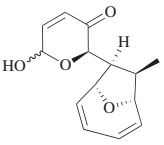
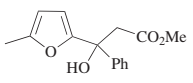
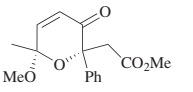
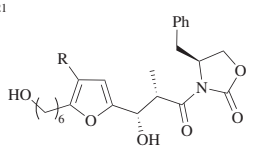
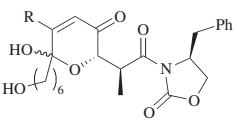
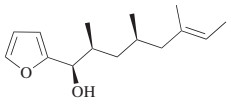
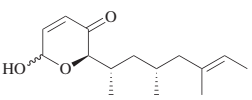
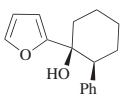
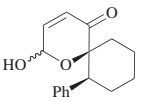
	*t*-BuOOH (6.0 eq), $VO(acac)_2$ (0.015 eq), CH_2Cl_2, 0°, 3 h	 (90)	507
	*t*-BuOOH (3.0 eq), $VO(acac)_2$ (0.02 eq), CH_2Cl_2, 0°, 3.5 h	 (76)	495
	1. *m*-CPBA (1.6 eq), CH_2Cl_2, 0°, 6 h 2. Ag_2O (1.0 eq), MeI (15 eq)	 (77)	808
C_{14-21}			
	NBS (34.6 eq), $NaHCO_3$ (104 eq), NaOAc (52 eq), THF/H_2O (4:1), rt, 1 h; then PPTS, CH_2Cl_2, 40–45°, 2 h		R: H (100); Br (100); 4-MeC_6H_4 (100) — 151
C_{15}			
	*t*-BuOOH, $VO(acac)_2$ (0.05 eq), CH_2Cl_2, 0°; then 0° to rt, 0.67 h	 (69)	839
	*m*-CPBA, CH_2Cl_2, 10°, 4 h	 (—)	455

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

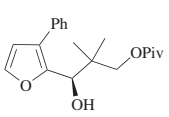
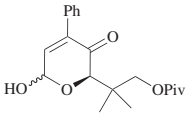
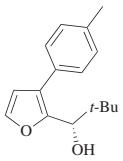
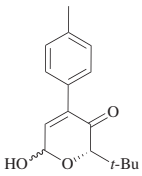
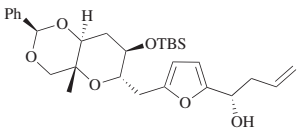
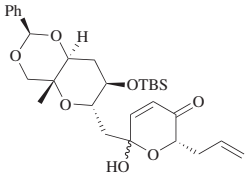
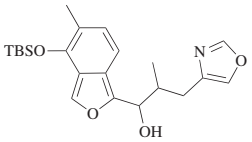
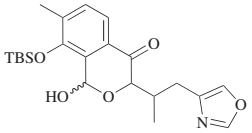
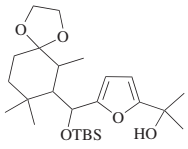
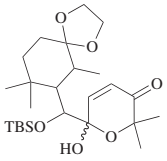
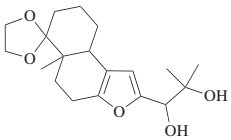
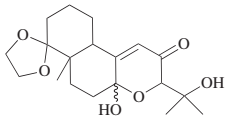
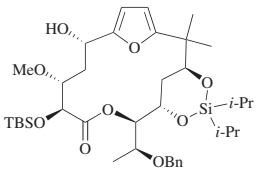
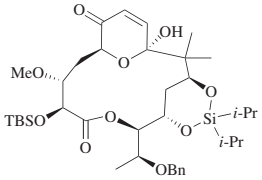
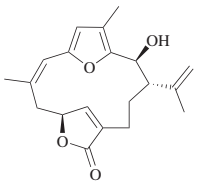
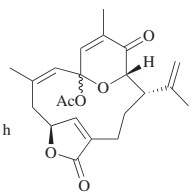
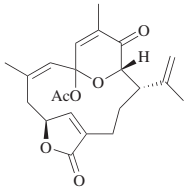
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	NBS (2.86 eq), EtOAc, reflux, 4 h	 (82)	610
C_{16} 	*m*-CPBA (2.0 eq), CH_2Cl_2, 0°; then rt, 1 h	 (91)	840
	$NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, $CHCl_3/H_2O$/pH 4.0 buffer/ *t*-BuOH (1:1:2:1), 40°, 7 h	 (58)	535
	*m*-CPBA (1.1 eq), CH_2Cl_2, 0°, 2 h	 (94)	841
C_{17} 	*m*-CPBA, CH_2Cl_2, 0° to rt, 12 h	 (92)	446
	*m*-CPBA (1.1 eq), CH_2Cl_2, 0°; then rt, 5 h	 (93)	842
C_{18} 	*m*-CPBA (1.3 eq), CH_2Cl_2, rt, 1 h	 (64)	843
C_{20} 	*m*-CPBA (1.0 eq), CH_2Cl_2, 0°; then Ac_2O (2.5 eq), DMAP (0.1 eq), py (5.0 eq), rt, 2 h	 (81)	310, 10
	1. *t*-BuOOH (2.5 eq), $VO(acac)_2$ (0.16 mol %), CH_2Cl_2, –20°, 4 h 2. Ac_2O (4 eq), DMAP (0.4 eq), Et_3N (10 eq), CH_2Cl_2, 0° to rt, 2.5 h	 (30)	844

TABLE 7. SYNTHESIS OF 6-HYDROXY-2*H*-PYRAN-3(6*H*)-ONES (*Continued*)

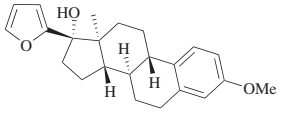
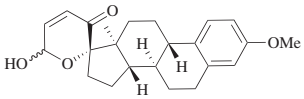
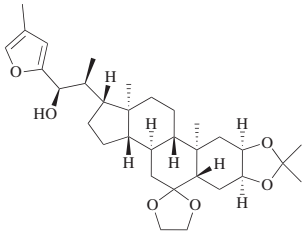
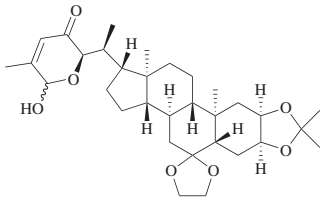
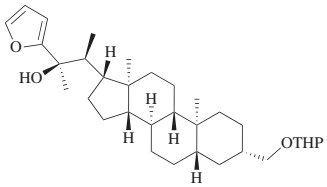
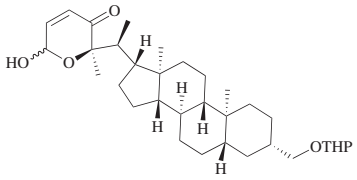
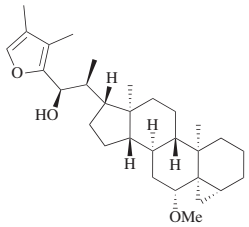
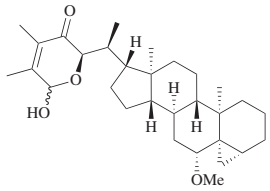
	Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{22}		CH_3CO_3H, AcOH	 (65)	432
C_{27}		NBS (1.18 eq), THF/H_2O (4:1), 0°, 30 min	 (92)	845, 461
C_{28}		*m*-CPBA (2.2 eq), NaOAc (2.0 eq), $CHCl_3$, 0°, 1.5 h	 (91)	439
		NBS (1.1 eq), NaOAc (1.1 eq), THF/H_2O (4:1)	 (84)	846, 847, 848

TABLE 8. SYNTHESIS OF 6-HYDROXY-1,2-DIHYDROPYRIDIN-3(6*H*)-ONES

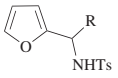
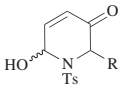
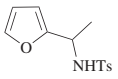
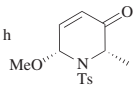
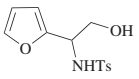
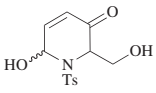
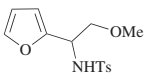
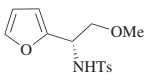
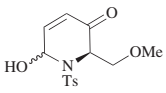
Furan	Conditions	Product(s) and Yield(s) (%)				Refs.
$C_{5–11}$						
	*m*-CPBA (2.1 eq), CH_2Cl_2, rt, 2 h		R	Temp	Time (h)	
			H	0°	2	(90) 540
			H	rt	2	(—) 538
			Me	0°	2	(97) 540
			Me	rt	2	(85) 554, 553, 538
			$AcOCH_2$	30°	4.5	(70) 539
			t-$BuPh_2SiOCH_2$	rt	2	(80) 437
			Et	0°	2	(51) 540
			n-Pr	0°	2	(78) 540
			i-Pr	0°	2	(36) 540
			t-$BuPh_2SiO(CH_2)_3$	rt	2	(80) 553, 849
			n-Bu	0°	2	(49) 540
			n-Bu	rt	2	(—) 538
			i-Bu	0°	2	(69) 540
			Ph	rt	2	(80) 437
C_6						
	1. *m*-CPBA (2.1 eq), CH_2Cl_2, rt, 2 h 2. $CH(OMe)_3$ (2.0 eq), $BF•Et_2O$ (0.1 eq), CH_2Cl_2, 0°, 3 h		(85)			551, 554, 553
	NBS, 4°, 4 h		(83)			539
	$Ti(Oi\text{-}Pr)_4$, L-(+)-DIPT, *t*-BuOOH, silica gel, CaH_2, CH_2Cl_2, rt, 3 d	 **I** (—)	+	 **II** (—)		564

TABLE 8. SYNTHESIS OF 6-HYDROXY-1,2-DIHYDROPYRIDIN-3(6*H*)-ONES (*Continued*)

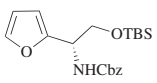
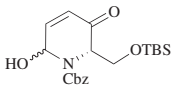
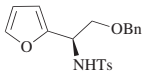
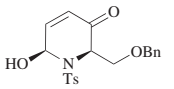
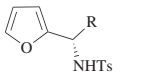
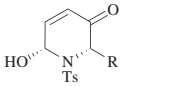
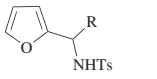
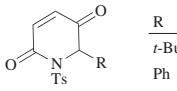
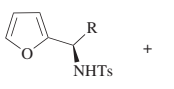
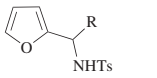
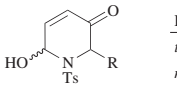
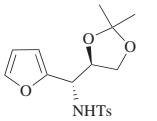
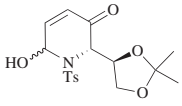
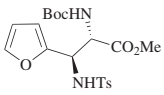
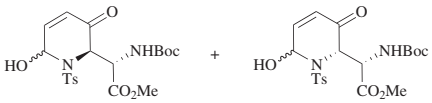
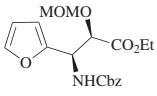
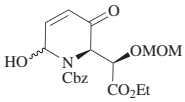
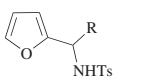
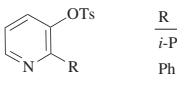
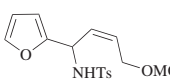
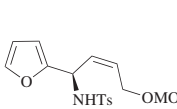
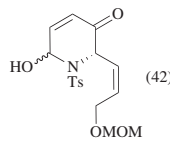
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	*m*-CPBA (2.0 eq), CH_2Cl_2, 0°, 3 h	 (87)	549
	*m*-CPBA (1.2 eq), CH_2Cl_2, rt, 16 h	 (82)	543, 542
$C_{6–8}$ 	*m*-CPBA (1.5 eq), CH_2Cl_2, rt, 4 h		
	R: Me; Time (h): 2	(85)	552, 550
	R: *t*-$BuMe_2SiOCH_2$; Time (h): 4	(92)	545, 556
	R: *t*-$BuPh_2SiOCH_2$; Time (h): 4	(94)	541, 544
	R: *n*-Pr; Time (h): 3	(74)	405
	R: Merrifield resin-O; Time (h): 4	(—)	537
$C_{6–11}$ 	1. *m*-CPBA (1.1 eq), CH_2Cl_2, rt, 3 h; 2. Jones reagent, acetone, rt, 0.25 h	 R: *t*-$BuPh_2SiOCH_2$ (93); Ph (96)	437
	Ti(O*i*-Pr)$_4$, D-(–)-DIPT, *t*-BuOOH, silica gel, CaH_2, CH_2Cl_2, rt, 3 d	 R: Me (—); *n*-Pr (—); *n*-Bu (—); *i*-Bu (—); Ph (—)	566
$C_{7–9}$ 	NBS (1.38 eq), NaOAc (1.28 eq), THF/H_2O (4:1), 0°, 3 h	 R: *t*-BuO_2CCH_2, THF/H_2O (99); *n*-Bu, CH_2Cl_2 (50); 2-furyl, THF/H_2O (83)	850, 558, 40
C_7 	*m*-CPBA (3.0 eq), CH_2Cl_2, rt, 1 h	 (62)	555
	NBS, $NaHCO_3$, NaOAc, 0°	 **I** **I + II** (65), **I/II** = 5:1 **II**	559
	*m*-CPBA (1.18 eq), CH_2Cl_2, rt, 8 h	 (88)	548
$C_{8–11}$ 	1. *m*-CPBA, CH_2Cl_2, 0°, 2 h; 2. $AlCl_3$, CH_2Cl_2, –78°; 3. Et_3N	 R: *i*-Pr (81); Ph (36)	154
C_8 	Ti(O*i*-Pr)$_4$, D-(–)-DIPT, *t*-BuOOH, silica gel, CaH_2, CH_2Cl_2, rt, 3 d	 (46) +  (42)	851, 42, 566

TABLE 8. SYNTHESIS OF 6-HYDROXY-1,2-DIHYDROPYRIDIN-3(6*H*)-ONES (*Continued*)

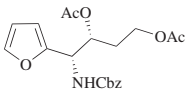
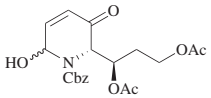
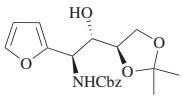
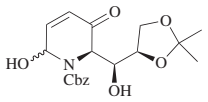
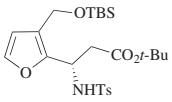
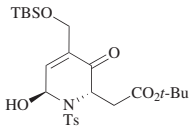
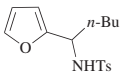
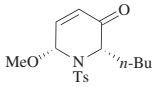
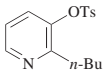
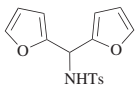
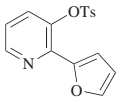
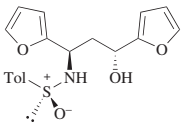
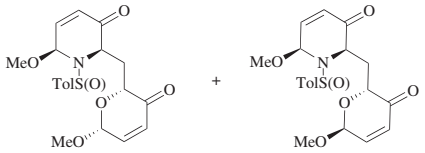
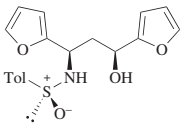
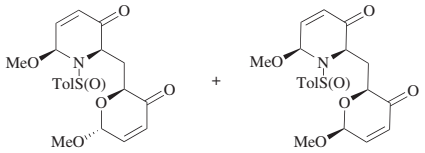
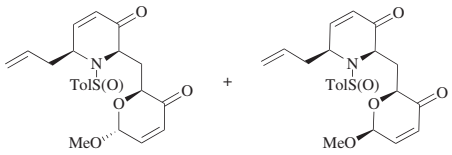
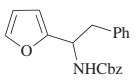
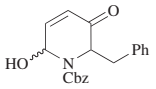
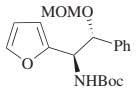
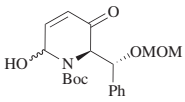
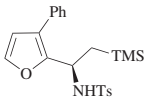
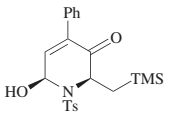
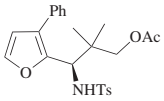
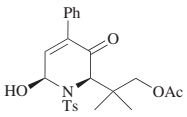
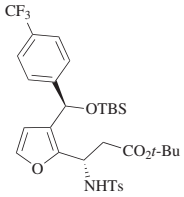
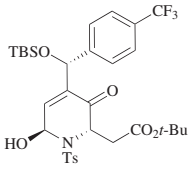
Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	*m*-CPBA (1.15 eq), CH_2Cl_2, rt, 16 h	 (88)	546, 852
	*m*-CPBA, CH_2Cl_2, rt, 20 h	 (72)	561
	NBS (0.67 eq), $NaOAc•3H_2O$ (0.86 eq), THF/H_2O (4:1), –5 to 0°, 3 h	 (83)	850
C_9			
	NBS (1.2 eq), $NaOAc•3H_2O$ (1.4 eq), THF/H_2O (1:1); then $CH(OMe)_3$ (2.0 eq), $BF_3•Et_2O$ (0.05 eq), CH_2Cl_2	 (85)	562
	1. NBS, NaOAc, THF/H_2O, 0° 2. $AlCl_3$ (1.2 eq), CH_2Cl_2, –78°, 0.5 h 3. Et_3N	 (92)	154
	NBS, NaOAc, THF/H_2O, 0°	 (50)	154
C_{11}			
	NBS (1.2 eq), $NaOAc•3H_2O$ (1.4 eq), THF/H_2O (1:1); then $CH(OMe)_3$ (2.0 eq), $BF_3•Et_2O$ (0.05 eq), CH_2Cl_2	 **I** **I + II** (29), **I/II** = 66:34 **II**	562, 563
	NBS (1.2 eq), $NaOAc•3H_2O$ (1.4 eq), THF/H_2O (1:1); then $CH(OMe)_3$ (2.0 eq), $BF_3•Et_2O$ (0.05 eq), CH_2Cl_2	 **I** **I + II** (34), **I/II** = 66:34 **II**	562, 563
	NBS (1.2 eq), $NaOAc•3H_2O$ (1.4 eq), THF/H_2O (1:1); then $CH(OMe)_3$ (2.0 eq), $BF_3•Et_2O$ (0.05 eq), CH_2Cl_2	 **I** **I + II** (30), **I/II** = 66:34 **II**	562
	NBS (1.2 eq), $NaOAc•3H_2O$ (1.4 eq), THF/H_2O (1:1); then $CH(OMe)_3$ (2.0 eq), $BF_3•Et_2O$ (0.05 eq), CH_2Cl_2, then, $allylSime_3$, BF_3, CH_2Cl_2	 **I** **I + II** (37), **I/II** = 66:34 **II**	562

TABLE 8. SYNTHESIS OF 6-HYDROXY-1,2-DIHYDROPYRIDIN-3(6*H*)-ONES (*Continued*)

Furan	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}			
	*m*-CPBA, CH_2Cl_2	 (69)	560
	*m*-CPBA, CH_2Cl_2	 (80)	547
	*m*-CPBA (2.0 eq), CH_2Cl_2, rt , 1 h	 (94)	557
C_{15}			
	*m*-CPBA (2.0 eq), CH_2Cl_2, rt, 1 h	 (83)	557
	NBS (0.67 eq), $NaOAc•3H_2O$ (0.86 eq) THF/H_2O (4:1), –5 to 0°, 3 h	 (64)	850

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CHAPTER 2

CYCLOADDITION AND ELECTROCYCLIC REACTIONS OF VINYLKETENES, ALLENYLKETENES, AND ALKYNYLKETENES

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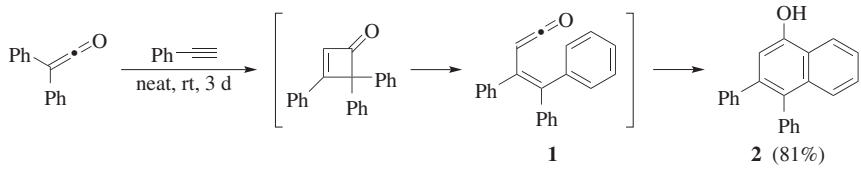
INTRODUCTION

Vinylketenes,[1,2,3] like arylketenes, are highly reactive and readily enter into cycloaddition reactions, a characteristic mode of ketene reactivity.[4−7] The reactivity of vinylketenes is attenuated by the presence of bulky groups and silyl substituents. The presence of a conjugated double bond in vinylketenes and allenylketenes, and a conjugated triple bond in alkynylketenes, allows a variety of additional cycloaddition pathways that are unavailable to simpler ketenes.

The earliest reference to a vinylketene remains unconfirmed.[5,8] The first substantial evidence for this class of ketenes, as well as a prescient proposal for the generation and electrocyclization of vinylketene **1**, was provided by Smith and Hoehn to explain the formation of 3,4-diphenyl-1-naphthol (**2**) from the reaction of diphenylketene with phenylacetylene (Scheme 1).[9,10] The authors suggest formation of an unobserved cyclobutenone via intermolecular [2+2] cycloaddition of diphenylketene with phenylacetylene. The cyclobutenone is in equilibrium with unobserved vinylketene **1** through 4π retro-electrocyclization. Naphthol **2** is then formed upon 6π electrocyclization of vinylketene **1**. Similar electrocyclization steps also occur with vinyl and alkynyl substituents, providing a simple and efficient route to highly valued six-membered ring compounds.

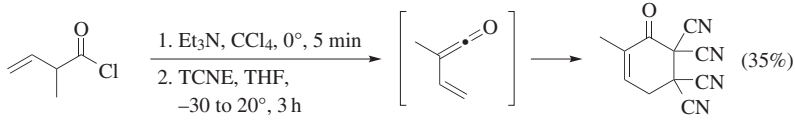


Scheme 1

The result shown in Scheme 1 initially went unnoticed and was not even cited until 1958, when a similar process was proposed for the reaction of diphenylketene with ethoxyacetylene.[11] Subsequent studies provided more evidence for the presence of vinylketenes as unobserved reaction intermediates from various sources,[12–14] and eventually these species were directly observed in several circumstances.[15–17] Studies of vinylketene cycloadditions have flourished since then.

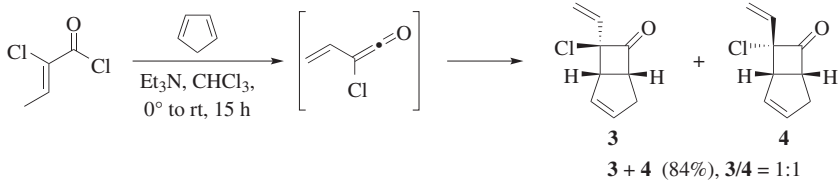
The formation and subsequent cyclization of a vinylketene via two electrocyclic processes is illustrated in Scheme 1. Amido-substituted vinylketenes generated by cyclobutenone ring opening react similarly, providing amido-substituted phenols that serve as precursors to quinolines, indoles, and other nitrogen-containing heterocycles.[18,19]

An example of intermolecular vinylketene [4+2] cycloaddition is the reaction of 2-methyl(vinyl)ketene (generated in situ by a dehydrochlorination) with tetracyanoethylene (Scheme 2).[20] The presence of vinylketenes is not always proven, especially as amines are known to react with ketenes to form zwitterions. The evidence for vinylketene formation in these and similar reactions is discussed in both the Mechanism and Scope and Limitations sections.



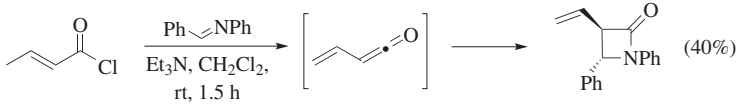
Scheme 2

Vinylketene cycloadditions with alkenes also may proceed without direct involvement of the vinyl group, as in the reaction of chloro(vinyl)ketene with cyclopentadiene to form vinyl cyclobutanones **3** and **4** by a [2+2] cycloaddition that proceeds efficiently but with no *exo*/*endo* selectivity (Scheme 3).[21]

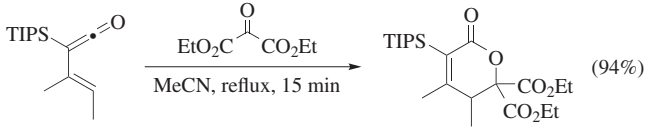


Scheme 3

Vinylketenes can react by both [2+2] and [4+2] pathways with imines and with carbonyl compounds. With imines, β-lactam formation is the preferred pathway (Scheme 4),[22] but with carbonyl compounds [4+2] cycloaddition is usually favored (Scheme 5).[23]

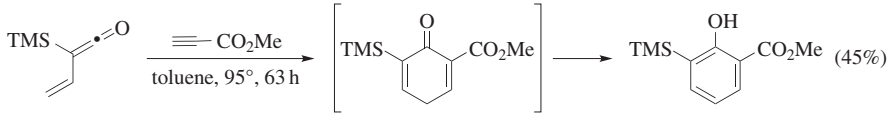


Scheme 4



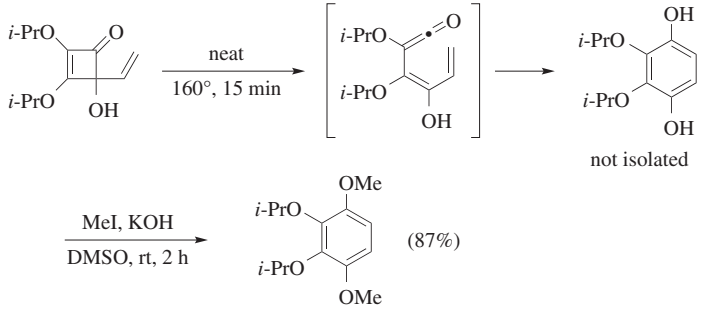
Scheme 5

Intermolecular [4+2] cycloaddition of a stable silyl(vinyl)ketene with methyl propiolate affords a 2,5-cyclohexadienone intermediate that tautomerizes to the phenol (Scheme 6).[24]



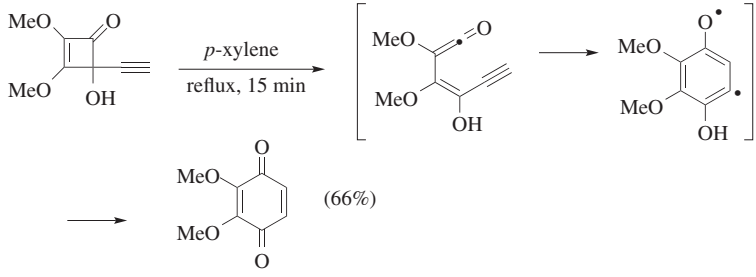
Scheme 6

Dienylketenes undergo 6π electrocyclizations readily, as shown in Scheme 7. The unobserved intermediate formed from a 4-vinylcyclobutenone leads to an intermediate hydroquinone that is subsequently methylated to generate the final product, which is used in the synthesis of echinochrome A.[25]



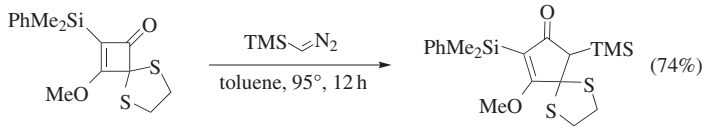
Scheme 7

In a related electrocyclization process an alkynyl-substituted vinylketene, generated by thermolysis of a 4-ethynylcyclobutenone, forms a diradical intermediate that provides the final 1,4-benzoquinone by hydrogen atom transfer (Scheme 8).[26]

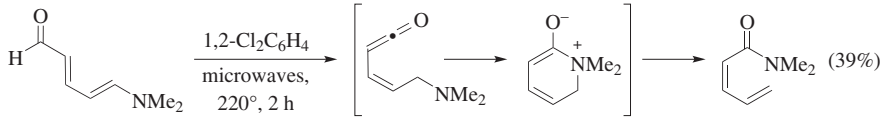


Scheme 8

Many vinylketene cycloadditions are polar processes that involve initial attack of a nucleophilic site onto the highly electrophilic ketene carbonyl. A discrete zwitterionic intermediate may be formed and, in a subset of reactions that are also covered in this chapter, that intermediate may fragment or rearrange. Examples include the formation of cyclopentenone derivatives from vinylketenes and diazo compounds (Scheme 9)[27] and the rearrangement of vinylketenes derived from Zincke aldehydes (Scheme 10).[28]



Scheme 9



Scheme 10

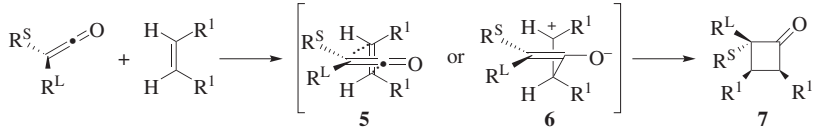
The formation and reactions of vinylketenes have been previously reviewed both specifically,[2–4,29,29a] and within reviews of other ketenes.[6,7,30] This chapter will discuss all cycloaddition and electrocyclization reactions of vinylketenes, allenylketenes, and alkynylketenes. The Tabular Survey includes all such reactions of vinylketenes known to the authors through July 2013. Inasmuch as vinylketenes and analogous species as reactive intermediates are often not identified in publications either graphically or by name, some examples have surely been missed.

MECHANISM AND STEREOCHEMISTRY

Theory of Ketene Cycloadditions and Electrocyclizations

Cycloaddition reactions are notable for their atom economy and for their ease of carbon–carbon bond formation, which often occurs with a high degree of regio- and stereoselectivity. Vinylketenes are activated by the vinyl group, which can interact conjugatively during cycloaddition reactions in the same way as the phenyl group in phenylketene. Kinetic studies of ketene reactivity show the order PhCH=CHCH=C=O > PhCH=C=O ≫ *n*-BuCH=C=O for addition both of water and of the stable free radical TEMPO.[31] Comparable kinetic data for cycloaddition reactions are not available, but as many of these processes involve a polarized transition structure, a similar order of reactivity is to be expected.

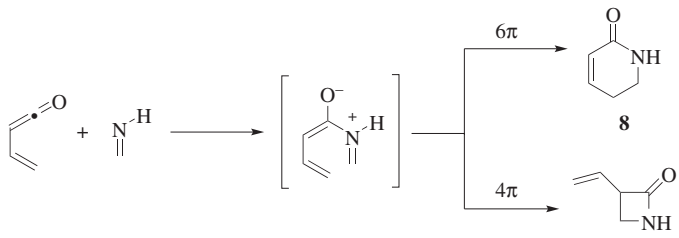
Ketene cycloadditions have been extensively reviewed[1,3,4,7,29,30,32] and will not be considered in detail in this chapter. Ketene [2+2] cycloadditions, including those of vinylketenes, are generally agreed to involve an initial orthogonal arrangement of the two reactants, with the smaller ketene substituent (R^S) closest to the alkene (Scheme 11). In a concerted reaction both bonds to the alkene are formed from the same side (suprafacial), while the bonds to the two carbons of the ketene are formed from opposite sides (antarafacial), as shown in structure **5**, and this leads to product **7** with the larger ketene substituent (R^L) *cis* to the larger substituents from the alkene. However, evidence shows that many ketene cycloadditions are not concerted, but involve a two-step process with the formation of a zwitterionic intermediate **6** (Scheme 11). This latter process is also consistent with the usual observation of selective formation of the thermodynamically less stable products without loss of the configurational homogeneity of the reactants. Thus, although the concerted pathway is consistent with the observed data in many cases, a stepwise process provides an equally convincing explanation of the results.



5 **6** **7**

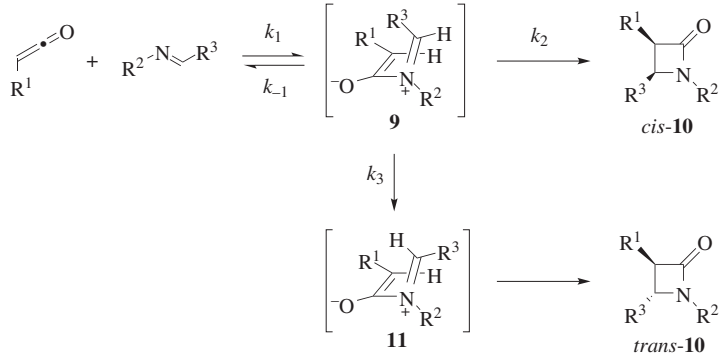
Scheme 11

Computational studies at the B3LYP/6-31G* level of the reaction of vinylketene with formaldimine find a concerted transition structure for formation of lactam **8**,[33] but other studies at this level find only a stepwise process for this reaction, with the formation of a zwitterionic intermediate (Scheme 12).[34] Both conrotatory and disrotatory transition structures of similar energy are found for the cyclization of the zwitterionic intermediate to lactam **8**, and both are considered possible for this reaction.[34] The competition between 6π and 4π pathways to form δ- and β-lactams, respectively, was also investigated in the reaction of vinylketene with formaldimine, and the 4π process was found to occur more readily.[33]



Scheme 12

The formation of β-lactams by [2+2] cycloadditions of ketenes with imines has received particular attention because of the presence of a 2-azetidinone ring in the most widely used class of antibacterial agents, and the importance of the stereochemistry about that ring for biological efficacy.[32] On the basis of computational and experimental studies,[35–37] these reactions are now generally interpreted by a mechanism wherein, for the major, product-determining pathway, the imine approaches the (monosubstituted) ketene from the side opposite the ketene substituent to form zwitterion **9**. This zwitterion either undergoes direct ring closure to form β-lactam *cis*-**10**, or isomerizes by bond rotation to afford zwitterion **11**, which undergoes ring closure to β-lactam *trans*-**10** (Scheme 13).[38]

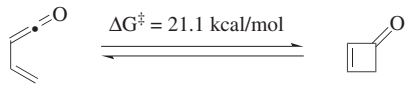


Scheme 13

As noted in the Scope and Limitations section (Scheme 30), electronic effects on the sense of rotation (torquoselectivity) in the ring opening and closing of cyclobutenones have been considered,[39] and this concept has been extended to the electrocyclization of the zwitterionic intermediates in the Staudinger β-lactam synthesis. Later work has, however, suggested that the theory of torquoselectivity cannot reliably be used to predict the stereochemical course of β-lactam formation.[40]

With respect to electrocyclizations of vinylketenes, the process for closure of the parent vinylketene into cyclobutenone is calculated at the MP4SDQ/6-31G**//HF/6-31G* level to be thermoneutral (Scheme 14), with a barrier in either direction of 21.1 kcal/mol.[41] The parent cyclobutenone is known to be thermally unstable at

room temperature,[42,43] and the instability may be due to spontaneous ring opening. 2-Bromocyclobutenone is also unstable and cannot be isolated.[44]



Scheme 14

The electrocyclization of conjugated dienylketenes into 2,4-cyclohexadienones is highly energetically favorable. The relative energies (kcal/mol) for the intermediates involved in the interconversion of phenol, 2,4-cyclohexadienone, and (*Z*)- and (*E*)-1,3,5-cyclohexatrienone (**12**), determined computationally at the B3LYP/6-311G(3df,3pd)//B3LYP/6-311G(d,p) level, are shown in Fig. 1.[45]

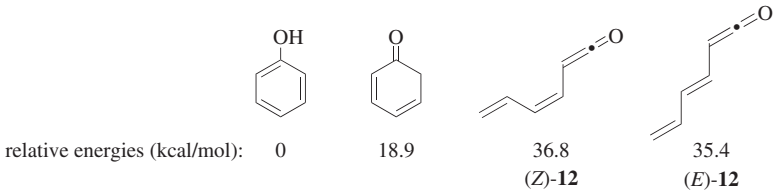


Figure 1. Relative calculated energies (kcal/mol) of vinylketene **12** and cyclic isomers.

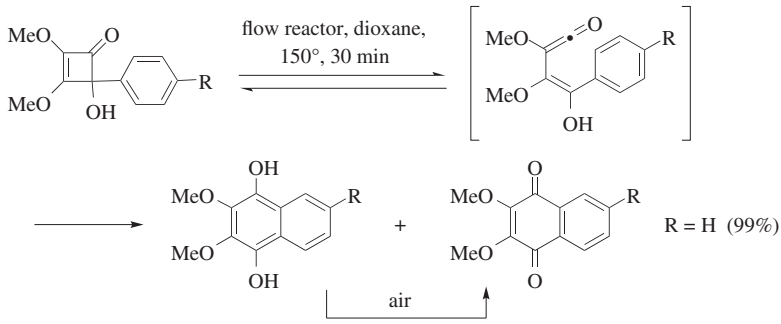
Cycloadditions and Electrocyclizations of Vinylketenes Involving Alkynyl Groups

As noted in the Introduction (Scheme 6), the intermolecular [4+2] cycloaddition of the stable vinyl(trimethylsilyl)ketene with methyl propiolate takes place to form a 1,4-cyclohexadienone that undergoes tautomerization to the phenol.[24] Electrocyclization processes that involve alkynyl groups are more complex, since a diradical is initially formed. The reaction shown in Scheme 8 is an example of the Moore cyclization[46] and is one of the most interesting vinylketene transformations, as the diradical can undergo further free radical reactions to provide a variety of different products depending upon the substitution pattern in the starting material. Such enyne electrocyclizations have been studied by computational methods and have been compared with related cyclizations.[47] The factors that favor formation of either 5- or 6-membered rings are also discussed below.

Cycloadditions and Electrocyclizations of Vinylketenes Involving Aryl Groups

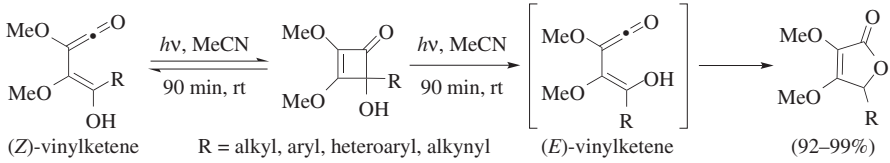
As shown in the Introduction (Scheme 1), electrocyclization of vinylketenes bearing aryl groups takes place readily in a process resembling the Friedel–Crafts reaction.[9,10] Thermal generation of arylvinylketenes in a flow reactor proceeds

efficiently to provide 1,4-naphthoquinones in high yield after exposure to air to convert any hydroquinone to the quinone (Scheme 15).[48] The rates of the reactions of substituted derivatives, determined using ^{1}H NMR analysis, show a reasonable correlation with σ_p parameters for the substituent R, a result interpreted in terms of reversible ring opening of the cyclobutenone, with electrocyclization as the rate-limiting step.



Scheme 15

When the reactions are conducted with photochemical activation of the cyclobutenone, a different course is followed and furanones (Scheme 16, R = alkyl, aryl, heteroaryl, and alkynyl) are formed.[49] This result is attributed to the reversibility of the competing electrocyclization of the (*Z*)-vinylketene, while formation of the furanone via cyclization of the (*E*)-vinylketene is irreversible.

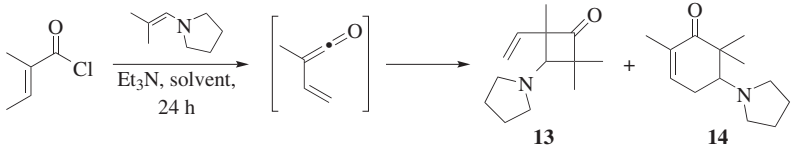


Scheme 16

Periselectivity: [2+2] vs [4+2] Cycloaddition Reactions

The question of competition between [4+2] and [2+2] cycloadditions in vinylketene–alkene cycloaddition chemistry has not yet been addressed in a systematic way. In some cases, obvious steric or geometric considerations greatly favor one over the other, in particular those that either prevent or favor a *cisoid* geometry for the vinylketene. The reactions of vinylketenes with alkenes often lead to [2+2] cycloadditions, but many examples of [4+2] pathways are also known. Methyl(vinyl)ketene reacts with enamines by both [2+2] and [4+2] pathways, forming an increasing amount of the [4+2] product **14** in hexane as compared to methylene chloride (Scheme 17).[50] The reaction is faster in methylene chloride and

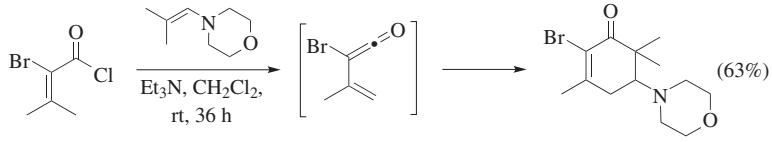
occurs at room temperature, compared to 70° in hexane, indicating stabilization of a more polar transition structure in the formation of product **13**. As shown in Scheme 17, both [2+2] and [4+2] vinylketene cycloadditions occur with attachment of the most nucleophilic atom of the ketenophile at the carbonyl carbon of the ketene. In certain cases with chiral nucleophilic catalysis, coordination with the catalyst at this position may occur first.[51,51a,32]



Solvent	Temp (°)	Yield (%) 13 + 14	13/14
CH_2Cl_2	rt	53	1:0
hexane	70	56	1:1

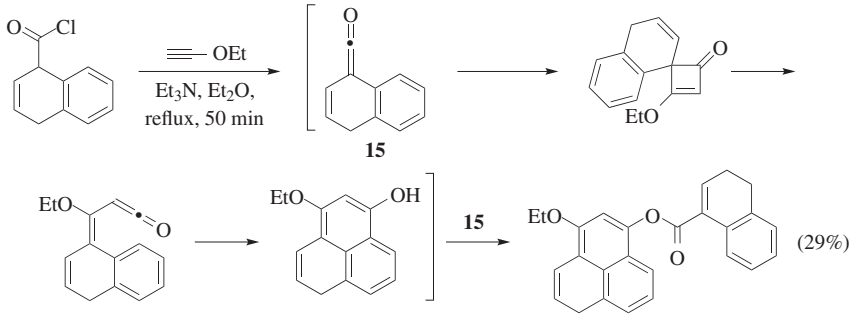
Scheme 17

Methyl substitution on C3 of the vinylketene directs a related enamine addition completely to the [4+2] pathway because the substitution retards the [2+2] pathway (Scheme 18).[50]



Scheme 18

In contrast, vinylketene **15**, generated in situ by a dehydrochlorination, is constrained in an s-*trans* conformation and can thus undergo only [2+2] cycloaddition with ethoxyacetylene to generate an unobserved cyclobutenone that ring opens to a new dienylketene. Electrocyclization followed by tautomerization to the phenol and final acylation forms the product (Scheme 19).[51]



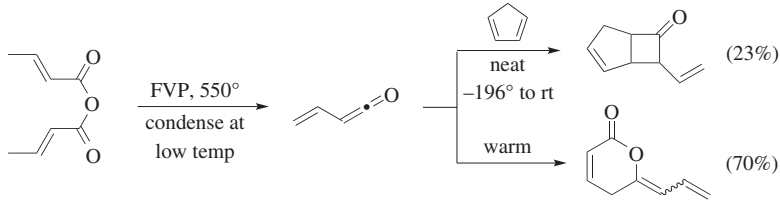
Scheme 19

SCOPE AND LIMITATIONS

Generation of Vinylketenes

The successful application of vinylketenes in organic synthesis depends upon effective means for their preparation, and the slow initial development of vinylketene chemistry reflects the lack of proven synthetic methods. The high reactivity of vinylketenes also precluded their identification and isolation for many years. However, almost all of the common methods of ketene formation prove to be applicable to vinylketenes, whereas cyclobutenone and cyclohexadienone ring openings provide versatile routes that are not available for the preparation of other types of ketenes. Synthetic applications of vinylketenes are inextricably bound up with their preparation, since in most cases the vinylketenes are not isolated but are formed as unobserved intermediates and react in situ with themselves or their desired reaction partners. Accordingly, this sub-section includes examples of their reactions that are complementary to those discussed below.

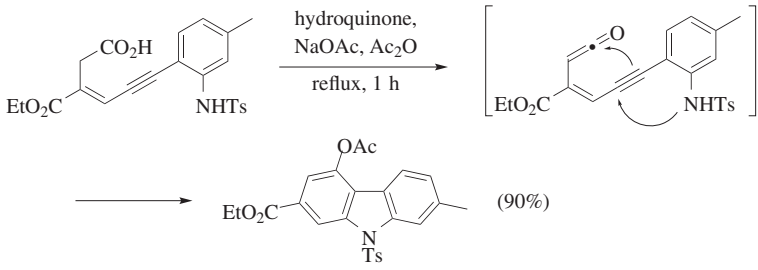
From Carboxylic Acids and Their Derivatives. Vinylketenes may be generated by dehydration of carboxylic acids by heating and also via elimination from in situ generated anhydrides. Flash vacuum pyrolysis (FVP) of crotonic anhydride forms the parent vinylketene, which is collected and characterized at low temperature and is also trapped in a cycloaddition reaction with cyclopentadiene (Scheme 20).[53] In the absence of a trapping agent, warming vinylketene forms the dimer (Scheme 20). *cis*- and *trans*-1-Propenylketenes are prepared by the pyrolysis of 3-pentenoic acid or 2,4-pentadienal at 600° and have been characterized by ^{1}H NMR spectroscopy.[54]



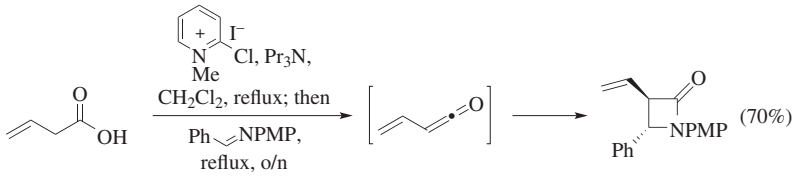
Scheme 20

Dehydration of unsaturated carboxylic acids by heating with sodium acetate and acetic anhydride is also used for forming vinylketenes, as in the generation of an unobserved alkynylvinylketene that cyclizes to form a carbazole (Scheme 21).[55]

Mukaiyama's reagent (2-chloro-1-methylpyridinium iodide) provides an alternative method for generating vinylketenes by dehydrating acids, and converts 3-butenoic acid into the parent vinylketene, which reacts in situ with an imine by [2+2] cycloaddition to yield a β-lactam (Scheme 22).[56] This reagent is particularly useful for generating ketenes when the acid precursors cannot conveniently be converted into acyl chlorides or similar derivatives.

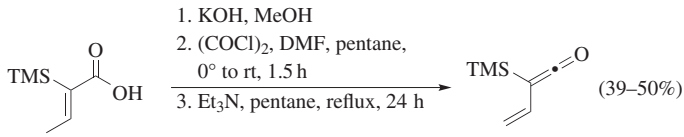


Scheme 21

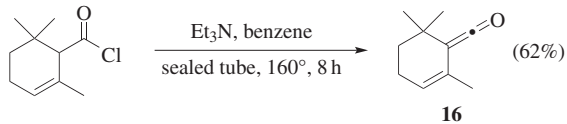


Scheme 22

Dehydrochlorination of unsaturated acid chlorides provides a useful route for the generation and utilization of many types of vinylketenes including the isolable α-trimethylsilyl derivative, which is stabilized by the trimethylsilyl substituent (Scheme 23).[24] Crowded acid chlorides may be unreactive and require higher temperatures for dehydrochlorination, as in the generation of vinylketene **16** from the acid chloride using triethylamine at 160° (Scheme 24).[57] Ketene **16** is also isolable because of the steric protection provided by the methyl groups.



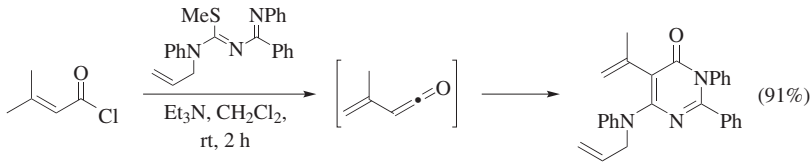
Scheme 23



16

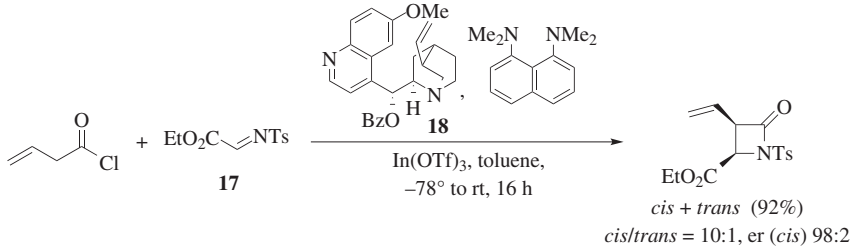
Scheme 24

Isopropenylketene is generated as an unobserved intermediate by dehydrochlorination of tiglyl chloride and reacts in situ with 1,3-diazadienes by selective [4+2] cycloaddition, forming pyrimidinones such as shown in Scheme 25.[58]



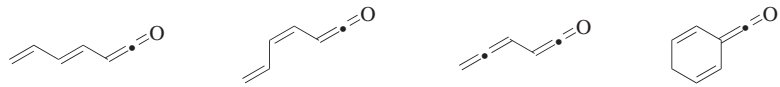
Scheme 25

The parent vinylketene is also prepared via dehydrochlorination of 3-butenoyl chloride using 1,8-bis(dimethylamino)naphthalene (Proton Sponge) as a stoichiometric base (Scheme 26).[51] Reaction with the electron-deficient imine **17** and benzoyl quinine **18**, which acts as both a shuttle base and a chiral catalyst, together with $In(OTf)_3$ as an electrophilic catalyst, results in highly stereoselective β-lactam formation. This reaction is suggested to proceed via formation of a chiral eneammonium enolate by reaction of the vinylketene with benzoyl quinine **18**, followed by reaction of the enolate with the imine. Catalytic, asymmetric cycloadditions of ketenes in general are the subject of a recent *Organic Reactions* chapter.[32]



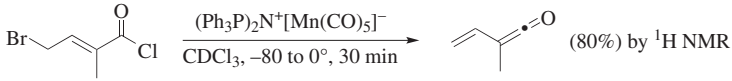
Scheme 26

Dehydrochlorination of 3-butenoyl chloride with 1,8-bis(dimethylamino)naphthalene at 0° in the absence of other reactants affords, in solution, the parent vinylketene, which exhibits the distinct ketene IR absorption at 2118 cm^{-1}.[59] The related ketenes **12**, **19**, and **20** have been observed under similar conditions and were characterized in solution.[59,60]



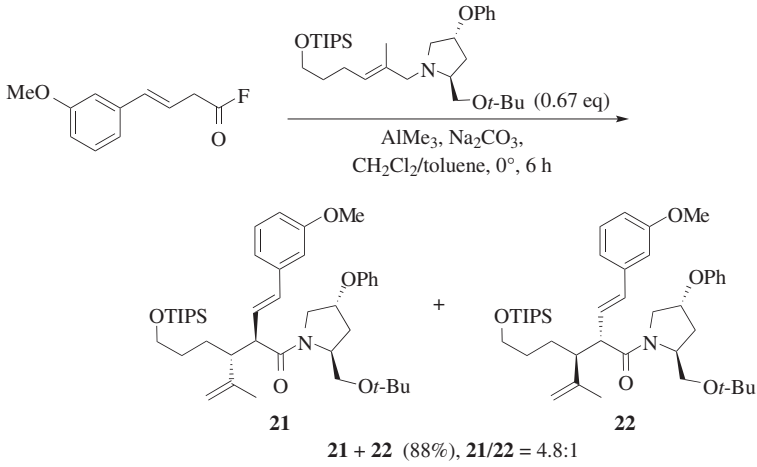
(*E*)-**12** (*Z*)-**12** **19** **20**

Reduction of a γ-bromo-α,β-unsaturated acid chloride with $(Ph_3P)_2N^+[Mn(CO)_5]^-$ generates methyl(vinyl)ketene at low temperatures in solution, permitting measurement of the ^1H NMR spectrum (Scheme 27).[61] This method of vinylketene generation is used infrequently, but is convenient on a small scale to generate observable intermediates.



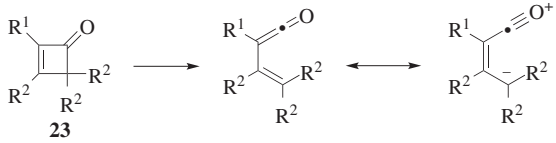
Scheme 27

Generation of a vinylketene from an acid fluoride in the presence of trimethylaluminum is used specifically to engage the ketene in a ketene-Claisen rearrangement with an allylic amine that carries a chiral auxiliary (Scheme 28).[62] Diastereomeric products **21** and **22** are obtained in 88% yield in a 4.8:1 ratio.



Scheme 28

From Cyclobutenones. Cyclobutenone ring opening is an unambiguous route to vinylketenes, and many examples are known. As noted in the Mechanism and Stereochemistry section, computational studies indicate that the ring opening of the parent cyclobutenone to form vinylketene has a low barrier and is essentially thermoneutral.[41] Experimental studies show large substituent effects on the rates of cyclobutenone ring opening in methanol. Thus, changing substituents on cyclobutenone **23** from R^1, R^2 = Me to R^1 = H, R^2 = Ph increases the rate of reaction by a factor of 2×10^4 (Scheme 29).[63] This rate increase can be attributed to stabilization of the vinylketene by conjugation. The results also indicate that an alkyl R^1 group versus hydrogen at the α-carbon of the ketene decreases the rate of ketene formation, which agrees with calculated substituent effects on ketene stability: electron-donating R^1 substituents, including methyl, are known to destabilize ketenes relative to a hydrogen substituent.[64] For example, methylketene is destabilized by 3.3 kcal/mol relative to the parent.



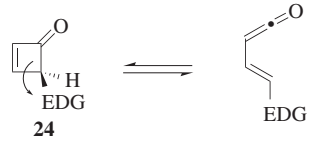
R^1	R^2	Relative Rate
Me	Me	1
H	Ph	2×10^4

23

Scheme 29

The rates of cyclobutenone ring opening are reduced in more polar solvents but the effects are small and, as a result, solvent choice for synthetic reactions is not restricted by polarity.[63] Nucleophilic solvents react with the ketenes and are used for this purpose as trapping agents, whereas inert solvents are used for reactions of the ketenes with added reagents.

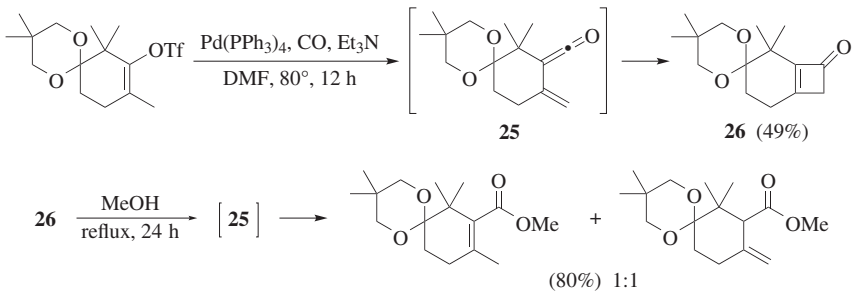
With 4,4-unsymmetrically substituted cyclobutenones the formation of stereoisomeric vinylketenes can occur. The torquoselectivity in the thermal ring opening of cyclobutenones **24** has been examined by computational means and proposed to occur with preferential outward rotation of electron donating groups (Scheme 30).[39] The torquoselectivity is usually not high, and the cyclobutenone opening and closing is reversible, so a steady-state concentration of the (*Z*)-vinylketene will also be present and may lead to observed products.



24

Scheme 30

Carbonylation of a triflate with catalysis by $Pd(PPh_3)_4$ is proposed to afford vinylketene **25** which cyclizes to form the isolable cyclobutenone **26** (Scheme 31).[65] Heating cyclobutenone **26** in MeOH reforms the ketene **25**, which is trapped to provide the ring-opened esters in 80% yield.

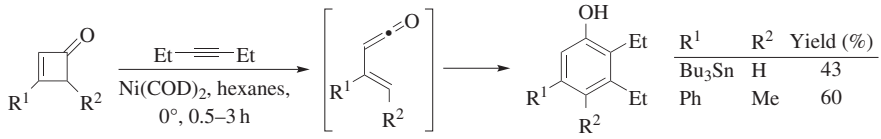


25 **26** (49%)

(80%) 1:1

Scheme 31

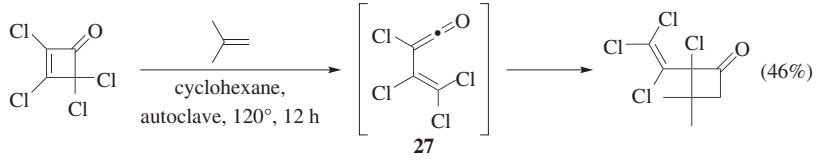
A nickel(0)-catalyzed cyclobutenone ring opening enables vinylketene [4+2] cycloadditions with alkynes to afford phenols below room temperature (Scheme 32).[66] The role of the catalyst has not been established.



R^1	R^2	Yield (%)
Bu_3Sn	H	43
Ph	Me	60

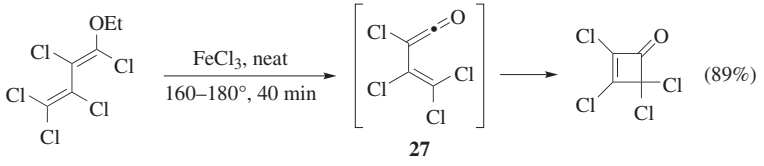
Scheme 32

The reactive perchlorovinylketene **27**, generated by cyclobutenone ring opening, reacts by [2+2] cycloaddition with 2-methylpropene in 46% yield (Scheme 33), as compared to a 26% yield when the same ketene is made by dehydrochlorination of 2,3,4,4-tetrachloro-3-butenoyl chloride.[67] Halogenated cyclobutanones formed in this way are useful intermediates in the synthesis of insecticidal pyrethroids. The cyclobutenone is the preferred isomer in the equilibrium process, and perchlorovinylketene generated in the absence of the alkene by a dealkylation–elimination method undergoes ring closure (Scheme 34).[68] Ring closure to the cyclobutenone is favored by the destabilizing effect of the α-chlorine of the ketene plus the stabilizing effect, by π-donation to the carbonyl, of chlorine at C3 of the cyclobutenone.[67]



27

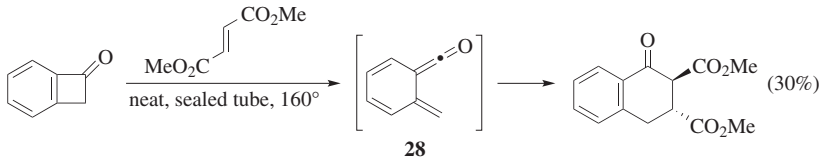
Scheme 33



27

Scheme 34

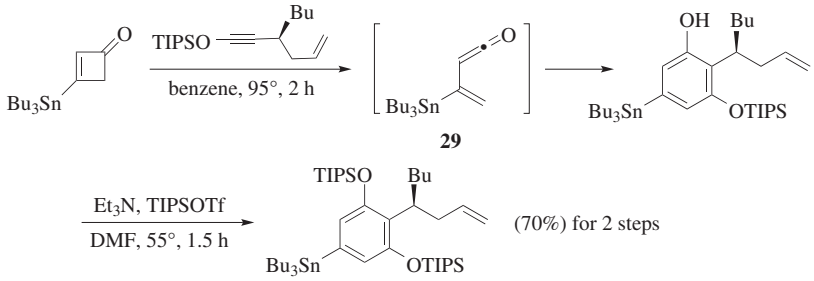
Heating benzocyclobutenone neat generates vinylketene **28** which reacts with an equimolar amount of dimethyl fumarate to form the [4+2] cycloaddition product (Scheme 35).[69]



28

Scheme 35

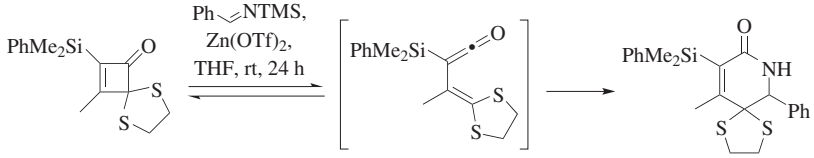
Stannylated vinylketene **29** is readily generated from the corresponding cyclobutenone and reacts selectively with the activated alkynyl group of a homoallyl silyloxyalkyne to afford a protected resorcinol derivative after silylation of the initially formed phenol (Scheme 36).[70]



29

Scheme 36

Just as for other silylketenes, silyl(vinyl)ketenes are stabilized and often may be observed as reactive intermediates and, in some cases, isolated in pure form. Even at room temperature slow conversion of cyclobutenone **30** to vinylketene **31** is observed, and is complete at 90° in toluene. In the presence of an *N*-silylimine and zinc(II) triflate, a [4+2] cycloaddition results in δ-lactam formation (Scheme 37).[27]

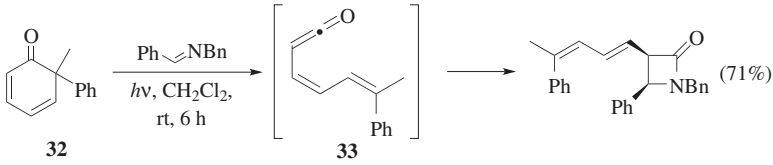


30 **31**

Scheme 37

From Cyclohexadienones. Photochemical ring opening of cyclohexadienones provides a unique route to dienylketenes, comparable to vinylketene formation from cyclobutenones. Because diversely substituted substrates are not as accessible as cyclobutenones this procedure has found more limited use. Photolytic cleavage of

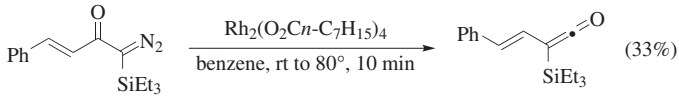
cyclohexadienones to form dienylketenes is readily confirmed both spectroscopically and by nucleophilic capture of the ketenes. Photolysis of cyclohexadienone **32** produces dienylketene **33** that is detected by UV spectroscopy and forms a *cis*-β-lactam by [2+2] cycloaddition when the reaction is conducted in the presence of *N*-benzyl phenyl imine (Scheme 38).[71]



32 **33**

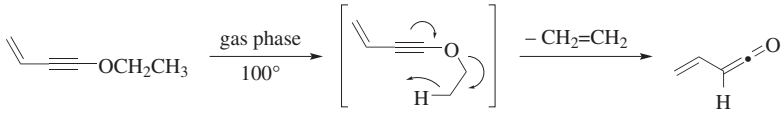
Scheme 38

From Diazo Ketones. The Wolff rearrangement of α,β-unsaturated diazo ketones, which may be carried out either by heating with or without a metal catalyst or by irradiation, provides a general route to vinylketenes.[2,3] Scheme 39 shows an example reaction that uses Rh(II) catalysis for the preparation of a stable silyl(vinyl)ketene.[72] Equivalent thermal reactions are scarce but examples are known, as shown in Scheme 63 (p. 283).



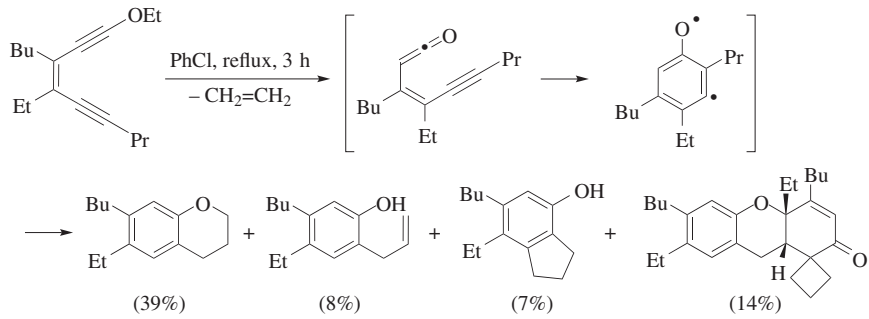
Scheme 39

From Alkynyl Ethers. Thermolysis of 4-ethoxy-1-butene-3-yne effects a retro-ene reaction to generate vinylketene for its direct observation in the gas phase (Scheme 40).[73]



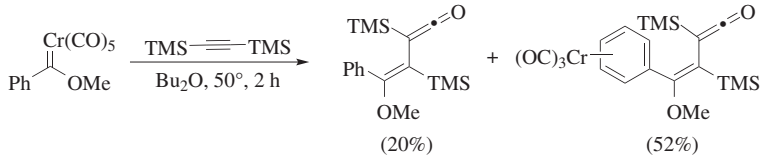
Scheme 40

A similar process takes place in solution, as exemplified by the reaction of the enediynyl ethyl ether shown in Scheme 41.[74] The alkynylvinylketene is formed as an unobserved intermediate that cyclizes to generate a diradical intermediate that leads to a variety of products.



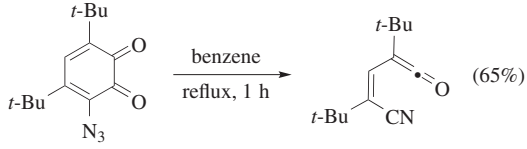
Scheme 41

From Metal Carbene Complexes. The reactions of Fischer carbene complexes with alkynes that form unobserved vinylketene complexes in synthetic transformations are reviewed elsewhere.[75] In a few instances isolable vinylketenes are obtained, as in the formation of a stabilized silyl(vinyl)ketene together with its $Cr(CO)_3$ complex, from the chromium carbene precursor (Scheme 42).[76]



Scheme 42

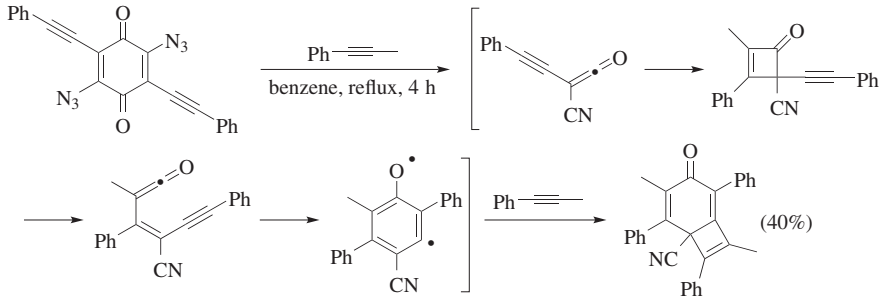
From Benzoquinones. Certain azido-1,2-benzoquinones provide vinylketenes upon thermolysis, including the remarkably stable, sterically protected vinylketene shown in Scheme 43.[77]



Scheme 43

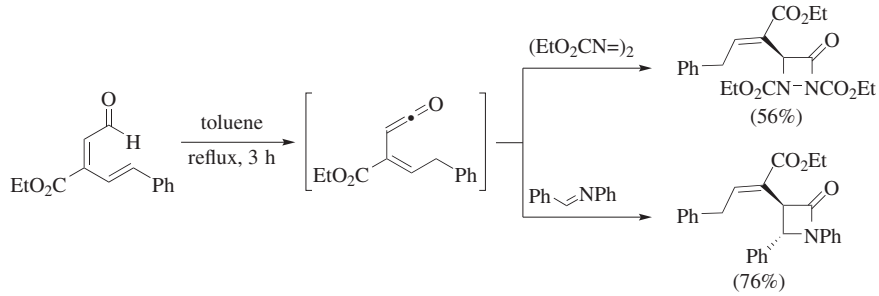
Vinylketenes that are not isolable are conveniently generated in situ by this method for cycloaddition reactions. Thermolysis of a 2,5-diazido-1,4-benzoquinone generates two molecules of an unobserved alkynyl(cyano)ketene, which react in situ by intermolecular [2+2] cycloaddition with 1-phenylpropyne, to form an intermediate

cyclobutenone. Ring opening affords a new vinylketene and electrocyclization forms a diradical intermediate which leads to the observed product by reaction with a second equivalent of the alkyne (Scheme 44).[78]



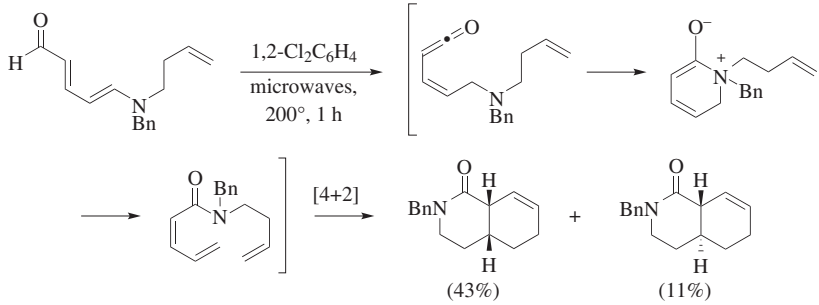
Scheme 44

From 2,4-Pentadienals. 1,5-Sigmatropic hydrogen shifts in unsaturated aldehydes that form vinylketenes have long been known[54,79–81] and have recently found synthetic applications.[82] Thermolysis of 3-ethoxycarbonyl-2,4-dienals in refluxing toluene causes a 1,5-shift of the formyl hydrogen to form vinylketenes which react by [2+2] cycloaddition with imines and diazenes, generating β-lactams and aza-β-lactams, respectively (Scheme 45).[83]



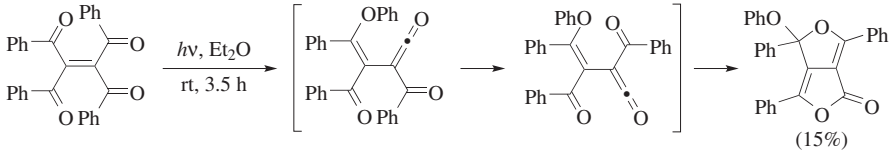
Scheme 45

As shown in the introduction, thermolysis of the Zincke aldehyde 5-dimethylamino-2,4-pentadienal results in rearrangement to *N,N*-dimethylpenta-2,4-dienamide.[28] A combined computational and experimental study indicates that a vinylketene intermediate is formed that generates a zwitterionic intermediate prior to electrocyclic ring opening (Scheme 10).[82] In the reaction of a related Zincke aldehyde, the reactive dienecarboxamide products undergo intramolecular cycloaddition reactions in situ when suitable dienophilic substituents are present (Scheme 46).[84]



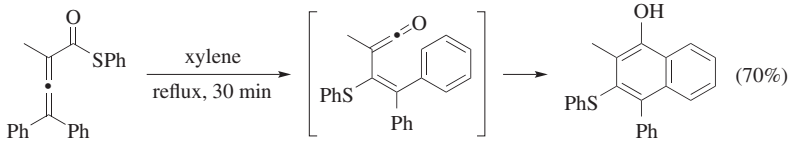
Scheme 46

From Other Sources. Photolysis of tetrabenzoylethylene in ether affords a cyclized product (isolated in 15% yield) that results from closure of a vinylketene generated by phenyl migration (Scheme 47).[85] The mechanism is confirmed by observation of the IR absorption of the vinylketene at 2110 cm^{-1} upon irradiation.[86]



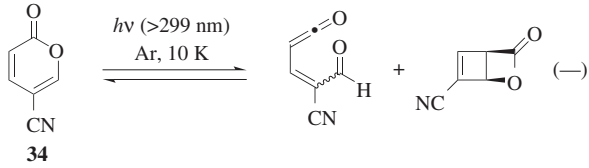
Scheme 47

Thermolysis of an allenyl thiocarboxylate results in thiophenyl group migration that forms an unobserved, intermediate vinylketene and this undergoes electrocyclization with the phenyl group to provide a naphthol (Scheme 48).[87]



Scheme 48

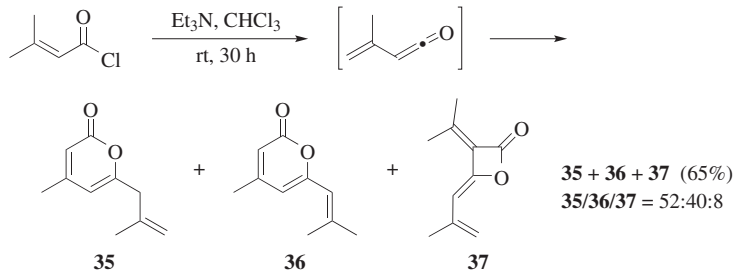
Photolysis of 2-pyranones under matrix-isolation conditions leads to reversible formation of observable vinylketenes in addition to Dewar lactones and cyclobutadienes, as exemplified by the reaction of the cyanolactone **34** (Scheme 49).[88] Several conformers and isomers of the ketene are detected by spectroscopy (with IR absorptions at 2146, 2140, 2134, 2118, and 2127 cm^{-1}) but could not be specified or isolated.



Scheme 49

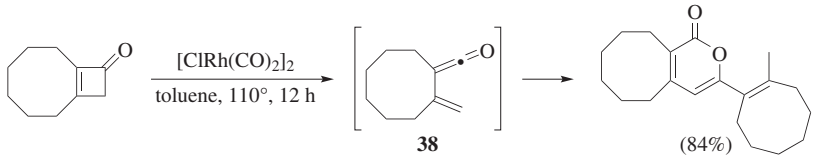
Cycloadditions and Electrocyclizations of Vinylketenes

Dimerization of Vinylketenes. A variety of dimerization processes for vinylketenes may be envisaged, but only a few of these have been observed. Pyranone formation by [4+2] cycloaddition is often favored, and 2-pyranones **35** and **36** are observed in the dimerization of isopropenylketene generated by dehydrochlorination of 3-methyl-2-propenoyl chloride. The methylene-substituted β-lactone **37** is also formed following the characteristic dimerization mode of most other ketenes (Scheme 50).[89] The pyrone dimer of the parent vinylketene is shown in Scheme 20 (p. 268). No examples of either [2+2] vinylketene dimerizations that form divinylcyclobutane-1,3-diones or involve [4+4] cycloadditions have been reported, and β-lactone formation is rare. Vinylketenes are usually generated in the presence of other reagents so that dimerization is precluded.



Scheme 50

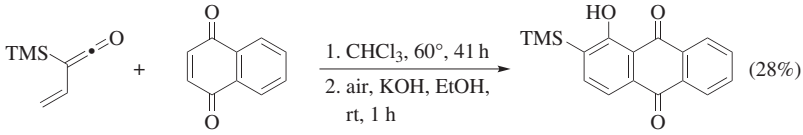
Ketene dimers are also formed in the rhodium-catalyzed ring opening of cyclobutenones, as shown in the generation of vinylketene **38** as an unobserved intermediate that forms the pyrone dimer (Scheme 51).[90]



Scheme 51

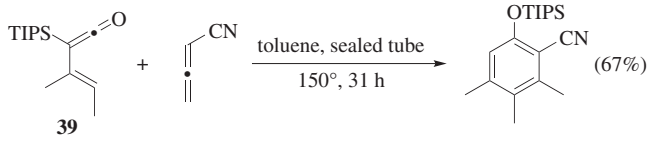
Intermolecular Cycloadditions of Vinylketenes with Alkenes. As noted in the Mechanism and Stereochemistry section, vinylketenes often favor [2+2] cycloaddition with alkenes, but many examples that proceed via the [4+2] pathway are also known and afford convenient routes to polysubstituted cyclohexene and benzene derivatives. Maleic anhydride provides a [4+2] cycloadduct with a stable silylketene (Scheme 52), and the analogous reaction with 1,4-naphthoquinone affords an anthraquinone after air oxidation of the initial product (Scheme 53).[24]

Scheme 52



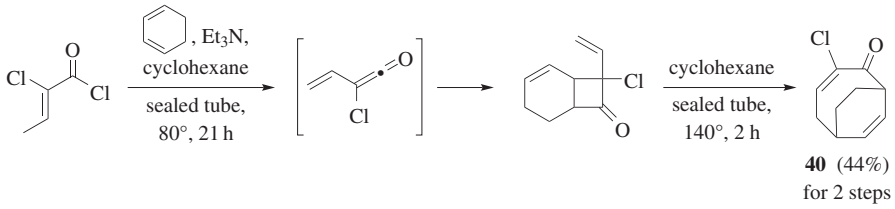
Scheme 53

Reaction of the more crowded silylketene **39** with cyanoallene requires a much higher temperature and proceeds with silyl migration (Scheme 54).[91]



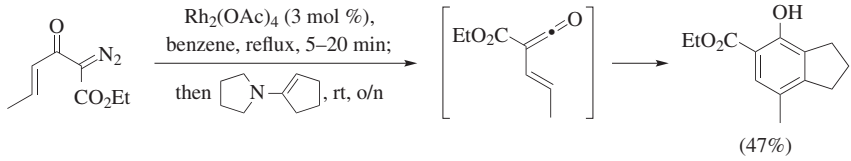
Scheme 54

At elevated temperatures the reactions of vinylketenes with conjugated dienes may lead to bridged 1,5-cyclooctadien-3-ones, but not by a direct [4+4] cycloaddition. For example, chloro(vinyl)ketene, formed by dehydrochlorination, undergoes [2+2] cycloaddition with 1,3-cyclohexadiene to produce an intermediate divinylcyclobutanone that undergoes a Cope rearrangement to form bicyclic ketone **40** (Scheme 55).[92]



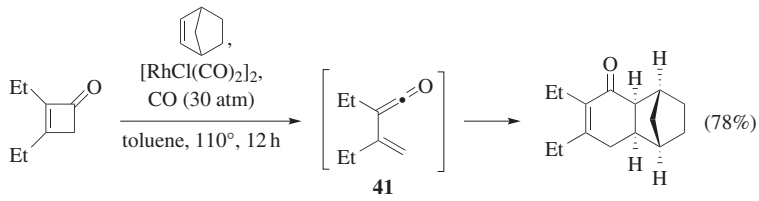
Scheme 55

Rhodium catalysis of the rearrangement of a diazo keto ester in refluxing benzene promotes the generation of ethoxycarbonyl(1-propenyl)ketene in solution. This vinylketene reacts at room temperature with added enamines by [4+2] cycloaddition followed by spontaneous elimination with aromatization to form a salicylate ester (Scheme 56).[93]



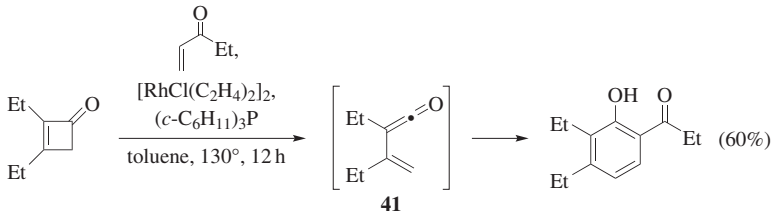
Scheme 56

Heating 1,2-diethylcyclobutenone under CO pressure and in the presence of a rhodium catalyst affords the intermediate vinylketene **41**, which reacts with norbornene by a [4+2] cycloaddition (Scheme 57).[90] Without the CO atmosphere a decarbonylated hydrocarbon is obtained.



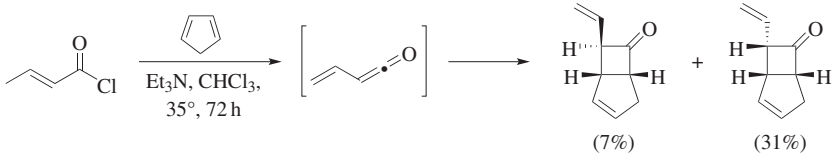
Scheme 57

Generating the same vinylketene **41** using a different rhodium catalyst and a phosphine co-catalyst in the presence of ethyl vinyl ketone results in [4+2] cycloaddition followed by dehydrogenation to produce a 2-acylphenol (Scheme 58).[94]



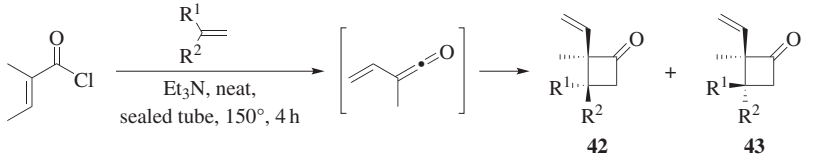
Scheme 58

[2+2] Cycloadditions with a variety of alkenes provide 2-vinylcyclobutanone derivatives. As is the case with other ketenes, the parent vinylketene reacts with cyclopentadiene by a [2+2] cycloaddition that favors the less stable *endo*-product (Scheme 59).[95]



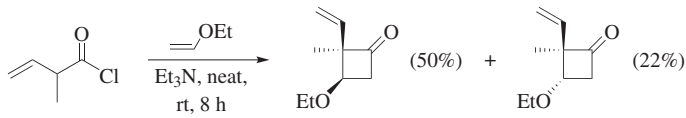
Scheme 59

The 2-vinylcyclobutanone products from reactions of methyl(vinyl)ketene with alkenes are usually a mixture of isomers with a preference for the bulkier substituent in the more crowded position, *cis* to the methyl group. This selectivity is shown in the reaction with 1-heptene to form a 7:3 mixture of products **42** and **43** (Scheme 60).[96,97] Stereoselectivity is lost and the yield is low with a 1,1-disubstituted alkene (Scheme 60).[96,97] The reaction of methyl(vinyl)ketene with the electron-rich ethyl vinyl ether is more facile and also generates a mixture of stereoisomers (Scheme 61).[20]



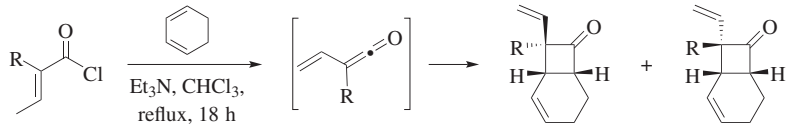
R^1	R^2	**42** + **43** (%)	**42/43**
n-C_5H_{11}	H	40	7:3
Bu	Me	11	1:1

Scheme 60



Scheme 61

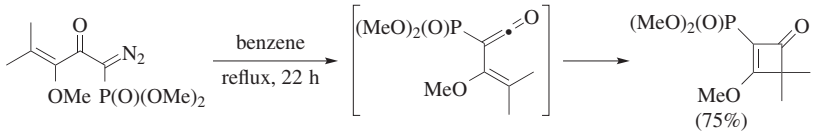
The preference for formation of the more crowded products is also seen in reactions of 2-substituted vinylketenes with 1,3-cyclopentadiene and 1,3-cyclohexadiene, as exemplified by the ratio of products **44** and **45** in Scheme 62.[95,21]



R	**44** + **45** (%)	**44/45**
Me	57	65:35
Bu	42	97:3

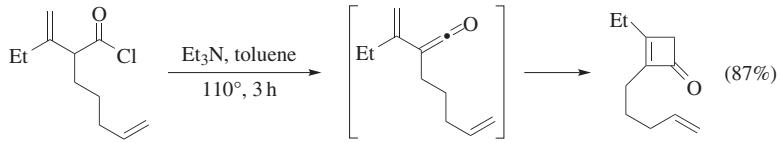
Scheme 62

Intramolecular Cycloadditions and Electrocyclizations of Vinylketenes Bearing Alkenyl Groups. A wide array of products can arise from intramolecular additions of vinylketenes to pendant alkenes in reactions that include straightforward closure by [2+2] and [4+2] processes, as well as other reactions that compete with these cyclizations, and further transformations of initial products under the reaction conditions. The equilibrium between a vinylketene and the corresponding cyclobutenone involves one of the simplest of these processes. As discussed earlier, vinylketenes are similar in stability to their isomeric cyclobutenones with rather low barriers for interconversion and the cyclobutenone may be isolated when it is the favored isomer. For example, the thermal Wolff rearrangement of a phosphoryl diazo ketone leads to vinylketene formation followed by electrocyclization to a cyclobutenone that is stabilized, relative to the vinylketene, by the methoxy group (Scheme 63).[98]



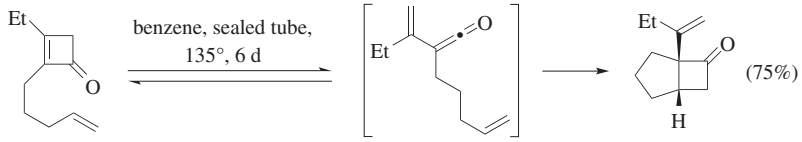
Scheme 63

Vinylketene **46**, generated by dehydrochlorination in refluxing toluene, also undergoes electrocyclization to afford the cyclobutenone (Scheme 64).[98] The process is reversible and at a higher temperature vinylketene **46** is reformed and closes irreversibly with the remote vinyl group via [2+2] cycloaddition to form a bicyclo[3.2.0]heptanone (Scheme 65).[98]



46

Scheme 64

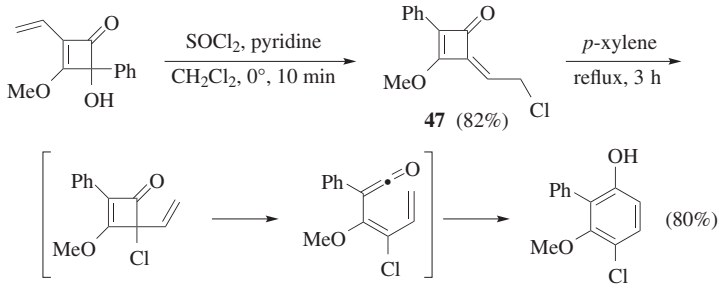


46

Scheme 65

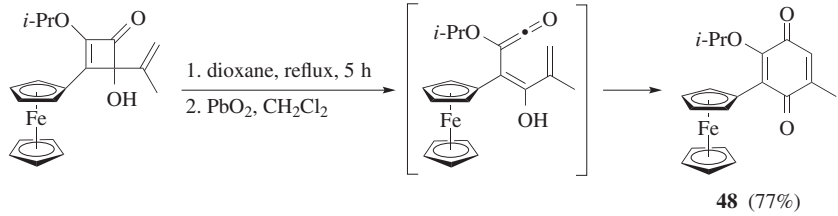
Chloro-substituted products are accessible using appropriately substituted cycobutenones or acid chlorides as the vinylketene precursors. Cyclobutenone **47** is

formed from the hydroxycyclobutenone by treatment with thionyl chloride. Compound **47** undergoes thermal ring opening via the allylic isomer to form a dienylketene that electrocyclizes to produce a 4-chlorophenol derivative (Scheme 66).[100]



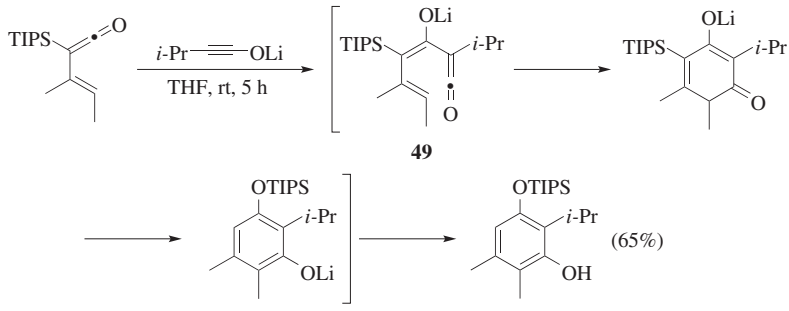
Scheme 66

Vinylketene–alkene cyclizations are also possible when a ferrocenyl substituent is present. Thermolysis of a ferrocenyl-substituted cyclobutenone in refluxing dioxane followed by oxidation with lead dioxide forms the corresponding 1,4-benzoquinone **48** by way of a dienylketene intermediate (Scheme 67).[101] The oxidizing agent is chosen to avoid competitive oxidation of the ferrocenyl group.



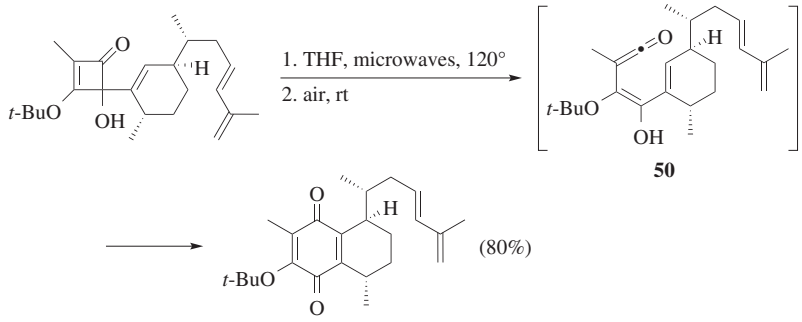
Scheme 67

A novel ynolate reaction with a stable silyl(vinyl)ketene generates dienylketene **49**, which undergoes an electrocyclization followed by carbon to oxygen silyl migration to afford a phenol (Scheme 68).[102,103]



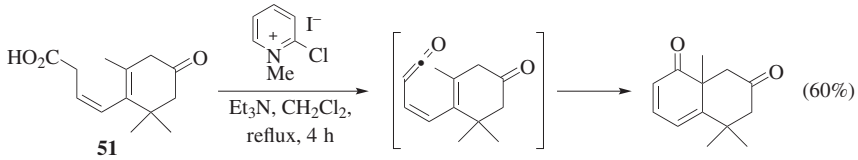
Scheme 68

In a more complex system, dienylketene **50** is formed from the corresponding cyclobutenone by microwave-assisted heating and undergoes electrocyclization (Scheme 69).[104] Subsequent air oxidation affords a quinone that is used in the synthesis of the diterpenes (−)-colombiasin A and (−)-elisapterosin B.



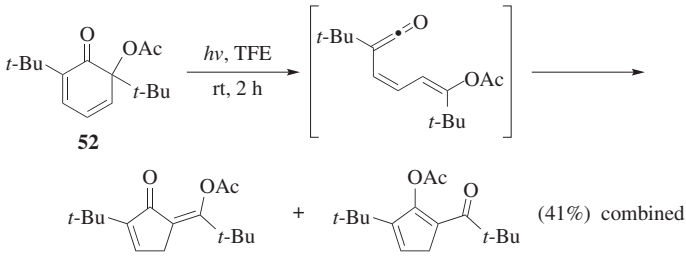
Scheme 69

When aromatization is prevented, cyclohexadienones are obtained from dienylketenes, as shown in the dehydration of carboxylic acid **51** using Mukaiyama's reagent (Scheme 70).[105]



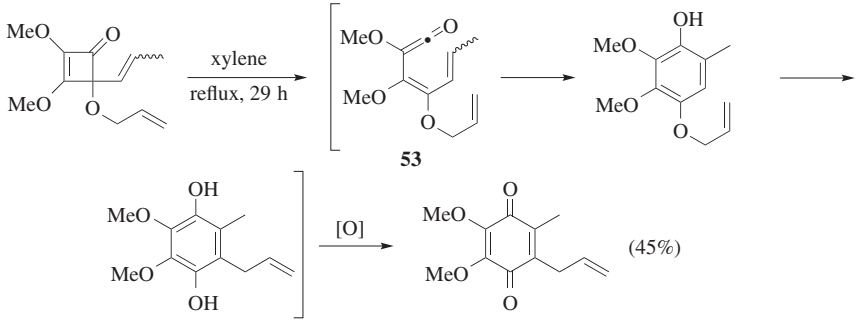
Scheme 70

Other cyclization modes for intermediate vinylketenes are also encountered. Irradiation of cyclohexadienone **52** in 2,2,2-trifluoroethanol (TFE) generates a dienylketene intermediate, which cyclizes to form two isomeric products, apparently as an equilibrating mixture (Scheme 71).[71]



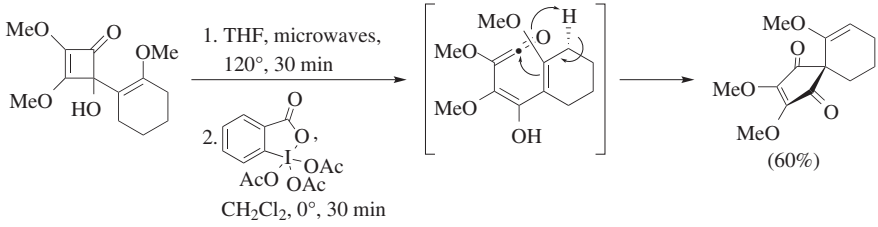
Scheme 71

Incorporation of an *O*-allyl group in the starting cyclobutenone results in a sequence that is suggested to involve electrocyclization of intermediate **53** followed by a Claisen rearrangement and oxidation of the hydroquinone under the reaction conditions by unspecified means, leading to the final 1,4-benzoquinone (Scheme 72).[106]

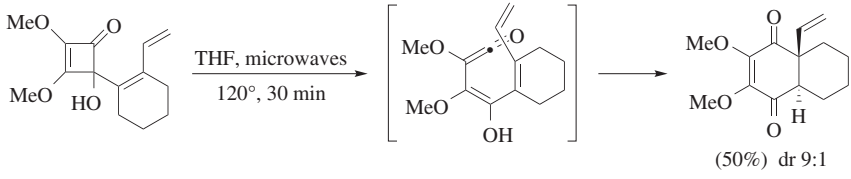


Scheme 72

The formation of a dienylketene by thermolysis of a 4-hydroxy-4-(2-methoxy-1-cyclohexenyl)-2-cyclobutenone followed by oxidation of the initial product with the Dess-Martin periodinane forms a spirocyclic 1,3-dione (Scheme 73).[107] The reaction is proposed to involve a carbonyl ene reaction of the initially formed vinylketene. Activation of the hydrogens allylic to the enol ether is proposed to be important to the course of the reaction, as dienylketenes from less activated substrates, such as the vinyl-substituted system in Scheme 74, afford cyclohexene-1,4-diones by the more typical electrocyclization of the dienylketene.[107]

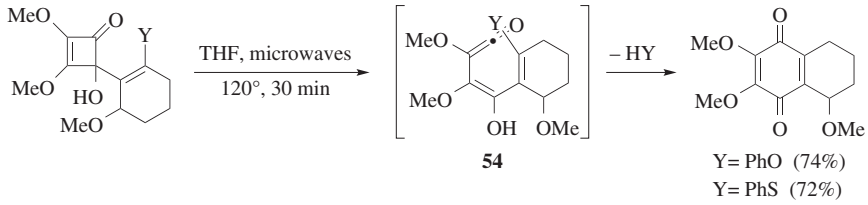


Scheme 73



Scheme 74

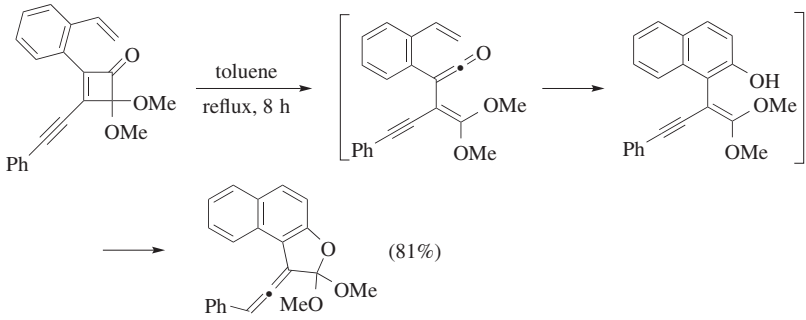
These competing processes are delicately balanced. If the cyclohexenyl MeO group is replaced by PhO or PhS, the allylic hydrogens in the vinylketene intermediates **54** are not as strongly activated and the ene reactions of the dienylketenes do not occur (Scheme 75).[107] Instead, electrocyclization followed by elimination affords the corresponding benzoquinones. Earlier examples also show that benzoquinones are commonly encountered products from electrocyclizations of dienylketenes and can arise either from an elimination step as in Scheme 75, or by oxidation of an intermediate hydroquinone.



54

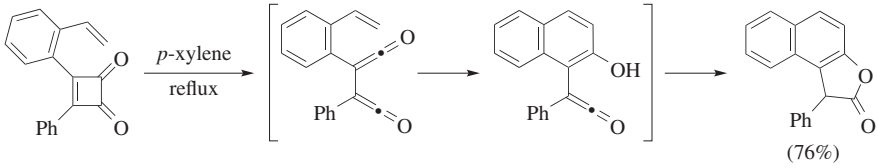
Scheme 75

When a suitably positioned, electrophilic acceptor group is present, phenolic hydroxy groups that are generated by the initial cyclization of a vinylketene can participate in further ring closures. An example involving an electron-rich olefin is shown in Scheme 76.[108]



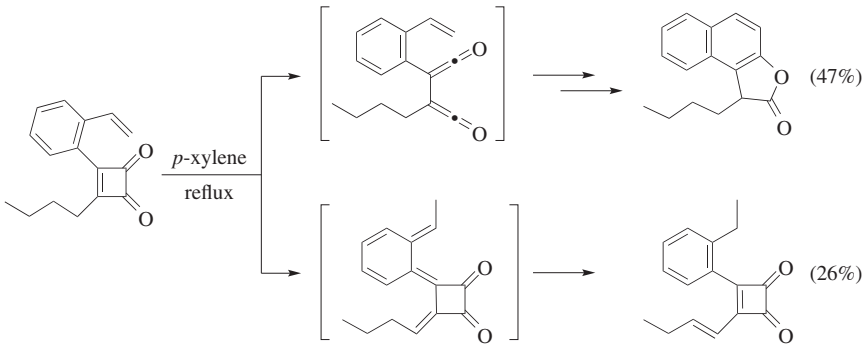
Scheme 76

Phenolic hydroxy groups may also be involved in lactone ring formation, as shown in Scheme 77.[109] Heating a cyclobutenedione in refluxing *p*-xylene results in the generation of a 1,2-bis(ketene) which undergoes electrocyclization to a naphthol-substituted monoketene that closes to produce a lactone.



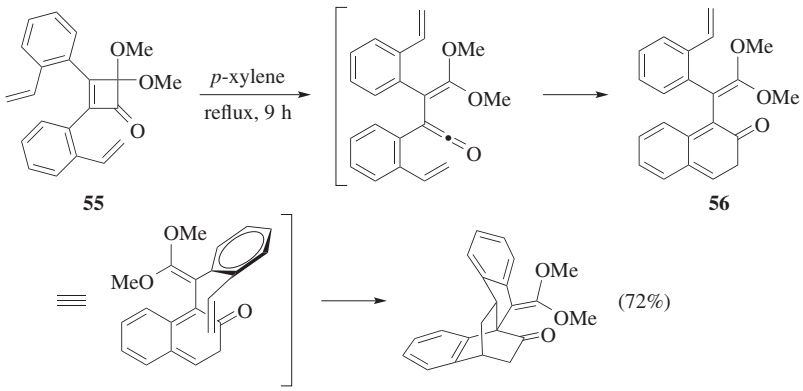
Scheme 77

Replacing the phenyl group in the foregoing substrate with an *n*-butyl group results in the formation of both the corresponding lactone (47%) and a new cyclobutenedione (26%) that is proposed to form from the intermediate generated by a 1,7-sigmatropic hydrogen shift (Scheme 78).[109] Formation of the bis(ketene)s is expected to be an equilibrium process favoring the cyclobutenedione, so the product distribution reflects a competition between the cyclization and hydrogen transfer processes.



Scheme 78

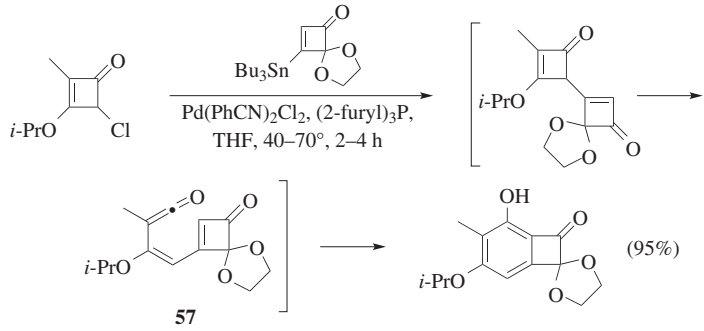
A further mode of secondary cyclization is shown in Scheme 79. Thermolysis of the cyclobutenedione monoketal **55** leads to a vinylketene that undergoes the usual electrocyclization to form intermediate **56**. This intermediate, however, does not aromatize but instead undergoes an intramolecular Diels–Alder reaction to afford a pentacyclic product.[109]



Scheme 79

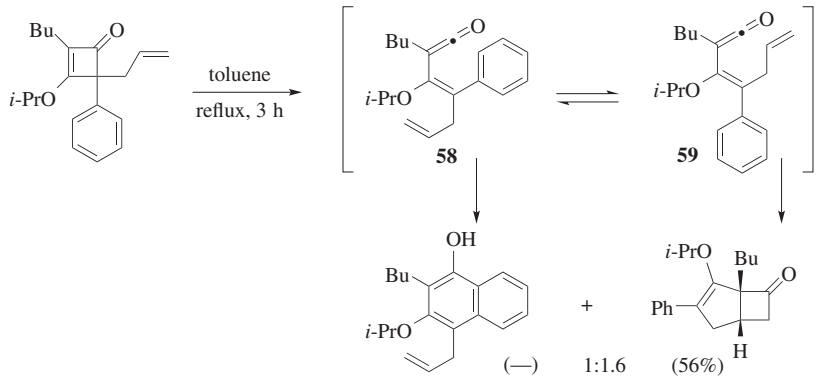
In situ generation of a bis(cyclobutenone) by palladium-catalyzed coupling of a 4-chlorocyclobutenone with a stannylcyclobutenedione monoketal is followed by ring opening to intermediate dienylketene **57**, which undergoes electrocyclization with

the alkenyl group of the remaining cyclobutenone to form a benzocyclobutenone (Scheme 80).[110] Benzocyclobutenones obtained by this route can be used in subsequent vinylketene cycloadditions.



Scheme 80

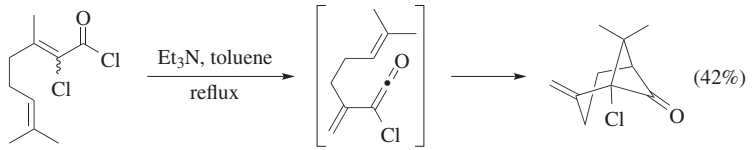
The competition between electrocyclization onto an aryl group (via isomer **58**) versus [2+2] cycloaddition with an allyl group (via isomer **59**) is shown in Scheme 81. The reaction forms the naphthol and the cyclobutanone in a ratio shown by NMR to be 1:1.6.[111] The naphthol could not be purified because of its propensity for air oxidation. The ratio of the two products is attributed to the effect of the electronic and steric properties of the substituents on the equilibrium between the vinylketene geometrical isomers **58** and **59** and in the cyclization steps.



Scheme 81

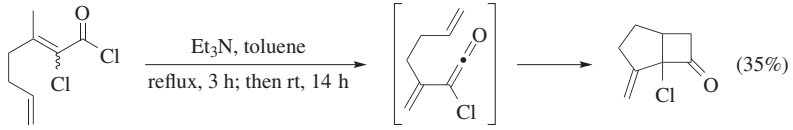
2-Chloro-substituted vinylketenes are activated for cycloadditions. Ketene **60** generated by dehydrochlorination undergoes intramolecular [2+2] cycloaddition with the alkenyl group leading selectively to the bicyclo[3.1.1]heptanone (Scheme 82); this regiochemical outcome can be explained by frontier molecular orbital analysis.[112]

By contrast, ketene **61** with a monosubstituted double bond forms the bicyclo[3.2.0] product (Scheme 83).[112]



60

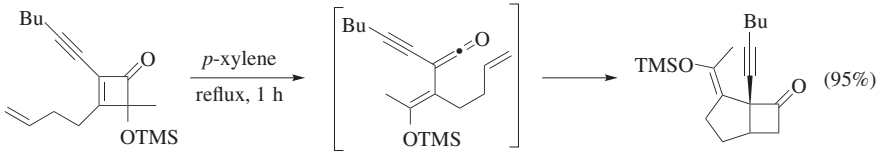
Scheme 82



61

Scheme 83

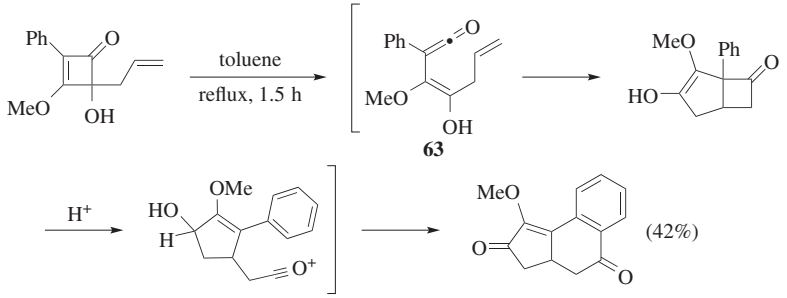
The multiply unsaturated vinylketene intermediate **62**, generated by heating the corresponding cyclobutenone in refluxing *p*-xylene, undergoes a very efficient [2+2] cycloaddition with the remote alkenyl group to yield a highly functionalized bicyclo[3.2.0]heptanone (Scheme 84).[113] A related system with a vinyl substituent replacing the alkynyl group also cyclizes in excellent yield.[114]



62

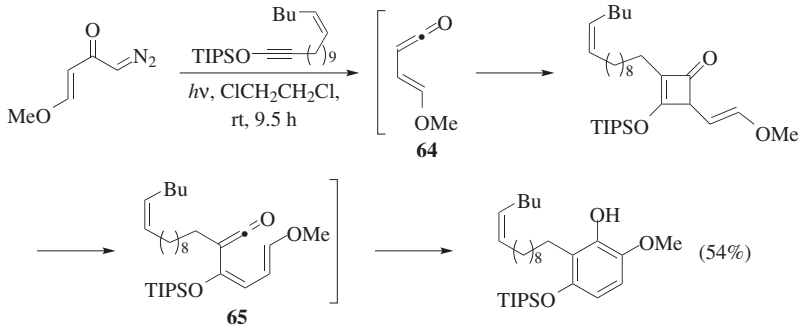
Scheme 84

Aryl groups also participate in secondary transformations. The ultimate production of the tricyclic product shown in Scheme 85 is proposed to involve formation of vinylketene **63** by cyclobutenone thermolysis, followed by an intramolecular [2+2] cycloaddition to afford an unobserved cyclobutanone intermediate. Subsequent cleavage and recyclization is suggested to involve the presence of adventitious acid, forming an intermediate acylium ion that cyclizes and is oxidized under the reaction conditions to afford the observed product of *C*-acylation of the phenyl group (Scheme 85).[115]



Scheme 85

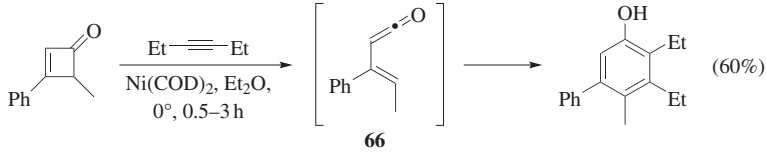
Intermolecular Cycloadditions of Vinylketenes with Alkynes. A simple intermolecular [4+2] cycloaddition involving a stable silyl(vinyl)ketene and methyl propiolate is shown in Scheme 6. However, [2+2] cycloaddition is the more typical mode of reactivity for vinylketenes with alkynes. Such processes form cyclobutenones that are prone to facile ring opening to form new vinylketenes that may react further, creating a versatile vinylketene pericyclic reaction cascade (see Scheme 1).[9,10] Scheme 86 illustrates a more sophisticated case in which generation of ketene **64** by photochemical rearrangement in 1,2-dichloroethane and in situ [2+2] cycloaddition with an alkynyl ether forms a cyclobutenone.[116] Subsequent photochemical or thermal ring opening leads to dienylketene **65** which affords the phenol by 6π electrocyclization. The product serves as a precursor in the synthesis of maesanin. In this example, a constitutionally isomeric phenol would be formed if the original cycloaddition with the alkyne took place by a [4+2] pathway.



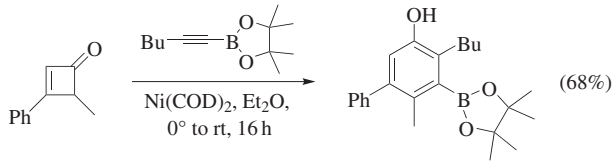
Scheme 86

bis(1,5-Cyclooctadienyl)nickel catalyzed ring opening of a cyclobutenone at low temperature is suggested to provide vinylketene **66** which reacts by [4+2] cycloaddition with 3-hexyne to afford a phenol (Scheme 87).[66] The cycloaddition reaction is catalyzed by $Ni(COD)_2$ and fails with activated alkynes containing alkoxy or acyl substituents because they are oligomerized by the catalyst. Unsymmetrical alkynes in

which neither of the substituents is strongly activating yield mixtures of cycloaddition products in this reaction.[66] Similar $Ni(COD)_2$ catalyzed reactions are also effective with alkynyl boronates, affording products for further elaboration (Scheme 88).[117]



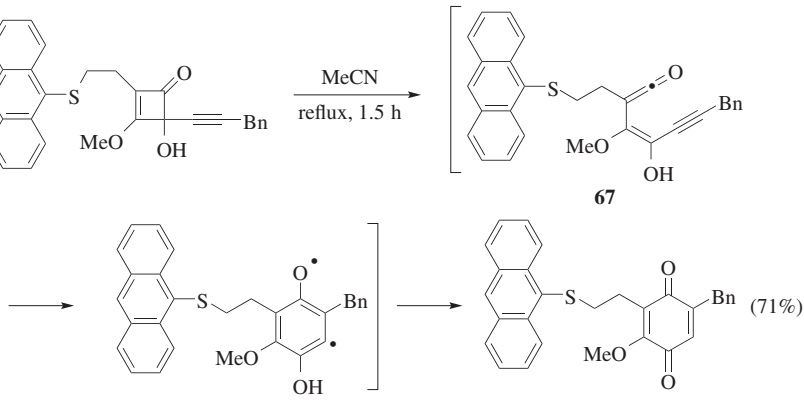
Scheme 87



Scheme 88

Electrocyclizations of Vinylketenes Bearing Alkynyl Groups. The chemistry of these reactions is very diverse and many examples are known. As discussed in the Mechanism and Stereochemistry section, and in contrast to the analogous electrocyclization with alkenyl groups, the initial product of an electrocyclization involving an alkynyl residue is a diradical. In suitable systems the reactive aryl radical can either add to a pendant group or abstract a hydrogen atom to form a new radical, ultimately leading to the production of relatively complex ring systems.

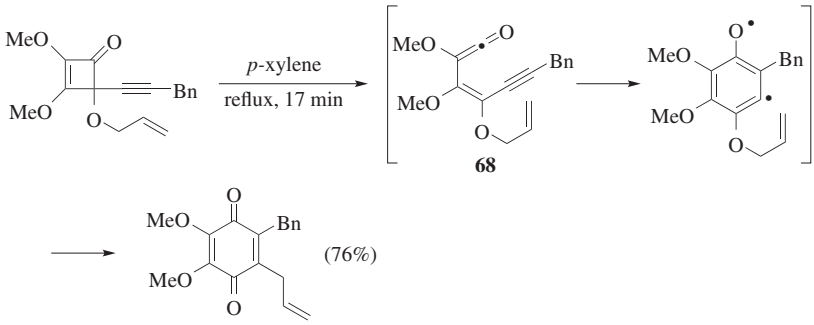
In a straightforward example, heating a 2-[2-(9-anthracenyl)thioethyl]cyclobutenone in acetonitrile causes efficient ring opening to form an alkynylvinylketene that electrocyclizes to form the expected benzoquinone (Scheme 89).[118] DNA cleavage



Scheme 89

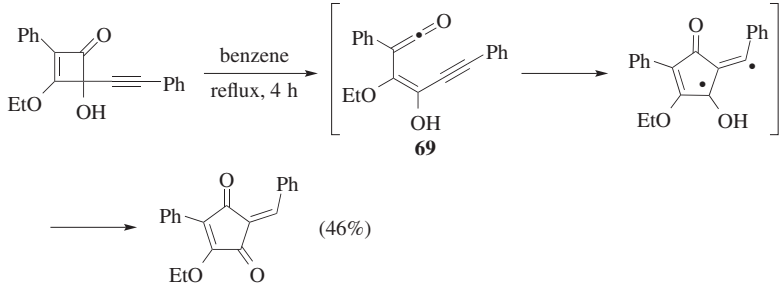
is observed when the reaction is carried out in the presence of supercoiled DNA in TRIS buffer (tris(hydroxymethyl)aminomethane), providing evidence of a diradical intermediate formed from alkynylvinylketene **67**.

A different fate for the diradical species is shown in Scheme 90. Allyloxy-substituted alkynylvinylketene **68**, generated by cyclobutenone ring opening, electrocyclizes to a diradical that undergoes allylic rearrangement to the final product.[26]



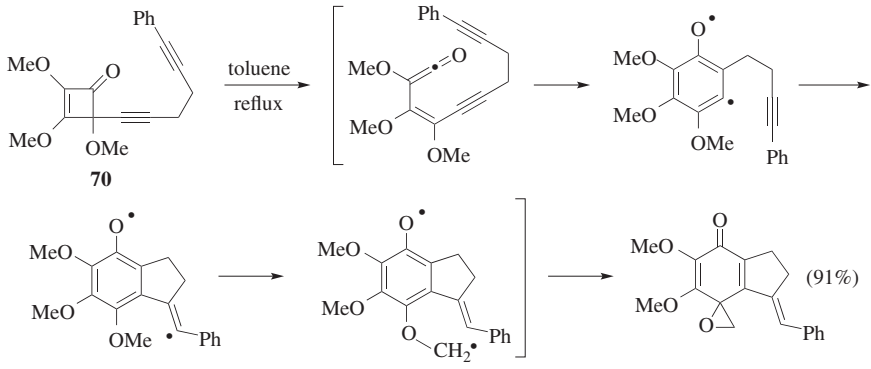
Scheme 90

The radical-stabilizing phenyl group in alkynylvinylketene **69**, generated by thermolysis, directs the subsequent cyclization to form a 5-membered-ring diradical intermediate that leads to a 2-benzylidene-1,3-cyclopentenedione derivative (Scheme 91).[26]



Scheme 91

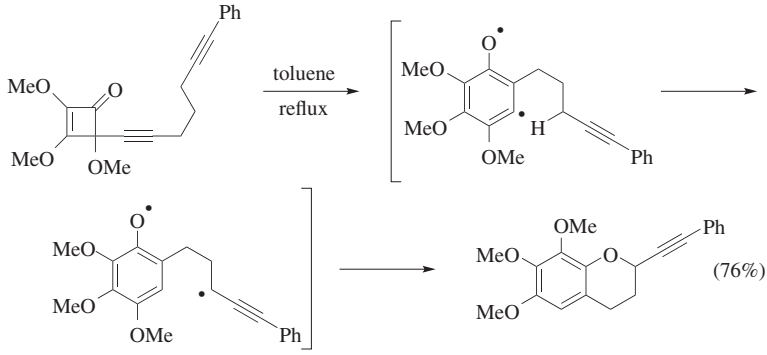
Chain length affects the balance between cyclization and hydrogen-atom abstraction processes in the intermediate radical. Both of these processes prefer a 6-atom separation of the reacting centers but smaller rings can form as shown in Scheme 92. The 4-(6-phenylhexa-1,5-diynyl)-2-cyclobutenone **70**, when heated in toluene, leads to an epoxide in a process envisaged to involve initial cyclization of the diradical, followed by hydrogen-atom transfer and a final ring closure (Scheme 92).[119]



70

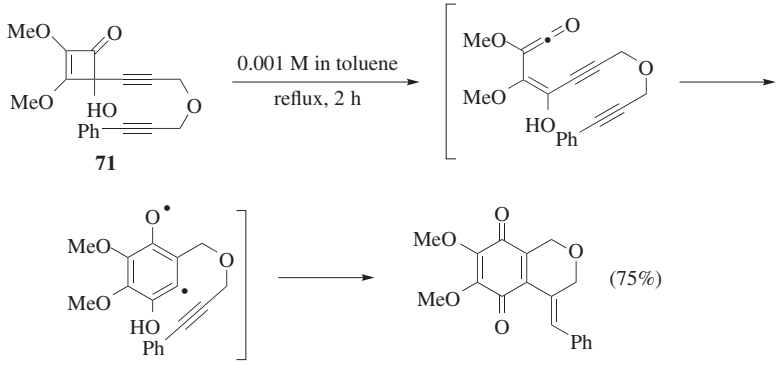
Scheme 92

However, in a substrate with a three-carbon tether between the two alkynes, an abstraction–recombination route forms a benzopyran (Scheme 93).[119]



Scheme 93

The diyne-substituted cyclobutenone **71**, upon ring opening at high dilution, affords a pyranobenzoquinone (Scheme 94).[120] This pathway is favored at low

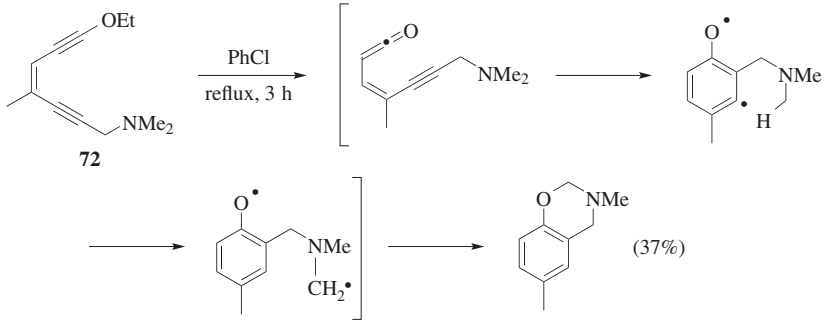


71

Scheme 94

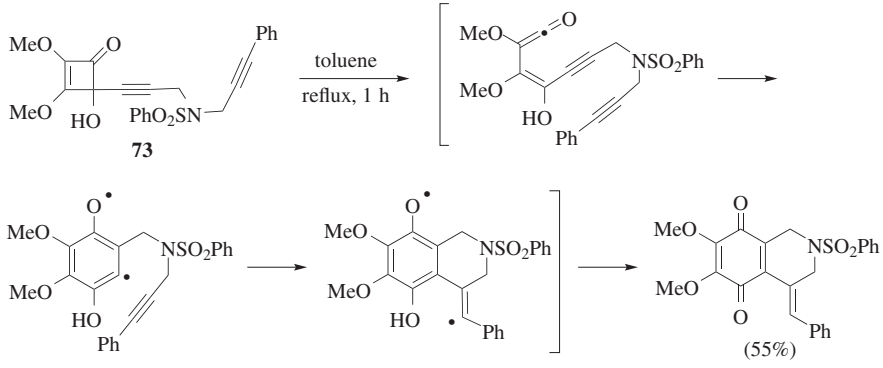
concentrations because formation of a six-membered ring by radical addition is favored over the bimolecular hydrogen-atom transfer that leads directly to a monocyclic quinone.

Heteroatom substituents in a side chain can facilitate hydrogen-atom abstraction following the initial electrocyclization. Enediyne **72**, upon heating in chlorobenzene, produces a diradical intermediate which, by intramolecular hydrogen-atom abstraction, generates a new diradical that undergoes ring closure (Scheme 95).[74]



Scheme 95

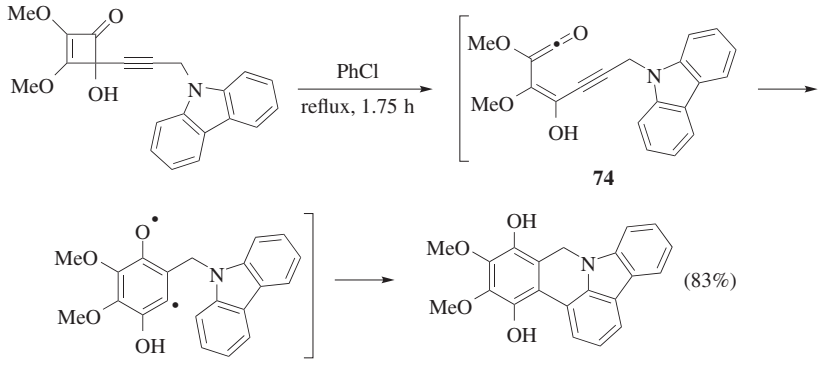
The thermal ring opening and subsequent cyclization of 4-[4-aza-1,6-alkadiynyl]cyclobutenone **73** is an example of a general route to *N*-heterocyclic quinones and hydroquinones wherein the diradical formed from the alkynylvinylketene adds to a pendant alkynyl group, in this case with the ultimate formation of a piperidinoquinone (Scheme 96).[121] It should be noted that these quinone-forming reactions do not require an oxidation step.



Scheme 96

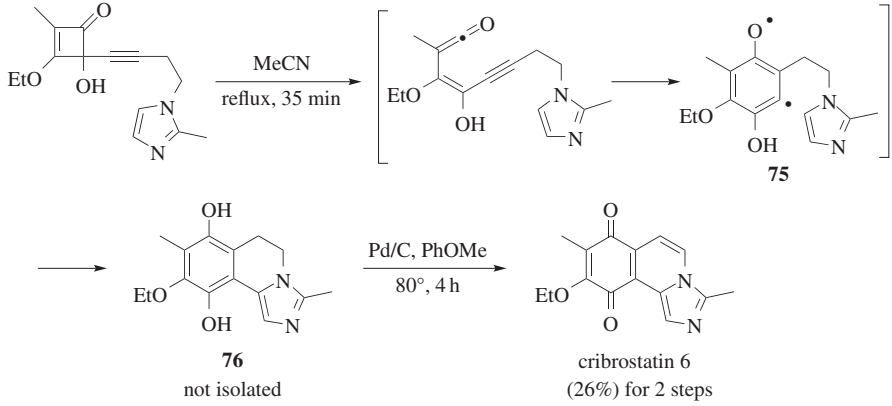
Cyclizations of the intermediate aryl radical onto aromatic rings are also encountered. Alkynylvinylketene **74**, which is formed by cyclobutenone ring opening in

refluxing chlorobenzene, electrocyclizes to a diradical, that then cyclizes further onto an aryl ring, forming a light-blue indolophenanthridine (Scheme 97).[121]



Scheme 97

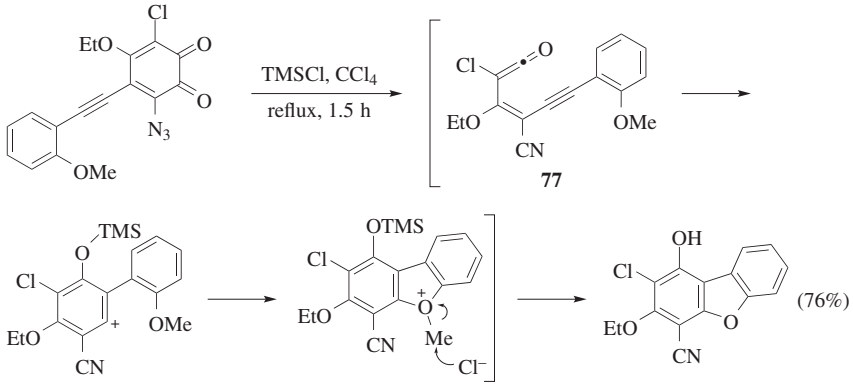
Secondary cyclizations of diradical intermediates onto heterocyclic rings also produce synthetically useful, polycyclic products. Diradical **75** formed in the alkynylvinylketene electrocyclization shown in Scheme 98 undergoes intramolecular aromatic substitution with the tethered 2-methyl-1-imidazolyl group to provide hydroquinone **76**. This crude hydroquinone is subjected to dehydrogenation with palladium on carbon to afford the tricyclic benzoquinone cribrostatin 6.[122]



Scheme 98

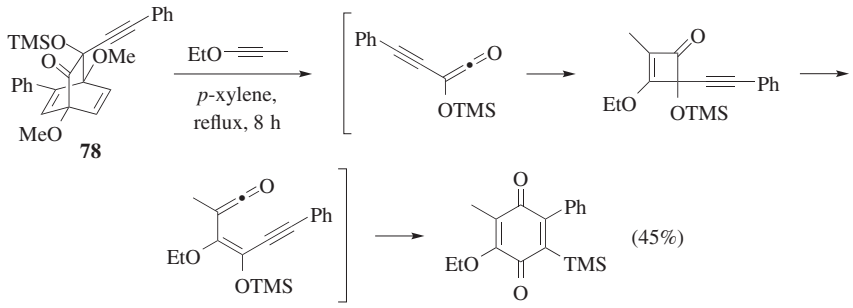
Formation of a new ring by attack of oxygen takes place in a cyclization that is conducted in the presence of chlorotrimethylsilane (Scheme 99).[123] Alkynylvinylketene **77** generated from an azido-1,2-benzoquinone forms a dibenzofuran by a process envisaged as cyclization to a silylated intermediate with electrophilic character.

Further cyclization followed by displacement of the methyl group by chloride ion affords the observed product in good yield.



Scheme 99

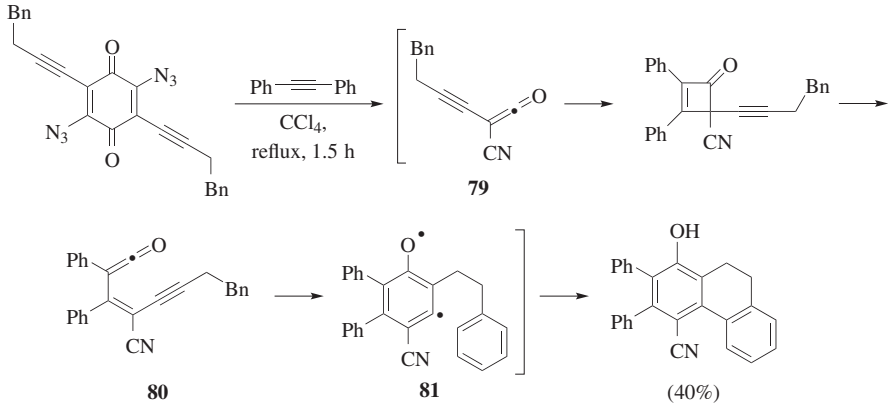
Cascade sequences involving two alkynylketenes are also possible. Heating ketone **78** in *p*-xylene generates an alkynylketene as an unobserved intermediate, which reacts by [2+2] cycloaddition with ethoxypropyne to form an intermediate cyclobutenone (Scheme 100).[124] Ring opening under the reaction conditions to an alkynylvinylketene and subsequent cyclization followed by oxygen-to-carbon silyl migration results in formation of the final benzoquinone.



Scheme 100

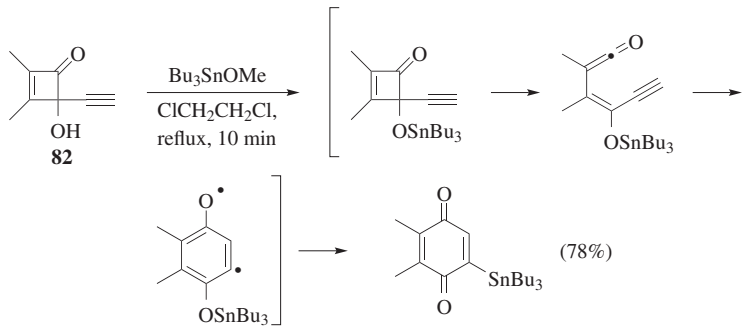
The generation of reactive cyano-substituted vinylketenes further expands the substituent scope for cascade processes. Two moles of alkynylketene **79** are obtained from the thermolysis of 2,5-diazido-1,4-benzoquinone, and these react with diphenylacetylene to form an alkynylcyclobutenone that undergoes ring opening to the alkynylvinylketene **80** (Scheme 101).[78] Electrocyclization forms diradical **81**,

which undergoes intramolecular arylation onto the pendant phenyl ring and yields a bridged biphenyl.



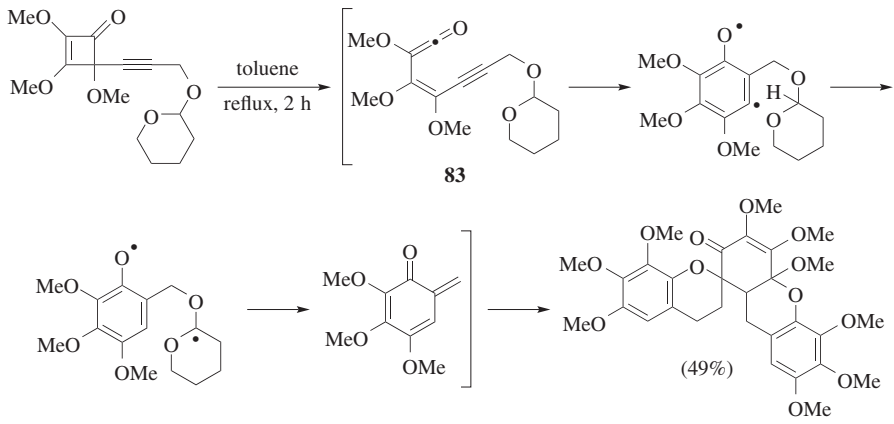
Scheme 101

A new carbon–tin bond can also be formed following the cyclization step. Heating cyclobutenone **82** in refluxing 1,2-dichloroethane in the presence of tri(*n*-butyl)methoxytin generates an *O*-stannylated alkynylvinylketene that undergoes electrocyclization to a diradical followed by oxygen-to-carbon migration of the tri-*n*-butyltin group to form the final benzoquinone (Scheme 102).[125] The tin substituent on the product provides a reactive center for further elaboration.[126]



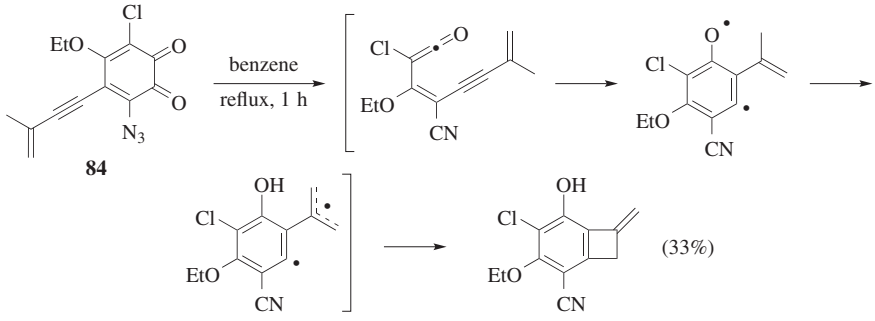
Scheme 102

Fragmentations of intermediate radicals can lead to unexpected products (Scheme 103).[120] Generation and electrocyclization of the alkynylvinylketene **83** is followed by hydrogen-atom transfer from C2 of the THP protecting group. The resulting diradical undergoes a fragmentation that is driven by carbonyl-group formation and provides an *o*-quinomethide, which undergoes trimerization.



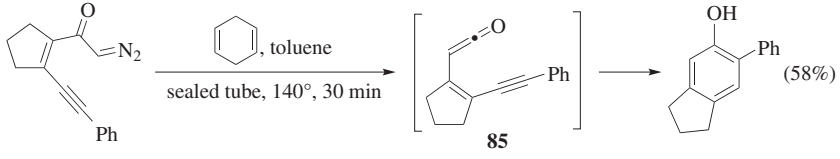
Scheme 103

The fully substituted 1,2-benzoquinone **84** upon thermolysis in refluxing benzene forms an unusual benzocyclobutene, illustrating another fate for a diradical derived from the electrocyclization of an alkynylvinylketene (Scheme 104).[123]



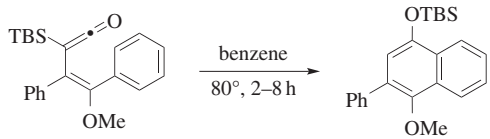
Scheme 104

Reductive conditions can also be used to quench the initially formed diradical. Thermal rearrangement followed by electrocyclization of the alkynylvinylketene **85** in the presence of 1,4-cyclohexadiene functioning as a hydrogen-atom donor affords the phenol (Scheme 105).[127]



Scheme 105

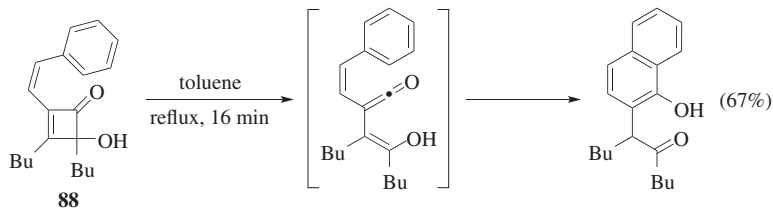
Electrocyclizations of Vinylketenes Bearing Aromatic Groups. Intermolecular reactions of vinylketenes with arenes have not been observed, but intramolecular reactions with pendant aryl groups have proven to be quite useful in synthesis. For example, the isolable, silyl-substituted vinylketene **86** undergoes electrocyclization followed by 1,5-hydrogen shift and 1,3-silyl migration to form naphthol **87** (Scheme 106).[128]



86 **87** (96%)

Scheme 106

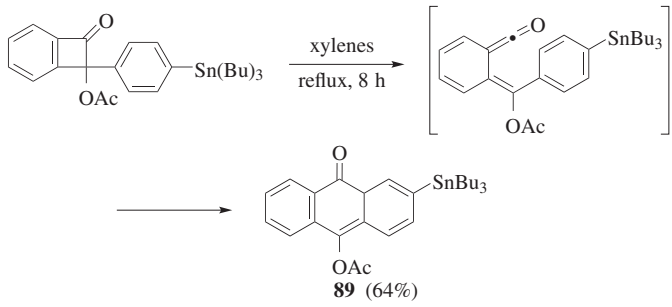
The vinylketene formed from thermolysis of cyclobutenone **88** engages in electrocyclization with the ketenophilic styryl group to form a 1-naphthol (Scheme 107).[129] Lactone formation by reaction of the hydroxyl group with the ketene is not observed.



88

Scheme 107

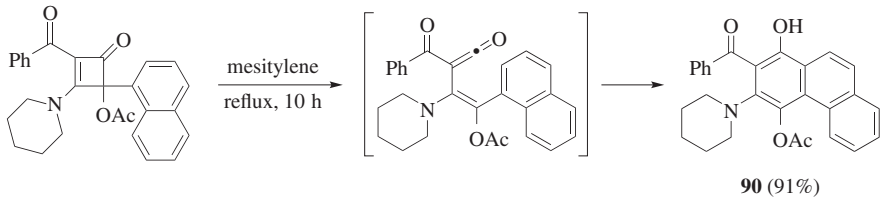
Vinylketenes derived from benzocyclobutenones also undergo electrocyclization. In the example shown in Scheme 108, the product is reported to possess the nonaromatized structure **89**.[130] Treatment of product **89** with K_2CO_3 and MeI affords the expected methoxyanthracene.



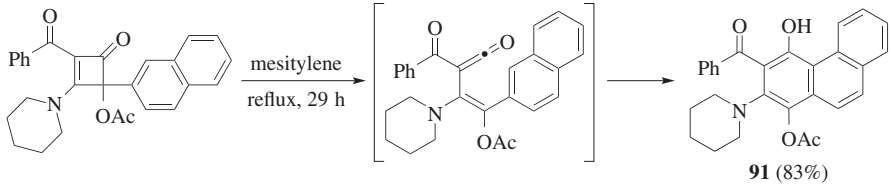
89 (64%)

Scheme 108

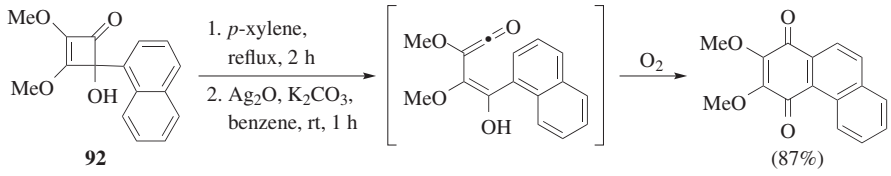
Positional selectivity in the electrocyclization of vinylketenes with aryl groups is observed in the reactions of the isomeric 1- and 2-naphthylcyclobutenones that form phenanthrene isomers **90** (Scheme 109) and **91** (Scheme 110), respectively, via acyl-substituted vinylketenes.[131] Cyclization of the vinylketene derived from the 2-isomer to provide exclusively product **91** reflects the general trend for electrophilic attack at the 1-position in naphthalene derivatives,[132] and none of the anthracene derivative that would have been produced by cyclization onto C3 is seen. This electrocyclization also occurs with 4-hydroxy-2,3-dimethoxy-4-(1-naphthyl)-2-cyclobutenone (**92**) (Scheme 111) and the corresponding 2-naphthyl analogue.[133] The isomeric vinylketenes afford, after oxidation of the crude product, the same phenanthrenequinone.



Scheme 109

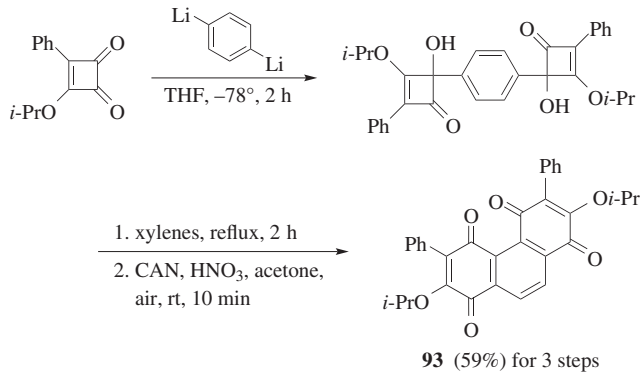


Scheme 110



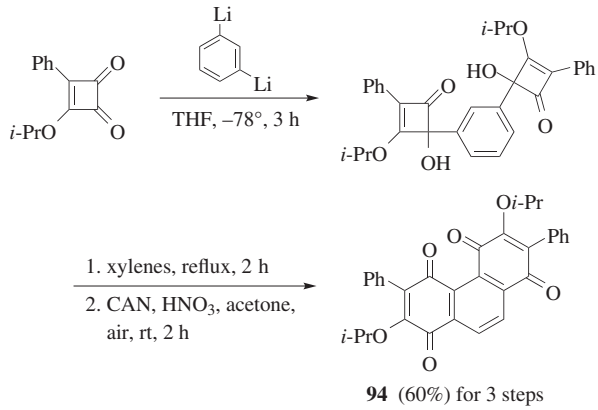
Scheme 111

Upon thermolysis, 1,4- and 1,3-bis(cyclobutenyl)benzenes provide substituted phenanthrenes **93** and **94**, respectively, in processes involving successive electrocyclizations of vinylketenes with the benzene nuclei (Schemes 112 and 113).[130]



93 (59%) for 3 steps

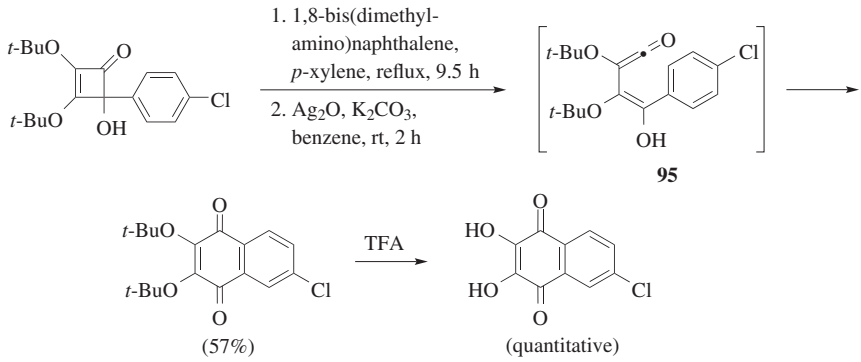
Scheme 112



94 (60%) for 3 steps

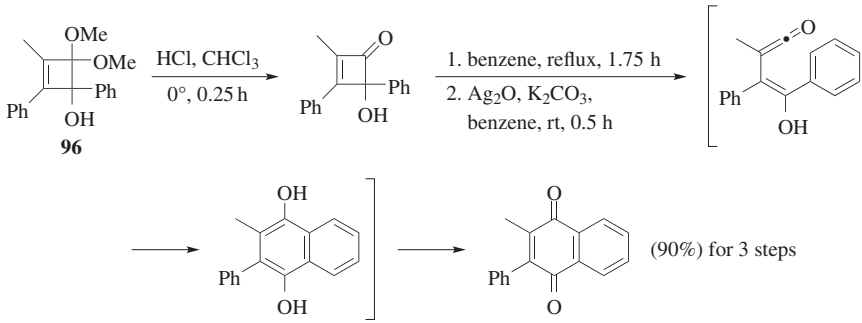
Scheme 113

The availability of a variety of ethers of squaric acid allows these sequences to be conducted with easily removable protecting groups on the final, phenolic alcohols. The generation and cyclization of vinylketene **95** provides the naphthoquinone in 57% yield along with 36% of recovered starting material (Scheme 114).[134] The presence of 1,8-bis(dimethylamino)naphthalene during the cyclization step is necessary to prevent competitive *tert*-butyl ether cleavage during the reaction. The *tert*-butyl groups in the product are easily cleaved under acidic conditions to afford the dihydroxynaphthoquinone.



Scheme 114

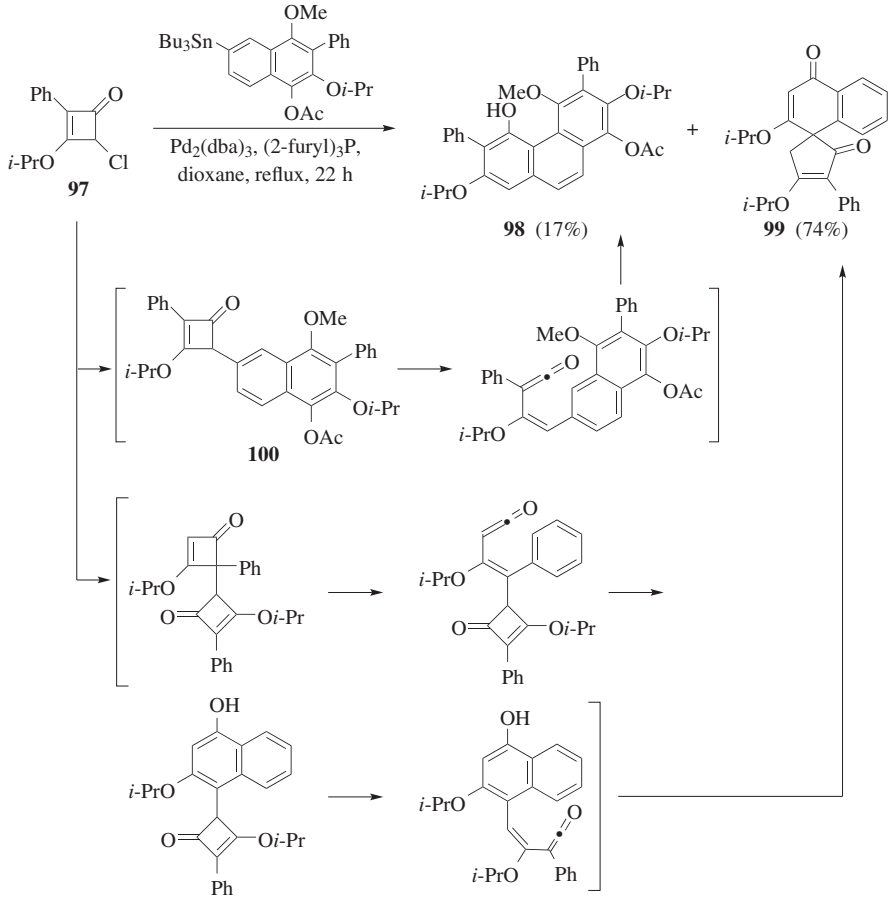
In some cases the use of a protected ketone is necessary for the selective synthesis of the required intermediate and subsequent transformations may be accomplished without further purifications, as shown in Scheme 115.[135] Hydrolysis of cyclobutene monoketal **96** leads to an intermediate cyclobutenone that undergoes thermal ring opening to the vinylketene followed by electrocyclization to an unisolated hydroquinone intermediate. Oxidation provides the final naphthoquinone.



Scheme 115

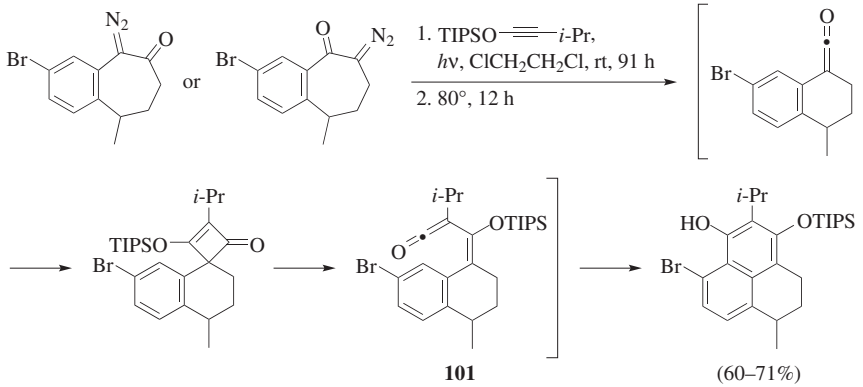
Stille couplings with 4-chlorocyclobutenones are normally efficient reactions for the in situ generation of precursors to vinylketenes (Scheme 116). However, homocoupling can be an issue, as shown for the coupling of cyclobutenone **97** with a stannylnaphthalene (Scheme 116).[130] Formation of product **98** occurs via the expected Stille coupling that provides cyclobutenone **100**, which ring opens to form the vinylketene and undergoes electrocyclization. The formation of spiro-product **99** evidently occurs by an initial reductive dimerization of 4-chlorocyclobutenone

97 to form a bis(cyclobutenone) that reacts by successive vinylketene formation, electrocyclization, and generation of a second vinylketene, which undergoes a unique electrocyclization (Scheme 116).



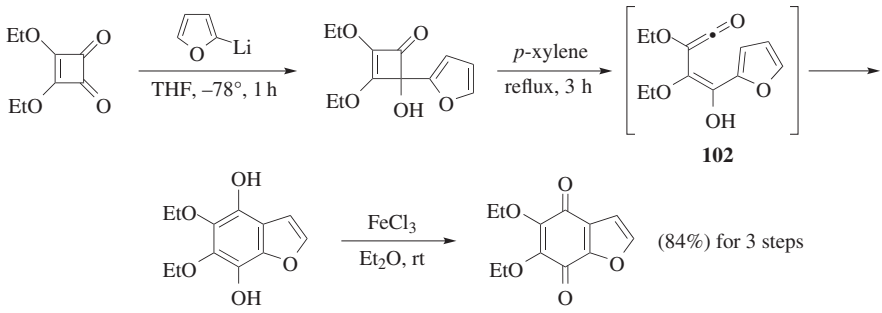
Scheme 116

Wolff rearrangements are also used to generate vinylketenes for cyclization onto arenes. In the tandem process shown in Scheme 117,[136] isomeric diazo ketones form the same ketene upon irradiation, which reacts in situ with 1-triisopropylsilyloxy-3-methyl-1-butyne by [2+2] cycloaddition to form an intermediate cyclobutenone. Upon continued irradiation or with the assistance of heating, the cyclobutenone affords vinylketene **101**, which undergoes electrocyclization to generate a dihydrophenalene that is used in the synthesis of salvilenone. The efficiency of the photochemical ring opening of the cyclobutenone may be compromised by deposition on the cell walls, so heating is used to ensure completion of this step.



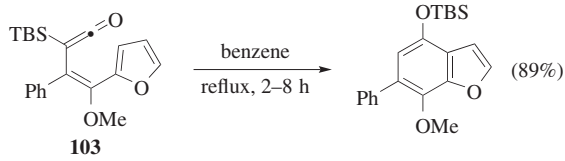
Scheme 117

Electrocyclizations of Vinylketenes Bearing Heteroaromatic Groups. Reactions that generate vinylketenes with pendant heteroaromatic rings positioned for electrocyclizations provide access to a variety of bi- and polycyclic products. If the vinylketene is generated from a cyclobutenone, it is frequently possible to take advantage of the facile metalation of diverse heterocycles for the synthesis of the vinylketene precursor, as shown in Scheme 118.[137] In a multistep sequence, without purification of intermediates, the reaction of diethyl squarate with 2-furyllithium followed by hydrolysis provides the crude hydroxycyclobutenone, which upon refluxing in *p*-xylene is reversibly converted to the vinylketene **102**. Electrocyclization of vinylketene **102** to a hydroquinone and final oxidation using ferric chloride in ether affords 5,6-diethoxybenzofuran-4,7-dione in excellent yield.



Scheme 118

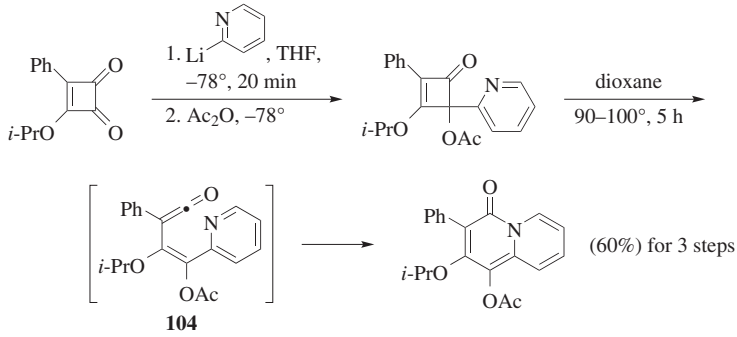
Heating the isolable, TBS-substituted vinylketene **103** in benzene forms a 4-silyloxybenzofuran by electrocyclization followed by hydrogen transfer and silyl group migration (Scheme 119).[128]



103

Scheme 119

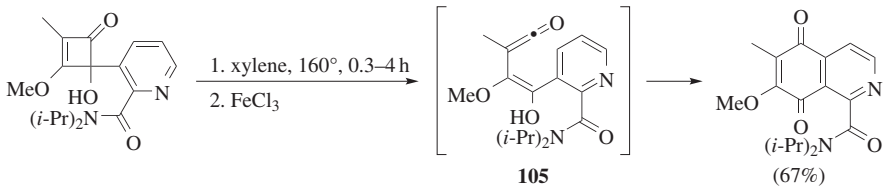
In some systems a carbon–nitrogen bond will form in preference to a carbon–carbon bond, affording a simple route to products with a ring-fused nitrogen. Reaction of a cyclobutenedione with 2-pyridyllithium followed by in situ acetylation and subsequent heating of the crude product in dioxane forms vinylketene **104**, which undergoes electrocyclization onto the carbon–nitrogen bond to form a quinolizidinone derivative (Scheme 120).[138]



104

Scheme 120

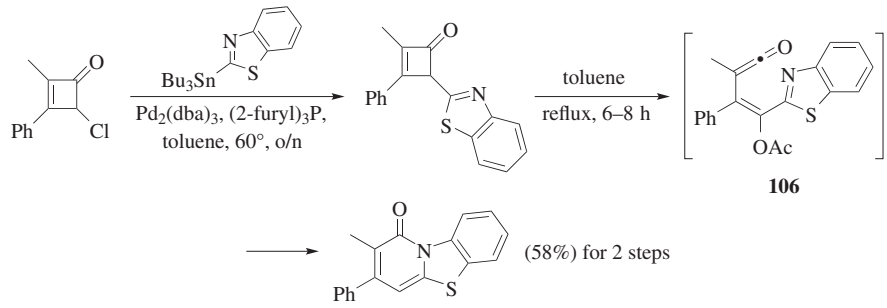
If the nitrogen is not suitably positioned, ring closure with carbon–carbon bond formation still occurs readily, even when an additional electron-withdrawing group is present on the pyridine acceptor ring. Thus, electrocyclization via vinylketene **105** followed by oxidation of the crude cyclization product affords the isoquinoline-5,8-dione system (Scheme 121).[139]



105

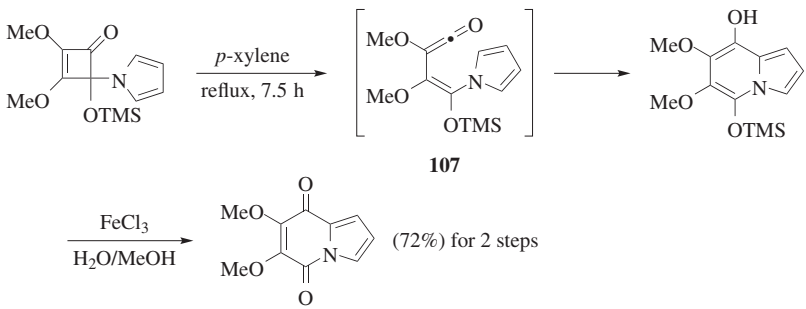
Scheme 121

Coupling 2-(tributylstannyl)benzothiazole with a 4-chlorocyclobutenone followed by heating in refluxing toluene provides a route to a 1-oxopyridobenzothiazole via vinylketene **106** (Scheme 122).[138] Similar procedures afford the corresponding furan and thiophene derivatives.[140]



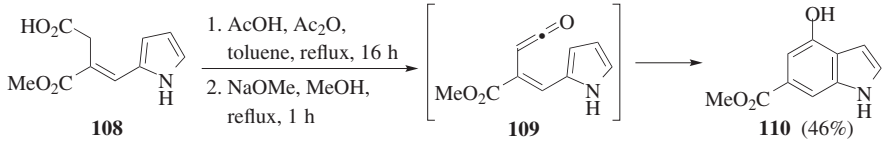
Scheme 122

The stability of hemiaminals derived from cyclobutenediones is used to advantage in an alternative route to the indolizine system by a cyclization that forms a carbon–carbon bond. Vinylketene **107** is generated from a protected 2-(1-pyrrolyl)-2-hydroxycyclobutenone and electrocyclizes with formation of a 5-trimethylsilyloxy-8-indolizinol, which is not isolated but is oxidized to the indolizine-5,8-dione with ferric chloride (Scheme 123).[141]



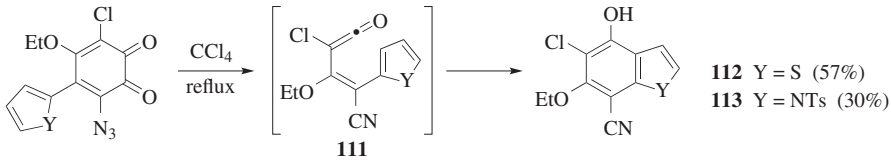
Scheme 123

Other modes of vinylketene generation are also applicable to electrocyclizations onto heterocycles. Heating β,γ-unsaturated carboxylic acid **108** with acetic acid and acetic anhydride causes dehydration via the mixed anhydride and generates vinylketene **109**, which undergoes electrocyclization to afford 4,6-disubstituted indole **110** (Scheme 124).[142] Cyclization onto the poorly nucleophilic, unsubstituted ring nitrogen is not seen.



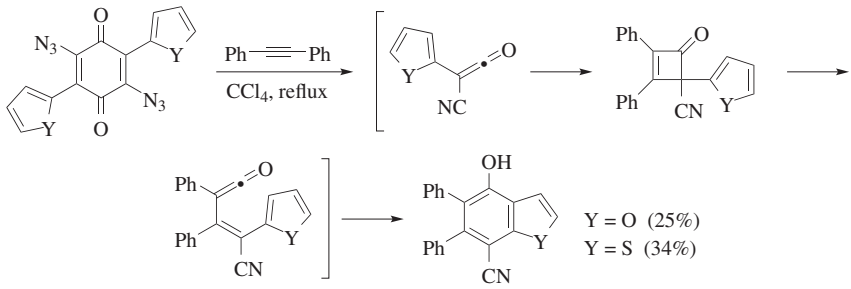
Scheme 124

Generation of vinylketenes **111** by heating the appropriate 4-heteroaryl-3-azido-1,2-benzoquinone in carbon tetrachloride affords benzo[*b*]thiophene **112** or indole **113** (Scheme 125).[143]



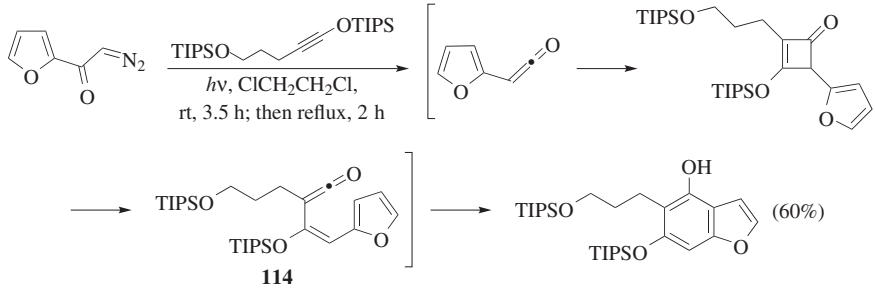
Scheme 125

2,5-Diazido-1,4-benzoquinones substituted with 2-furyl or 2-thienyl groups react in refluxing carbon tetrachloride to form two molecules of the respective heteroaryl(cyano)ketenes, which react in situ with diphenylacetylene via [2+2] cycloaddition to form heteroaryl-substituted cyclobutenones (Scheme 126).[143] These intermediates undergo ring opening under the reaction conditions to form the heteroaryl-substituted vinylketenes, followed by electrocyclization to afford the corresponding benzofurans or benzothiophenes.



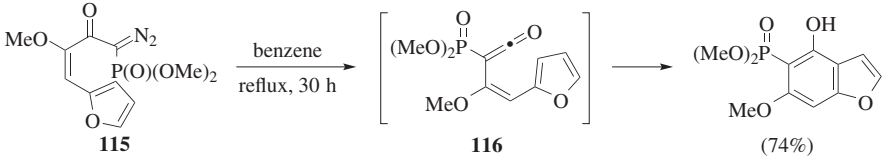
Scheme 126

A similar tandem process is achieved by irradiation of 2-diazo-1-(2-furanyl) ethanone in the presence of an alkyne. After in situ [2+2] cycloaddition followed by ring opening of the cyclobutenone to afford the intermediate 2-furylvinylketene **114**, a final electrocyclization provides the benzofuran (Scheme 127).[144]



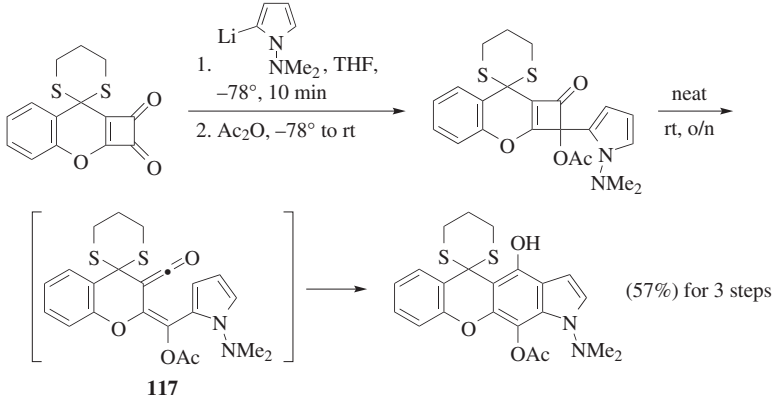
Scheme 127

A variety of functional groups can be incorporated in the precursor to the vinylketene. Thermal decomposition of diazo ketone **115** forms vinylketene phosphonate **116**, which reacts further by 6π electrocyclization with the furyl substituent to form a 4-hydroxy-5-benzofuranyl phosphonate (Scheme 128).[98]



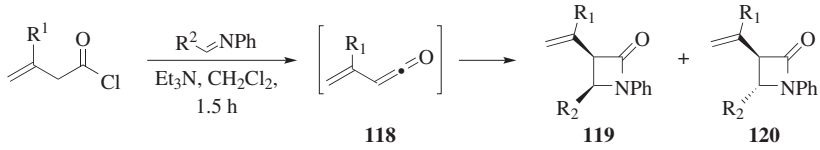
Scheme 128

An example involving a polycyclic vinylketene with differential protection is shown in Scheme 129.[145] The *N*-dimethylamino protecting group that facilitates the initial metalation does not interfere in the electrocyclization of intermediate **117** that generates the indole system.



Scheme 129

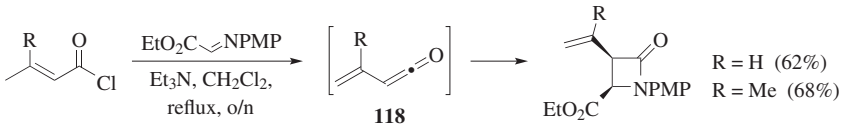
Cycloadditions of Vinylketenes with Imines and Diazenes. Reactions of ketenes with imines to form β-lactams date from the earliest days of ketene chemistry, and because of the importance of β-lactam antibiotics there is a strong, continuing interest in understanding and controlling the stereochemical course of these reactions. An empirical classification that relates the ketene substitution pattern to the stereochemical outcome in cycloaddition reactions with imines has been suggested,[146] with vinylketenes favoring *cis*-products. However, this classification lacks systematic validation, and the stereochemical course of these reactions shows a strong dependence on temperature, even completely reversing as the temperature is changed.[147] Predictions should be based only on very close analogy. As noted in the Mechanism and Stereochemistry section, application of the torquoselectivity theory to explain the stereochemical outcome of ketene–imine cycloadditions is also unreliable.[40] Vinylketenes **118** generated by dehydrochlorination react in situ with *N*-phenyl imines and preferentially form *trans*-β-lactams **120**. In the reaction with the imine derived from cinnamaldehyde, the product ratio is temperature-dependent, with increased formation of *cis*-β-lactam **119** at lower temperatures (Scheme 130).[22]



			Yield (%)	
R^1	R^2	Temp	**119**	**120**
H	Ph	20° to reflux	—	40
H	(*E*)-PhCH=CH	20°	25	5
H	(*E*)-PhCH=CH	reflux	7	35
H	2-furyl	reflux	—	70
Me	2-furyl	reflux	—	70

Scheme 130

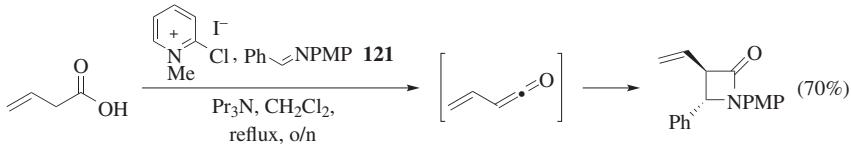
As shown in Scheme 131, vinylketenes **118** undergo [2+2] cycloaddition with the *N*-(4-methoxyphenyl)imine derived from ethyl glyoxylate to afford *cis*-β-lactams, a result that is not affected by varying the 3-substituent on the ketene.[148]



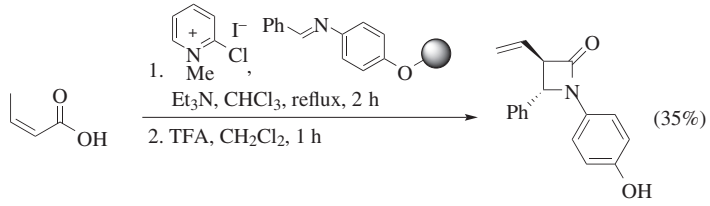
Scheme 131

In contrast, the parent vinylketene, generated from 3-butenoic acid with Mukaiyama's reagent, reacts with benzaldehyde-derived imine **121** to afford the *trans*-β-lactam (Scheme 132).[149] This reaction may also be carried out with a

polymer-bound imine, with production of the *N*-(4-hydroxyphenyl)-β-lactam after the final cleavage process (Scheme 133).[150]

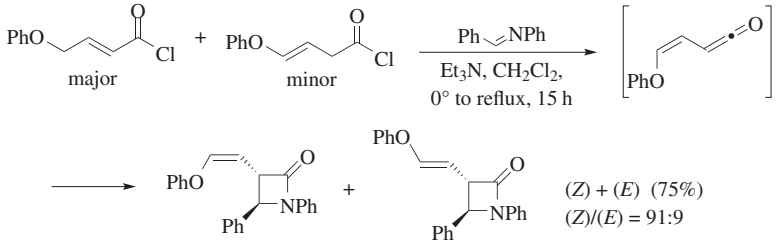


Scheme 132



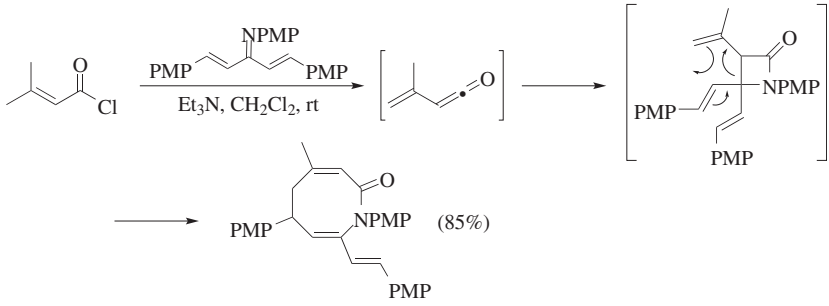
Scheme 133

Vinylketenes with a C4-heteroatom substituent (PhO, PhS, N_3, or phthalimido), generated from the corresponding acid chlorides, also undergo [2+2] cycloaddition with a variety of imines to provide *trans*-β-lactams predominantly (Scheme 134).[151] The (*Z*)-configuration of the double bond in the products is strongly preferred, a result that is attributed to heteroatom stabilization of that geometry in the intermediate vinylketene.[151]



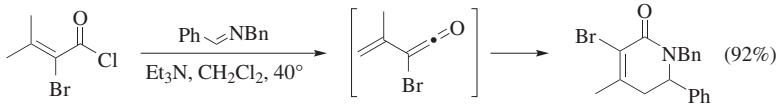
Scheme 134

bis(Vinyl)ketimines react with vinylketenes to afford 8-membered lactams in a process that is suggested to occur by a Cope rearrangement of the initially formed β-lactam cycloadducts (Scheme 135).[152] In some cases, the intermediate β-lactams are isolable at room temperature, and rearrange in toluene at 120°.[153]

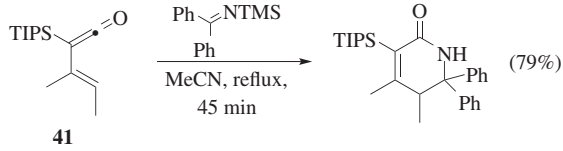


Scheme 135

Although a systematic study of substituent effects is not available, some vinylketenes do favor [4+2] cycloadditions with imines. Bromo(isopropenyl)ketene, generated by dehydrochlorination, reacts in situ with *N*-benzylbenzaldimine by [4+2] cycloaddition to form a δ-lactam (Scheme 136).[154] The tendency of vinylketenes with substituents on the vinyl group to favor [4+2] cycloaddition with some alkenes was noted earlier (Schemes 2 and 20). Stable silyl(vinyl)ketenes such as **41** also react with imines in a [4+2] fashion (Scheme 137).[23]

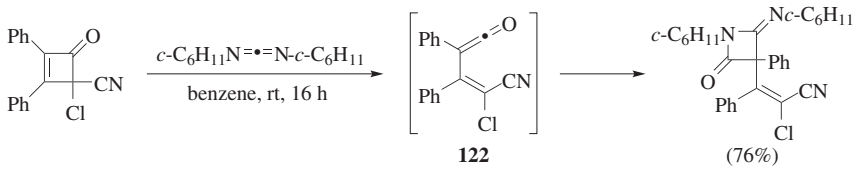


Scheme 136



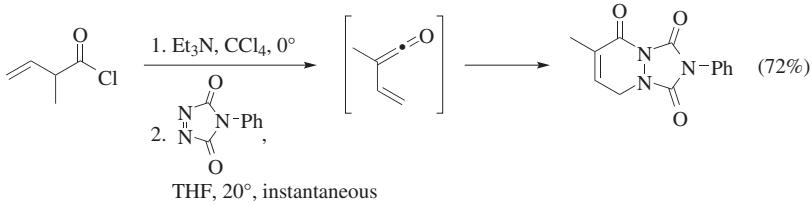
Scheme 137

Vinylketene **122**, generated by cyclobutenone ring opening in benzene at room temperature, reacts by [2+2] cycloaddition with *N*,*N*′-dicyclohexylcarbodiimide (DCC) to afford a 4-imino-β-lactam (Scheme 138).[155]



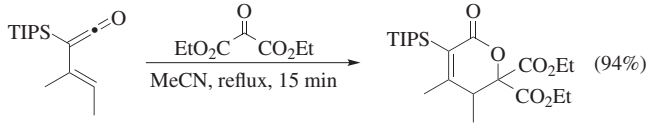
Scheme 138

Cycloadditions of vinylketenes with diazenes also take place readily. In situ generated methyl(vinyl)ketene reacts rapidly with *N*-phenyl-1,2,4-triazoline-3,5-dione by [4+2] cycloaddition (Scheme 139).[20] With diethyl azodicarboxylate, [4+2] cycloaddition is favored but some of the [2+2] cycloadduct is also formed.[20]



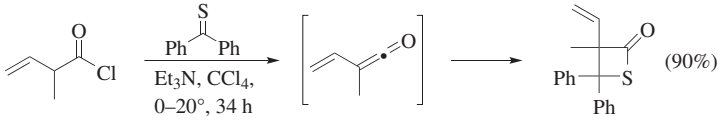
Scheme 139

Cycloadditions and Electrocyclizations of Vinylketenes with Carbonyl and Thiocarbonyl Groups. Uncatalyzed, intermolecular additions of vinylketenes to carbonyl compounds are limited in scope. Activated ketones undergo [4+2] cycloaddition with silyl(vinyl)ketenes (Scheme 140).[23] Similar additions of benzaldehyde and activated ketones to the extended vinylketene derived from thermal ring opening of benzocyclobutenone are known.[69]



Scheme 140

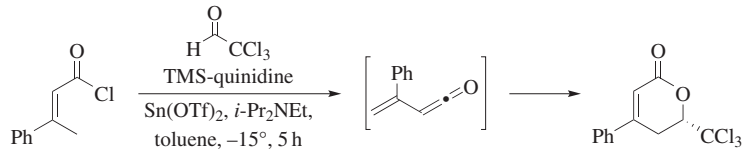
Thiobenzophenone reacts with methyl(vinyl)ketene, generated in situ by dehydrochlorination, via [2+2] cycloaddition to form a 2-thietanone in high yield (Scheme 141).[20]



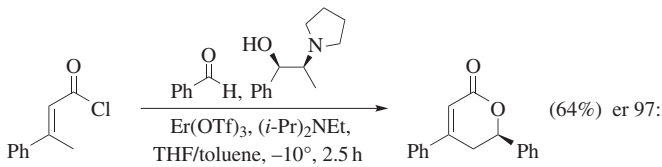
Scheme 141

Catalyzed, asymmetric additions to carbonyl compounds also result in formal [4+2] cycloadditions. Vinylketenes, generated in situ by dehydrochlorination, react with trichloroacetaldehyde in the presence of $Sn(OTf)_2$ and *O*-trimethylsilylquinidine as a chiral catalyst to afford δ-lactones such as **123** in good yields and with high enantiomeric purity (Scheme 142).[156,157,32] Reaction in the presence of MeOD provides the methyl ester with partial deuterium incorporation. This result is interpreted as

showing the involvement of both a vinylketene intermediate and a route that involves displacement of chloride by the amine catalyst followed by deprotonation to afford a dienolate intermediate, which leads to lactone products without a vinylketene intermediate. The corresponding reaction with benzaldehyde requires a different chiral catalyst for optimal results (Scheme 143).[156,158,32]

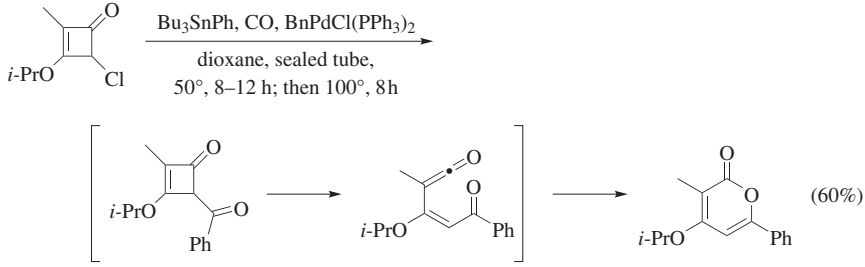


Scheme 142



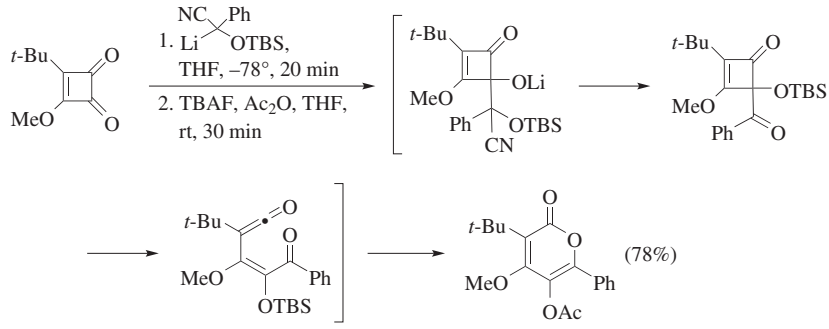
Scheme 143

A variety of methods generate 2-acylvinylketenes, which undergo 6π electrocyclization to afford 2-pyrones. Carbonylative Stille coupling of 4-chlorocyclobutenones affords 2-pyrones in a process that is believed to involve the formation and ring opening of a 4-acylcyclobutenone to generate the acylvinylketene (Scheme 144).[159]



Scheme 144

Alternatively, addition of an *O*-(trialkylsilyl)cyanohydrin anion to a cyclobutenedione brings about a sequence of silyl migration with loss of cyanide ion, ring opening to the acylvinylketene, and final 6π electrocyclization to the 2-pyrone (Scheme 145).[160]



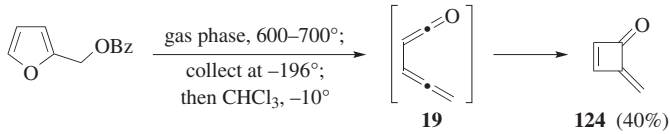
Scheme 145

Cycloadditions and Electrocyclizations of Allenylketenes and Alkynylketenes

Allenyl- and alkynylketenes are calculated to have stabilization energies similar to vinylketenes, and may be prepared by many of the same routes.[1,3,64,161] However, cycloaddition reactions of these ketenes have received scant attention in comparison to those of vinylketenes. A major reason for this is that the ring opening of cyclobutenones, which has provided a simple and convenient route to a wide variety of vinylketenes, is not applicable to the formation of alkynyl- or allenylketenes. Nevertheless, existing research suggests that further examination of alkynyl- and allenylketenes can provide unique synthetic methods to form a variety of interesting and useful products.

Alkynyl- and allenylketenes have been directly observed in a few instances, and one example of a stable allenylketene has been isolated and characterized by X-ray diffraction.[161] Several cycloaddition reactions of these ketenes have been reported, and with creative effort further studies could prove to be quite rewarding.

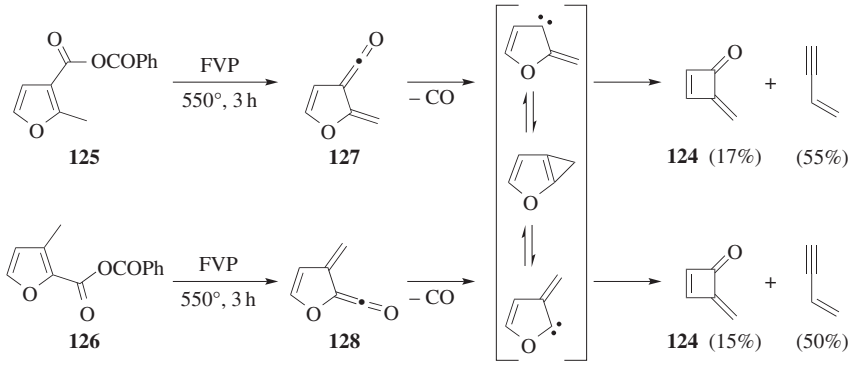
Allenylketenes. Allenylketenes are uncommon species, but this is not due to any fundamental instability or difficulty in preparation, but rather that there has been little effort devoted to their investigation. As noted earlier, the parent allenyl ketene **19** is formed in solution as an observable intermediate by dehydrochlorination of the acid chloride.[59] It is also formed and observed in an argon matrix by dehydrochlorination[162] and by irradiation of diazoacetylallene.[163] When generated by gas-phase pyrolysis of 2-(benzoyloxymethyl)furan, the parent allenylketene (**19**) cyclizes to methylenecyclobutenone (**124**) (Scheme 146).[164] This conversion is the analog of the ring closure of vinylketene to cyclobutenone (Scheme 14), and is calculated to have a barrier of 33.7 kcal/mol for closure of the *syn*-conformer



Scheme 146

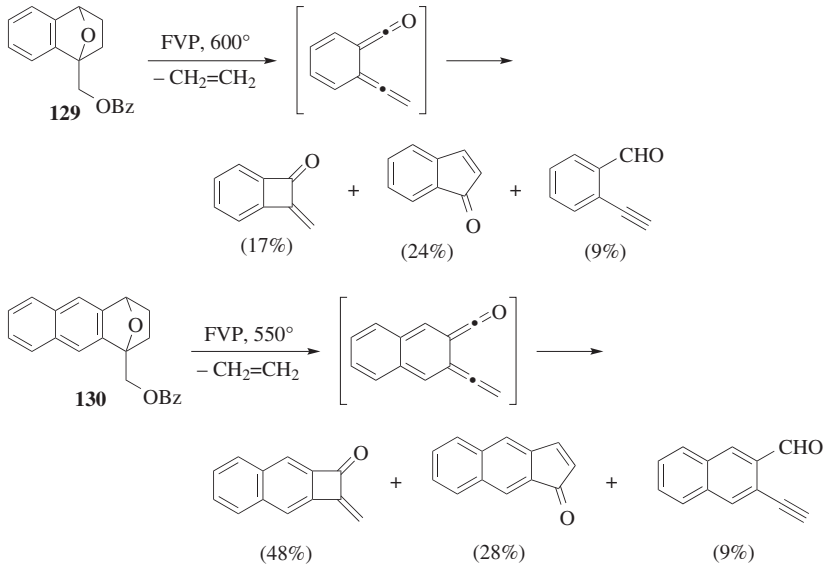
of allenylketene **19**, which is found by computational studies to be less stable than methylenecyclobutenone (**124**) by 11.8 kcal/mol.[161]

Methylenecyclobutenone (**124**) is also formed upon flash-vacuum pyrolysis of benzoic furoic anhydrides **125** and **126**, where the initial intermediates are isomeric vinylketenes **127** and **128**, respectively (Scheme 147).[165] Although the possibility of allenylketene formation was not considered in this report, the decarbonylation and rearrangement pathway that leads to methylenecyclobutenone (**124**) is likely to proceed via allenylketene **19**.



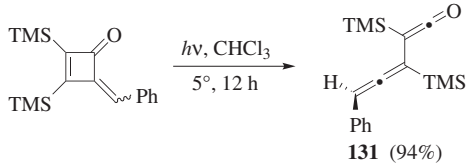
Scheme 147

Flash-vacuum pyrolysis also generates extended allenylketenes. The benzo- and 2,3-naphtho analogs of methylenecyclobutenone (**124**) are formed upon flash-vacuum pyrolysis of compounds **129** and **130** (Scheme 148).[166,167]



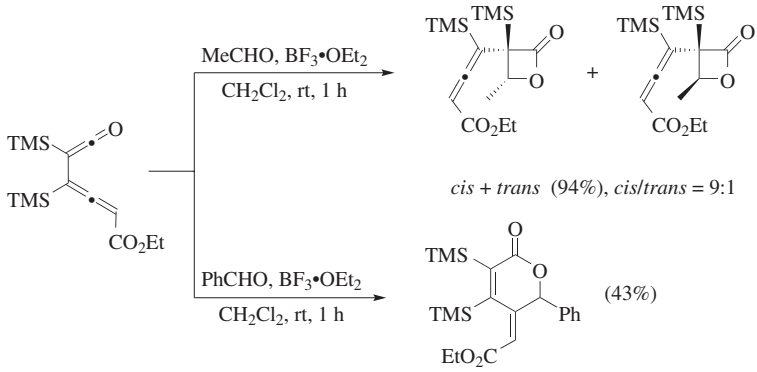
Scheme 148

tetrakis(Trimethylsilyl)allenylketene is generated by matrix irradiation of tetrakis(trimethylsilyl)cyclopentadienone and undergoes decarbonylation on extended irradiation.[168] Persistent allenylketenes that are stabilized by trimethylsilyl substituents are obtained by irradiation of 2,3-bis(trimethylsilyl)-substituted methylenecyclobutenones in solution (Scheme 149).[161] The X-ray crystal structure of allenylketene **131** confirms that these species prefer the coplanar *anti* conformation shown, as predicted computationally.[161] The use of the ketenyl and allenyl substituent stabilization parameters allows the prediction of the energy change for the generation of ketene **131**, and the experimentally measured equilibrium constant for ring closure is in reasonable agreement with these predictions.[161]



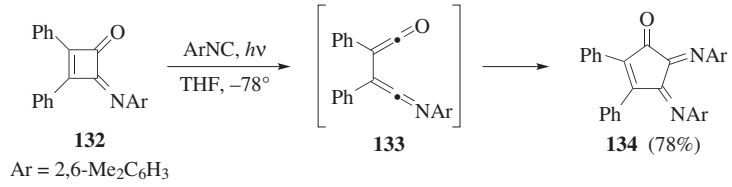
Scheme 149

2,3-Trimethylsilyl-substituted allenylketenes undergo [4+2] cycloadditions with tetracyanoethylene at room temperature.[169] These allenylketenes also undergo Lewis acid catalyzed addition to aldehydes. In these reactions, the substituent on the aldehyde determines whether products from a formal [2+2] or [4+2] pathway are obtained (Scheme 150).[169]



Scheme 150

The aza analog **133** of an allenylketene is generated by photochemical ring opening of 4-aryliminocyclobutenone **132** (Scheme 151) and is identified by its IR spectrum: 2091 cm^{-1} (C=O) and 2022 cm^{-1} (C=N).[170] Cycloaddition with 2,6-dimethylphenyl isocyanide provides cyclopentenone **134**.



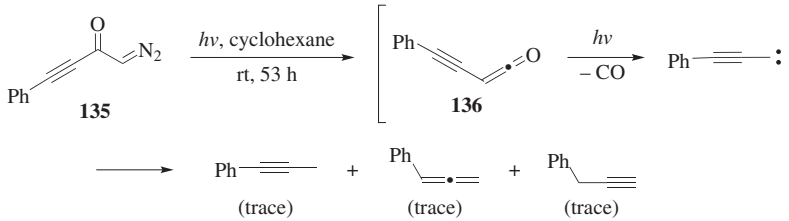
132
Ar = 2,6-$Me_2C_6H_3$

133

134 (78%)

Scheme 151

Alkynylketenes. The generation of phenylethynylketene (**136**) as an unobserved, reactive intermediate evidently occurs by rearrangement upon photolysis of the diazo ketone **135**, as shown by the formation of decarbonylation products (Scheme 152).[171]

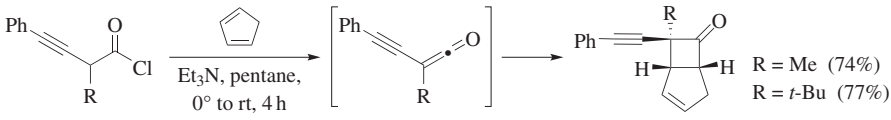


135

136

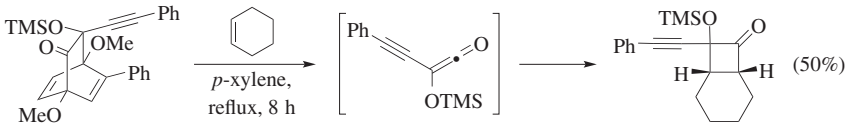
Scheme 152

Phenylethynylketene formed via flash photolysis is detected by UV[172] and by time-resolved IR spectroscopy by the characteristic absorption at 2130 cm^{-1} in acetonitrile.[173] Conventional photolysis in isooctane also allows IR detection.[174] In preparative reactions with added alkenes, 2-alkyl-substituted phenylethynylketenes undergo [2+2] cycloadditions to provide alkynyl-substituted cyclobutanones, and in reactions with cyclopentadiene, products with the alkynyl group in the *exo* position are the only observed products (Scheme 153).[175,176] This result reflects the previously discussed tendency for the formation of the more crowded adducts in vinylketene–alkene reactions together with the small steric requirements of the carbon–carbon triple bond.

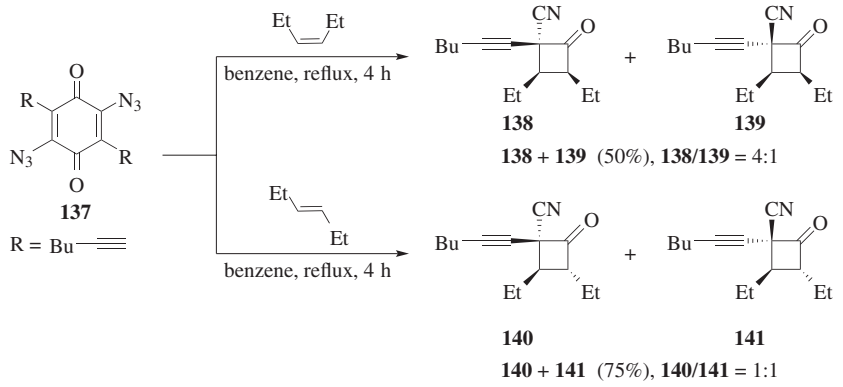


Scheme 153

In other [2+2] cycloadditions with alkenes, the alkynylketene is generated either by retro-Diels–Alder reaction (Scheme 154)[124] or by thermal decomposition of a 3,6-dialkynyl-2,5-diazido-1,4-benzoquinone **137**.[177,178,179] The latter reaction generates an alkynyl(cyano)ketene, which adds to (*Z*)-3-hexene to afford cyclobutanones **138** and **139** in a 4:1 ratio (Scheme 155).[178] The alkene stereochemistry is preserved in the cycloaddition, as the reaction with (*E*)-3-hexene affords products **140** and **141**.

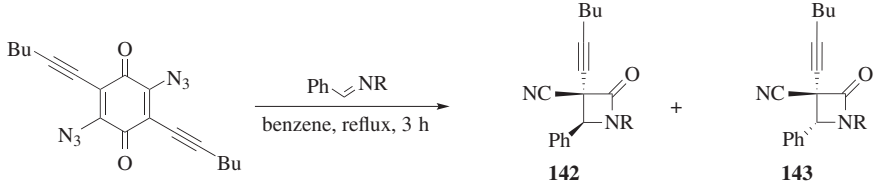


Scheme 154



Scheme 155

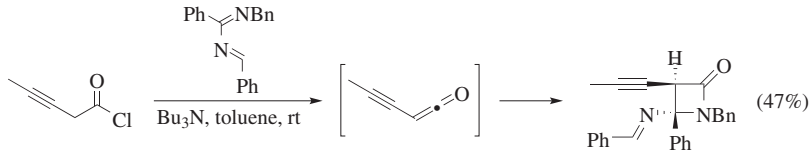
Additions of alkynylketenes to C=N bonds generate β-lactams that bear an alkynyl substituent. The alkynylketene obtained from thermolysis of compound **137** reacts with simple imines derived from benzaldehyde to afford β-lactams in good yields, with the ratio of product isomers **142** and **143** dependent on the nature of the *N*-substituent (Scheme 156).[180] With imines derived from cinnamaldehydes, mixtures of [2+2] and [4+2] cycloadducts are obtained.[179,180] Cycloadditions of alkynyl(cyano)ketenes with DCC provide the [2+2] cycloadducts.[178]



	Yield (%)	
R	**142**	**143**
t-Bu	14	51
c-C_6H_{11}	69	21
Ph	81	0

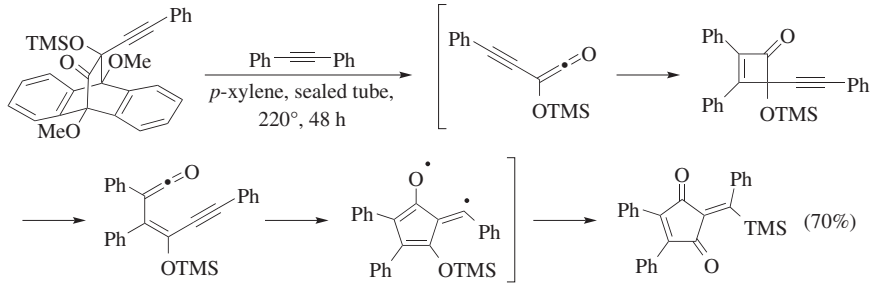
Scheme 156

The generation of an alkynylketene from an acid chloride in the presence of a 1,3-diazabuta-1,3-diene provides only the [2+2] adduct, an unusual 4-amino-2-azetidinone derivative (Scheme 157).[181]



Scheme 157

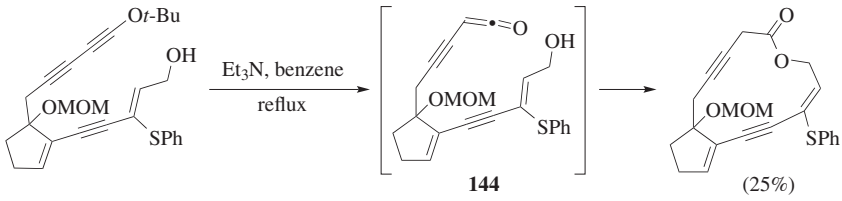
In the example shown in Scheme 158, an alkynylketene is generated by a retro-Diels–Alder reaction that is driven by the generation of an anthracene derivative. This alkynylketene reacts with diphenylacetylene in a reaction cascade that begins with a cycloaddition that forms an alkynylcyclobutenone.[177] Variations in the substitution pattern on the alkyne can result in competitive formation of a 6-membered ring in the cyclization step.[182]



Scheme 158

Other Reactions of Alkynylketenes

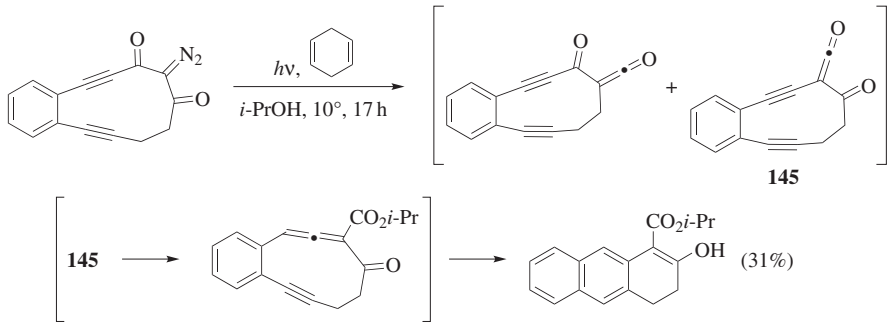
Alkynylketenes also feature in the formation of several polyunsaturated, macrocyclic lactones. Thermal decomposition of a 1-*tert*-butoxydiyne under mild conditions generates the alkynylketene **144**, which is captured by the terminal hydroxyl group (Scheme 159).[183]



Scheme 159

A photochemical rearrangement of a 2-diazo-1,3-dione in 2-propanol affords the alkynyl(acyl)ketene **145** along with the isomeric acylketene. The alkynyl(acyl)ketene

145 ultimately leads to a dihydroanthracene derivative in a sequence interpreted as isomerization of the initially formed ester to the allenic isomer, followed by a Myers–Saito electrocyclization (Scheme 160).[183,184]



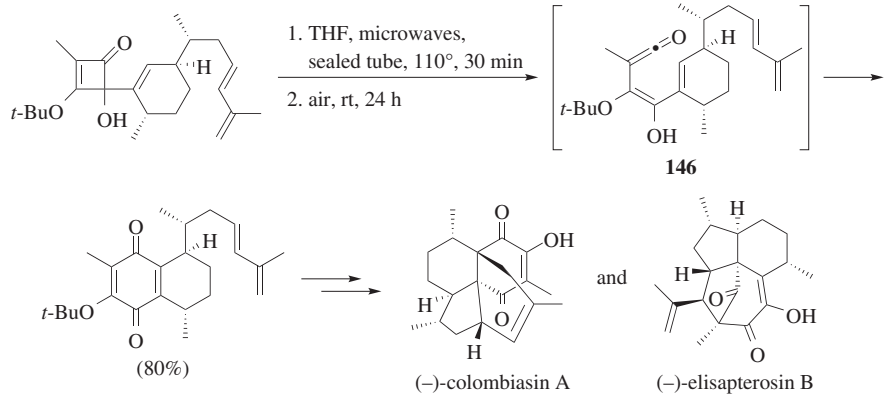
Scheme 160

APPLICATIONS TO SYNTHESIS

Vinylketene cycloadditions and electrocyclizations have proven useful for the synthesis of natural products, especially for those incorporating polyhydroxylated aromatic rings or their quinone equivalents.

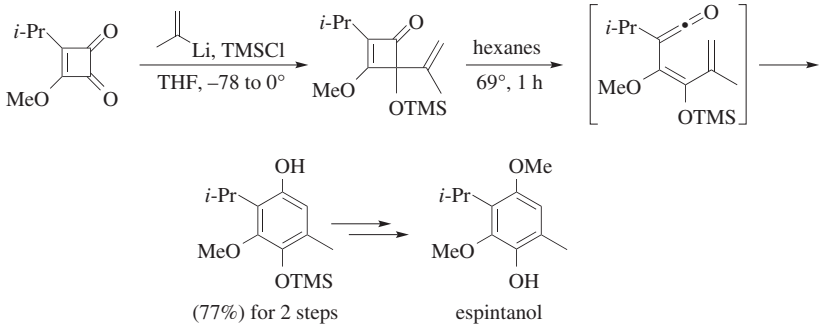
Electrocyclizations of Vinylketenes with Alkenes and Alkynes

The value of the electrocyclization of hydroxy dienylketenes to provide, after an oxidative step, 1,4-benzoquinone derivatives suitable for further elaboration is illustrated by the synthesis of a precursor to the diterpenes (−)-colombiasin A and (−)-elisapterosin B (Scheme 161).[104] Dienylketene **146**, formed from the cyclobutenone by microwave-assisted heating in THF, undergoes an electrocyclization, and subsequent oxidation by air affords a quinone that is used in the synthesis of the polycyclic diterpenes.



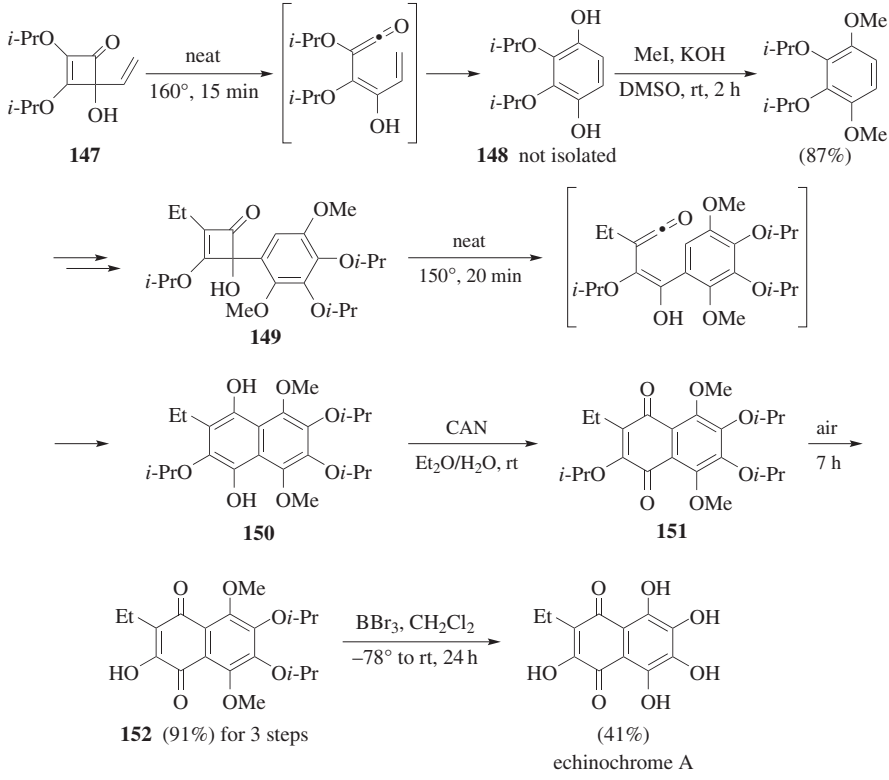
Scheme 161

A related electrocyclization of a protected hydroxy dienylketene is used in a synthesis of the antiparasitic monoterpene espintanol (Scheme 162).[185] *O*-Methylation and subsequent desilylation of the initially formed phenol generate the natural product.



Scheme 162

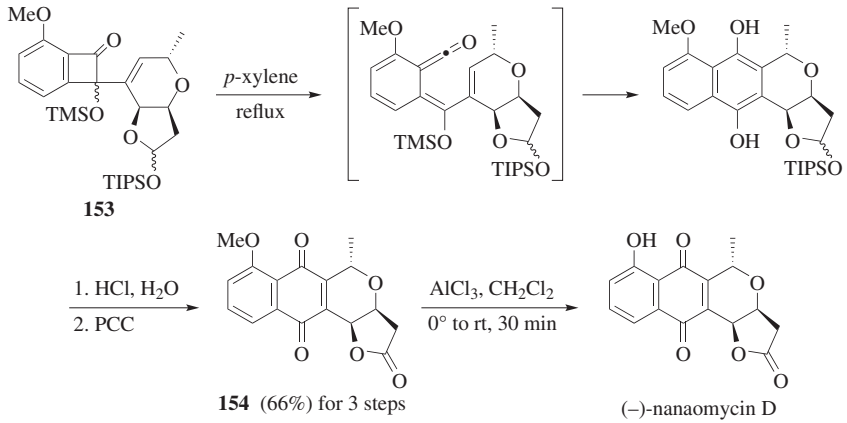
Two sequential vinylketene electrocyclizations are employed for the synthesis of echinochrome A, a highly oxygenated component of the pigments derived from sea urchins (Scheme 163).[25] The addition of vinylmagnesium bromide to diisopropyl



Scheme 163

squarate generates cyclobutenone **147**, which forms product **148** upon thermolysis. Due to its high propensity for air oxidation, product **148** is methylated in situ, then is further elaborated to cyclobutenone **149**. Heating intermediate **149** generates hydroquinone **150**, which undergoes in situ oxidation to naphthoquinone **151** followed by hydrolysis to naphthoquinone **152**. Final dealkylation affords the natural product.

The generation and cyclization of a benzo analog of a dienylketene is a key step in the synthesis of (−)-nanaomycin D (Scheme 164).[186] Thermolysis of compound **153** followed by desilylation and oxidation of the hydroquinone forms the *O*-methyl derivative **154**, which is converted into the natural product by treatment with $AlCl_3$.

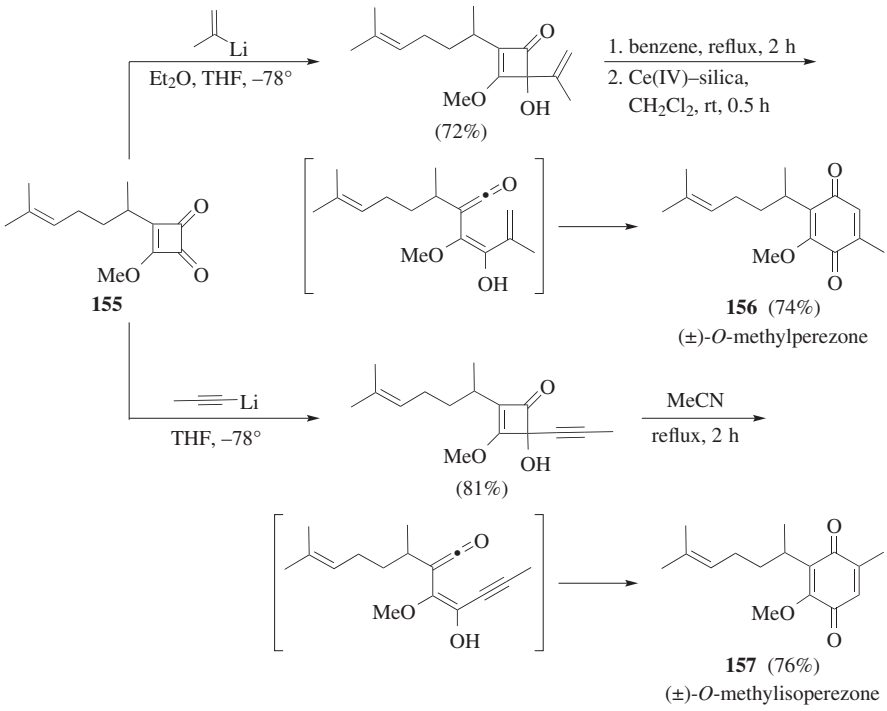


Scheme 164

The isomeric benzoquinones (±)-*O*-methylperezone (**156**) and (±)-*O*-methylisoperezone (**157**) are synthesized from the same cyclobutenedione **155** (Scheme 165).[106] Addition of 2-propenyllithium, cyclobutenone ring opening, electrocyclization, and a final oxidation affords product **156** via the dienylketene. The alternative addition of 1-propynyllithium to cyclobutenedione **155** followed by heating provides product **157** via the alkynylvinylketene.

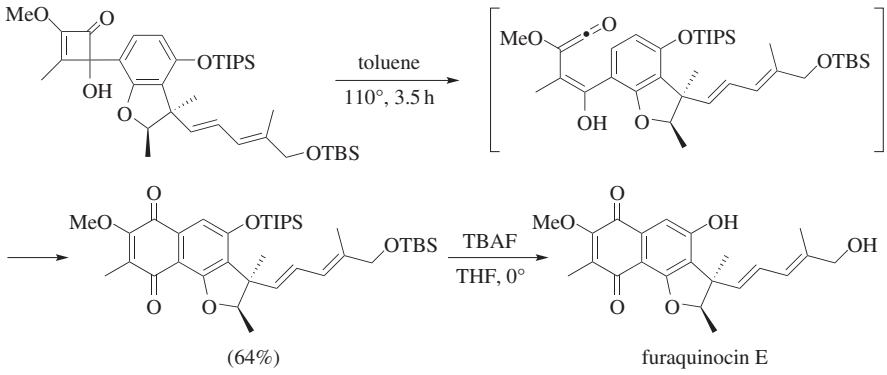
Electrocyclizations onto Aromatic and Heteroaromatic Rings

Both electrocyclizations of vinylketenes and cyclizations of the derived diradical species onto aromatic or heteroaromatic rings have found a number of applications in the synthesis of natural products. Furaquinocins are a class of antibiotics that exhibit a wide range of additional biological effects, including the inhibition of platelet aggregation and coagulation. The preparation of furaquinocin E (Scheme 166) employs the addition of a chiral, nonracemic fragment to 3-methyl-4-methoxycyclobutenedione.[187] Thermolysis followed by air oxidation generates a



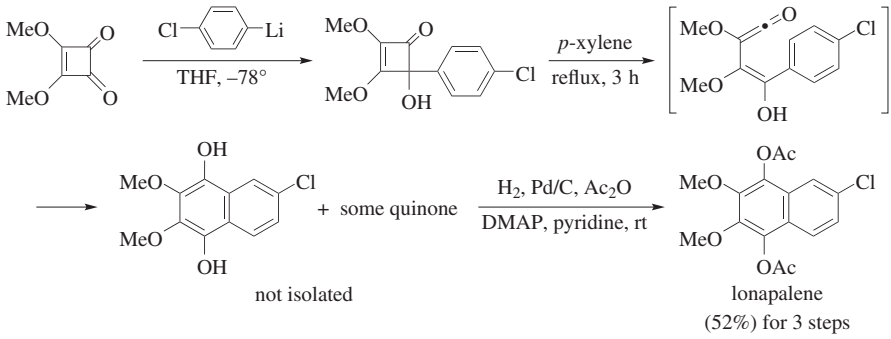
Scheme 165

quinone that affords the natural product after deprotection. A related furaquinocin is obtained using the addition of the enantiomeric organolithium reagent to dimethyl squarate as the first step in the sequence.[187]



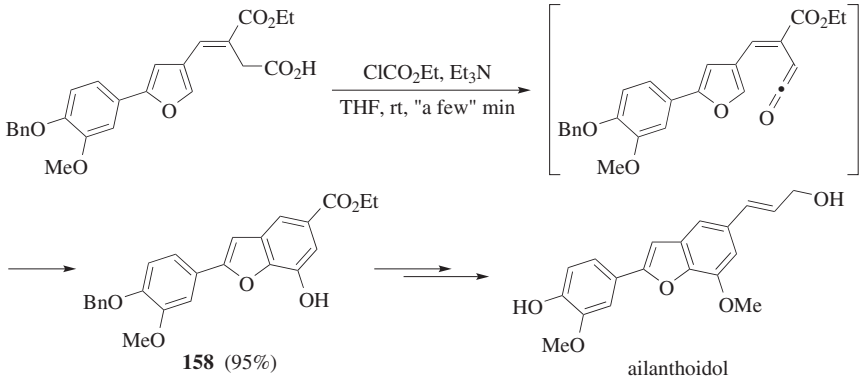
Scheme 166

A similar sequence is used in a concise synthesis of lonapalene, a topical antipsoriatic drug (Scheme 167).[133]



Scheme 167

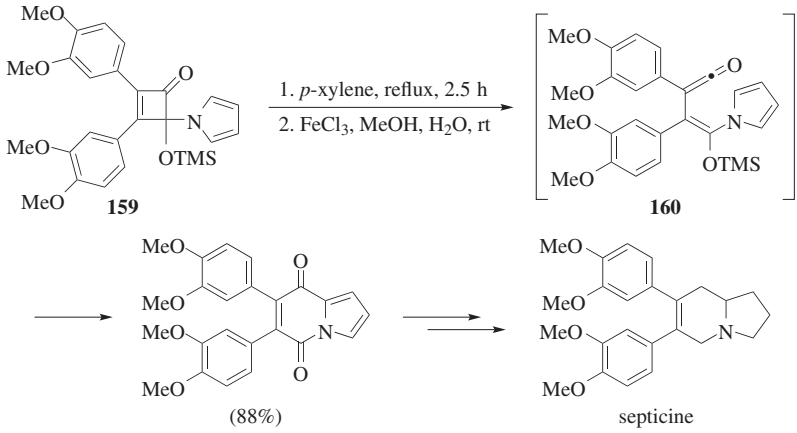
A vinylketene-based synthesis of 2-aryl-7-hydroxybenzofurans is employed for the synthesis of ailanthoidol, a naturally occurring neolignin (Scheme 168).[188] The vinylketene is generated from the carboxylic acid by the formation of a mixed anhydride followed by elimination, and undergoes a quantitative, in situ electrocyclization onto the furan ring to form product **158**. Methylation of the phenol followed by a chain-extension sequence then affords the natural product.



Scheme 168

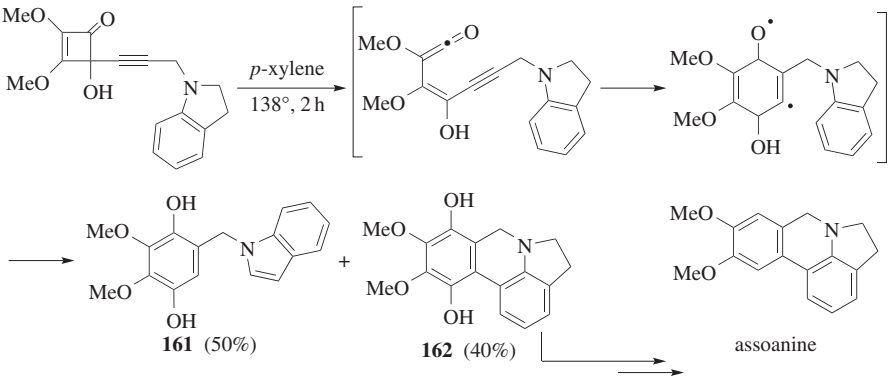
Septicine, an indolizidine alkaloid, is accessed via vinylketene electrocyclization involving the 2-position of a pyrrole ring. The precursor cyclobutenone **159** is derived from the addition of pyrrole anion to the corresponding diaryl cyclobutenedione (Scheme 169).[189] Heating cyclobutenone **159** in *p*-xylene forms vinylketene **160**,

and electrocyclization followed by oxidation forms the indolizine-5,8-dione in 88% yield. Subsequent reductions provide the natural product.



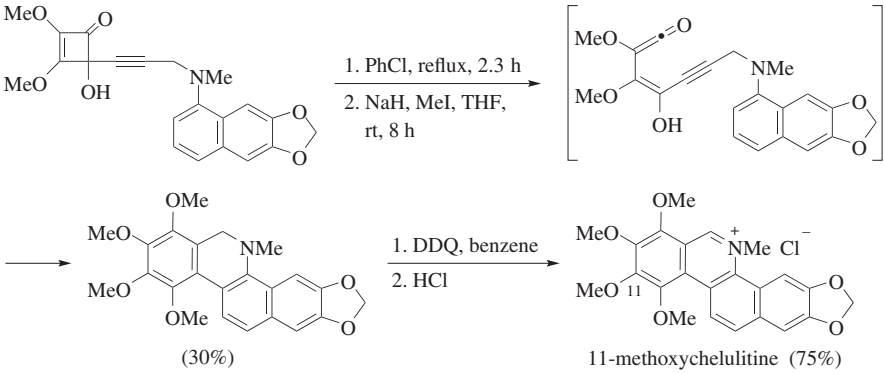
Scheme 169

The ability of the diradical species formed in the electrocyclization of an alkynylvinylketene to participate in further cyclization processes is featured in several alkaloid syntheses. The synthesis of assoanine, a biologically active pyrrolophenanthridine alkaloid, is shown in Scheme 170.[121] Addition of the anion derived from *N*-propargylindoline to dimethyl squarate affords the precursor to the alkynylvinylketene, which cyclizes to generate a mixture of the indole **161** and the tetracyclic compound **162**. The latter substance is further elaborated to the alkaloid.



Scheme 170

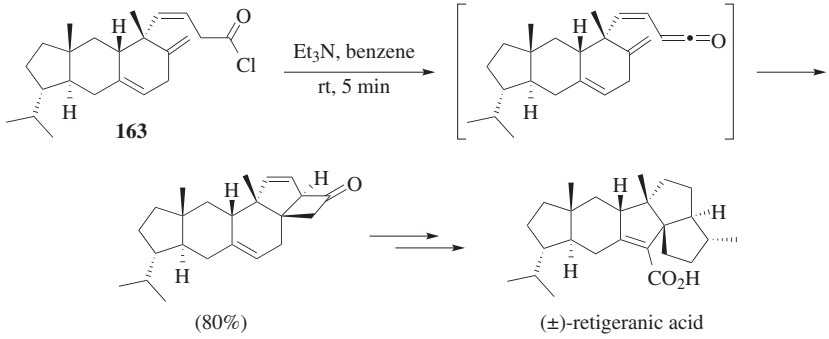
A related arylation process that starts with a 1-(propargylamino)naphthalene derivative is used to synthesize the 11-methoxy analogue of the benzophenanthridinium alkaloid chelilutine (Scheme 171).[190]



Scheme 171

[4+2] and [2+2] Cycloadditions

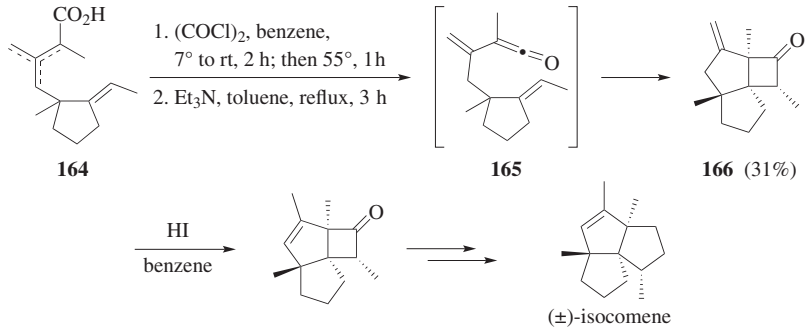
Several natural product syntheses utilize [2+2] cycloadditions of vinylketenes with olefins to generate cyclobutanones. A route to retigeranic acid, a sesquiterpene of novel structure found in various lichens from the Himalayas, is shown in Scheme 172.[191] Dehydrochlorination of the acid chloride **163** generates the vinylketene, which reacts by intramolecular [2+2] cycloaddition to provide a cyclobutanone. Subsequent elaborations that contract the cyclohexene ring and expand the cyclobutane ring form the natural product.



Scheme 172

Scheme 173 shows a formal total synthesis of another sesquiterpene, (±)-isocomene, that takes advantage of the fact that acid **164**, a mixture of double bond

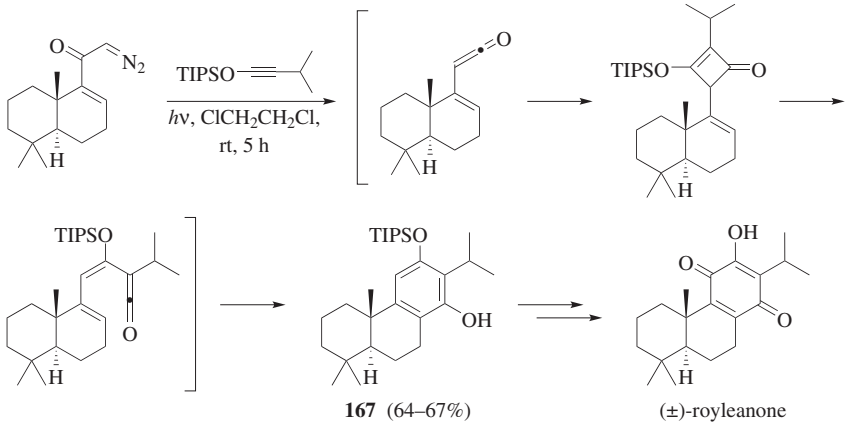
isomers, affords a single vinylketene **165**, which undergoes an intramolecular [2+2] cycloaddition to form product **166**.[192] Acid-catalyzed isomerization of cycloadduct **166** affords a known precursor[193] of the natural product.



164 **165** **166** (31%)

Scheme 173

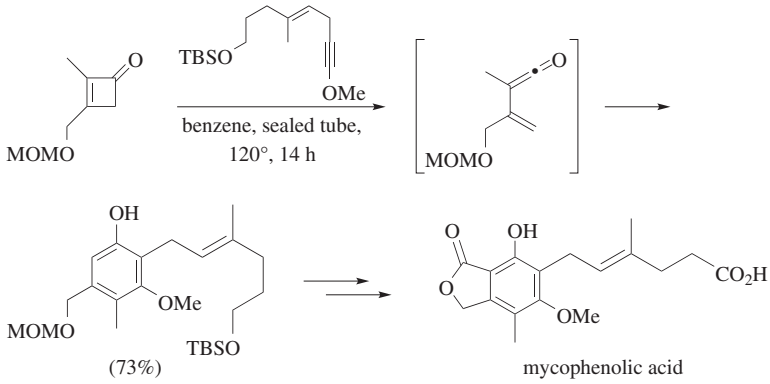
Royleanone is an angularly fused diterpenoid quinone with insecticidal, disinfectant, and modest antitumor properties. The vinylketene required for the synthesis of (±)-royleanone is generated by a Wolff rearrangement and undergoes intermolecular [2+2] cycloaddition to a silyloxyalkyne (Scheme 174).[194] Adduct **167** is then formed by ring opening of the cycloadduct to form a new vinylketene that undergoes final electrocyclization. Adduct **167** is readily elaborated to the natural product.



167 (64–67%) (±)-royleanone

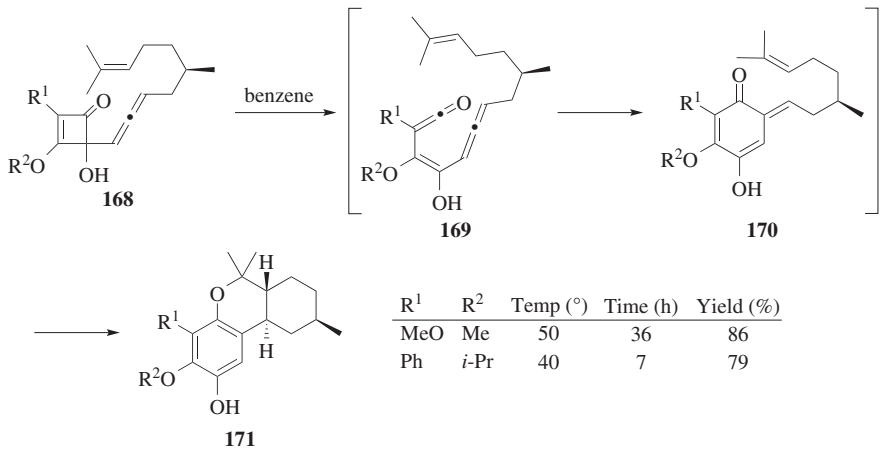
Scheme 174

The same tandem reaction sequence of intermolecular [2+2] vinylketene addition, cyclobutenone ring opening, and 6π electrocyclization is utilized in the synthesis of the antitumor antibiotic mycophenolic acid (Scheme 175).[195]



Scheme 175

A novel synthesis of cannabinoids is shown in Scheme 176.[196] Ring opening of cyclobutenone **168** to ketene **169** is followed by electrocyclization to generate the *o*-quinone methide **170**, which undergoes an intramolecular hetero-Diels–Alder reaction with the tethered olefin to directly form the hexahydrocannabinol analogs **171**. A different approach that involves the cycloaddition of a silyloxyalkyne to a cyclobutenone-derived vinylketene is used in a synthesis of Δ^6-tetrahydrocannabinol.[197]

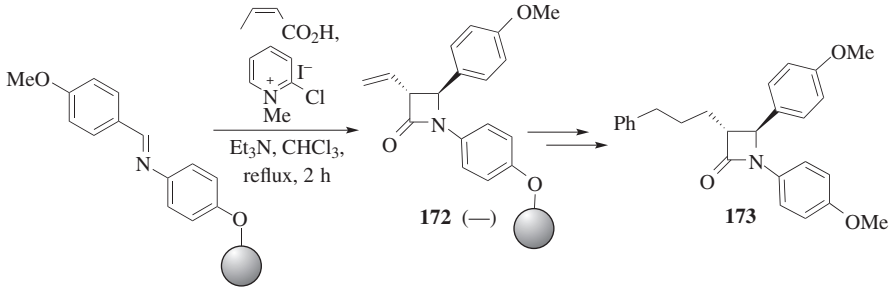


R^1	R^2	Temp (°)	Time (h)	Yield (%)
MeO	Me	50	36	86
Ph	*i*-Pr	40	7	79

Scheme 176

With respect to non-natural substances with valuable biological activity, a solid-phase approach to a known hypocholesterolemic agent **173** is shown in Scheme 177.[150] Vinylketene, generated by dehydration of crotonic acid, undergoes [2+2] cycloaddition with a polymer-bound imine to form β-lactam **172**

(Scheme 177). Subsequent olefin metathesis followed by cleavage from the resin, hydrogenation, and *O*-demethylation affords the active substance.

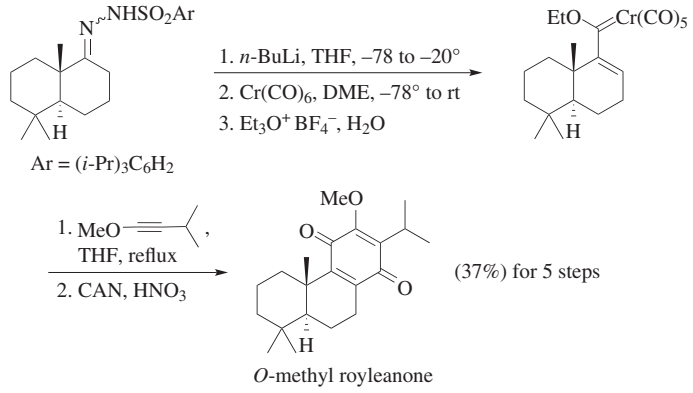


Scheme 177

COMPARISON WITH OTHER METHODS

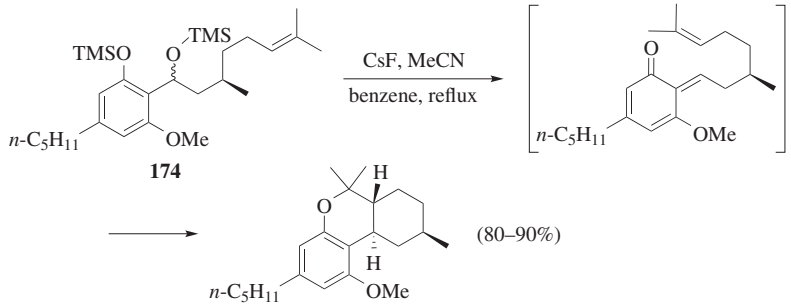
Vinylketene cycloadditions and electrocyclizations are very versatile and are used to make a wide variety of different types of compounds, including quinones, phenols, polycyclic aromatic and heteroaromatic compounds, cyclobutenones, cyclobutanones, cyclohexadienones, β-lactams and lactones, and 6-membered ring heterocycles. Although their utility to form 4-membered rings is shared with other ketenes, the formation of 6-membered rings is their most distinctive feature, and provides a route to these ubiquitous compounds from acyclic precursors via inter- and intramolecular [4+2] cycloadditions and electrocyclizations with a variety of reaction partners. In particular these reactions provide alternatives to Friedel–Crafts chemistry and nucleophilic aromatic substitution, whereas for β-lactams and β-lactones vinylketene cycloadditions are useful for products with specific substitution patterns.

A major synthetic route that complements some vinylketene cycloadditions is described in the earlier *Organic Reactions* chapter, "The Syntheses of Phenols and Quinones via Fischer Carbene Complexes".[75] These reactions proceed through metal-complexed vinylketene intermediates and provide a well-developed method for the preparation of these valuable substances. One example of the applications of this method is the synthesis of *O*-methyl royleanone (Scheme 178).[198] This process is judged to be somewhat shorter and higher-yielding than the vinylketene route shown in Scheme 174.[194] The Fischer carbene method does however lack the flexibility of routes utilizing free vinylketenes, which may be derived from diverse precursors and offer a wider variety of reaction pathways.



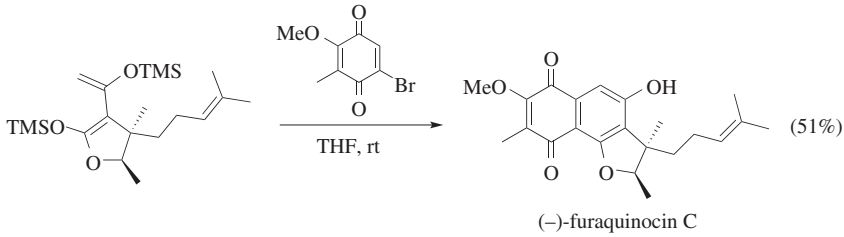
Scheme 178

The vinylketene route to hexahydrocannabinol analogs utilizes an electrocyclization that forms an intermediate *o*-quinone methide (Scheme 176).[196] For comparison, an alternative method of synthesis also involves an *o*-quinone methide intermediate, but in this case it is generated by fluoride-ion-induced desilylation and elimination from the substituted cyclohexadiene **174** (Scheme 179).[199]



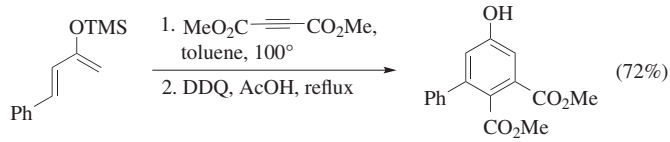
Scheme 179

Diels–Alder reactions can provide alternatives to vinylketene cyclizations. Furaquinocin E may be obtained via a vinylketene–arene cyclization (Scheme 166),[187] but an alternative approach to furaquinocin C uses intermolecular cycloaddition of an electron-rich diene to a 1,4-benzoquinone with subsequent elimination (Scheme 180).[200]



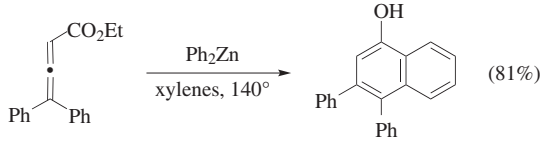
Scheme 180

Polysubstituted phenols are also obtained by the cycloaddition of alkynes to silyloxybutadiene derivatives followed by dehydrogenation (Scheme 181).[201]



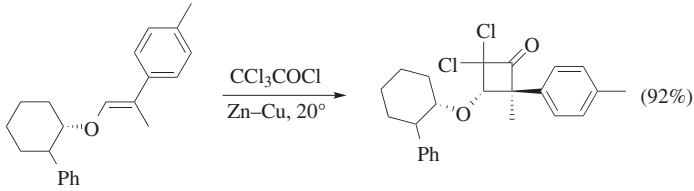
Scheme 181

1-Naphthols are obtained by Michael addition of arylzinc reagents to 3-arylallenecarboxylates via in situ electrocyclization of the initial addition products (Scheme 182).[202]



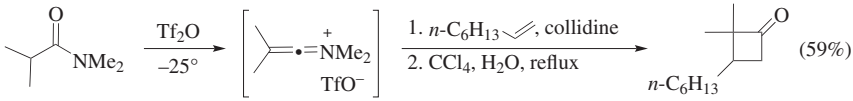
Scheme 182

Cyclobutanones are obtained by a variety of routes. Intermolecular ketene–alkene cycloadditions require activation of one or both of the components to secure good yields, as exemplified by the addition of dichloroketene to a chiral, nonracemic enol ether (Scheme 183),[203] a key step in a synthesis of cuparene, which has also been obtained by a vinylketene route.[204]



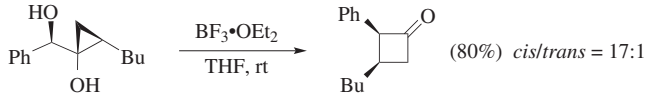
Scheme 183

Keteniminium salts are more reactive than the corresponding ketenes and are useful for reactions with less nucleophilic alkenes (Scheme 184).[205]



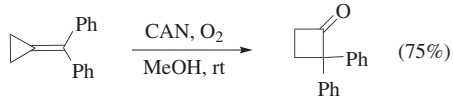
Scheme 184

Ring expansions also afford convenient routes to cyclobutanones. α-Hydroxycyclopropyl carbinols, which are readily prepared in two steps from 1-alkynyl boronate esters, undergo a stereoselective pinacol rearrangement (Scheme 185).[206]



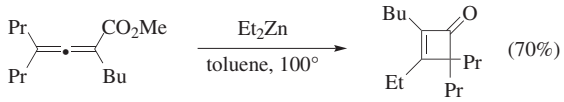
Scheme 185

Oxidative ring expansion of methylenecyclopropane derivatives using CAN under an oxygen atmosphere affords 2,2-diarylcyclobutanones in good yields (Scheme 186).[207]



Scheme 186

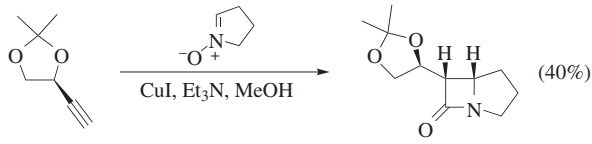
Organozinc reagents react with allenecarboxylates by Michael addition followed by a cyclization–elimination process, providing a route to polysubstituted cyclobutenones (Scheme 187).[208]



Scheme 187

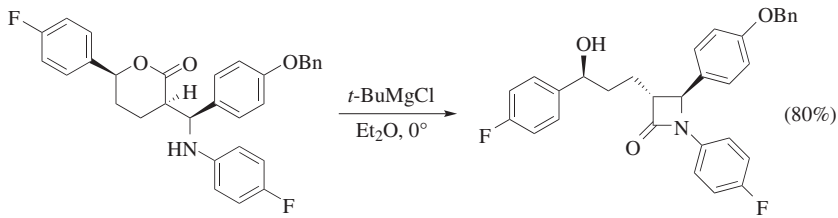
Synthesis of β-lactams is most commonly achieved by reactions of ketenes with imines. [1,3,32,37,209–211] Although the previously discussed additions of vinylketenes to imines form a modest fraction of the many examples of these reactions, they do uniquely provide 3-alkenyl azetidinones, which are not available by most alternative routes. Other routes to β-lactams have involved ring closure by almost all of the possible bond-forming modes, by ring expansion, and by cycloaddition approaches

different from the ketene–imine process. An example of the latter, the Kinugasa copper(I)-induced reaction of a chiral, nonracemic alkyne with a nitrone generates a carbapenam derivative (Scheme 188).[212]



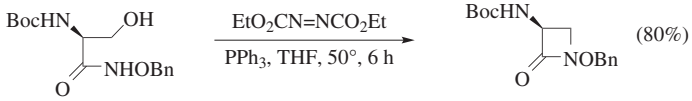
Scheme 188

A route to benzyl-protected ezetimibe, a potent inhibitor of cholesterol absorption, illustrates ring closure by formation of the N1–C2 amide bond (Scheme 189).[213] The δ-lactone is converted to the β-lactam via *O*- to *N*-acyl transfer.



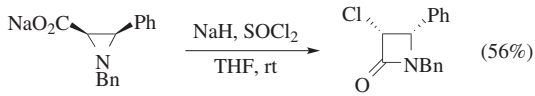
Scheme 189

Mitsunobu ring closure of the N1–C4 bond in *N*-alkoxy-β-hydroxyamides is an effective route to *N*-alkoxy β-lactams (Scheme 190).[214,215] The *N*-substituent is readily removed by reduction.



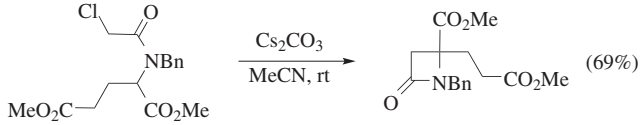
Scheme 190

β-Lactams are also formed by ring expansion of aziridinecarboxylic acids (Scheme 191).[216]



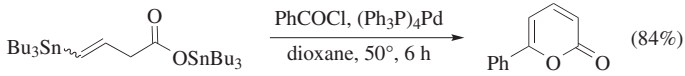
Scheme 191

C2–C3 ring closure reactions of α-chloro acetamides are also effective when an anion-stabilizing group is present (Scheme 192).[217]



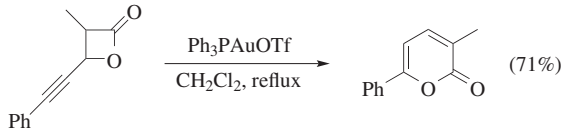
Scheme 192

The α-pyrone ring system is formed in a number of reactions of vinylketenes including dimerizations (Schemes 50 and 51) and cyclizations of in situ generated 2-acylvinylketenes (Schemes 144 and 145). In a method reminiscent of the latter process, α-pyrones are prepared from acid chlorides in one step utilizing a Stille coupling (Scheme 193).[218]



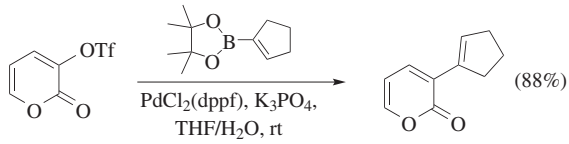
Scheme 193

Interest in developing new routes to the α-pyrone system is reflected in recent publications. A gold(I)-catalyzed rearrangement of β-alkynylpropiolactones enables a straightforward synthesis of substituted α-pyrones in good yields (Scheme 194).[219]



Scheme 194

3-Substituted-2-pyrones are obtained from the corresponding triflates using palladium-catalyzed cross-coupling reactions with boronic acid derivatives, as exemplified by the formation of the 3-cyclopentenyl derivative shown in Scheme 195.[220]



Scheme 195

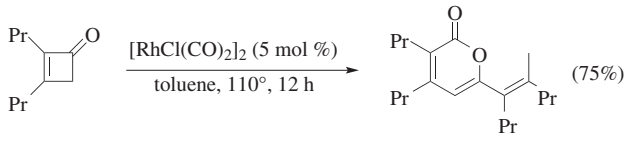
EXPERIMENTAL CONDITIONS

Many routes are available for the generation of vinylketenes, with thermal cyclobutenone ring opening, acid chloride dehydrochlorination, and Wolff rearrangement being the most frequently used methods. Elimination reactions from carboxylic acid derivatives other than acid chlorides often take place at room temperature or below, but may involve reagents or reaction products that can induce side reactions or hamper product purification. The use of stable vinylketenes is restricted to silyl-substituted derivatives, and to disubstituted ketenes with sufficient steric protection to prevent self-reaction.

Depending upon the particular precursors used, both thermal and photochemical generation of vinylketenes can be used. Generation of vinylketenes from diazo ketones may be done thermally or photochemically; sometimes both are used because photochemical reactions may be slowed as the reaction proceeds due to the formation of light absorbing products.

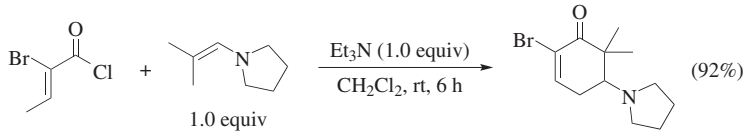
Ketene cycloadditions and electrocyclizations uniformly require anhydrous solvents and protection from the air, but otherwise may be carried out in almost all non-reactive solvents, including aliphatic and aromatic hydrocarbons, chlorocarbons, acetonitrile, and cyclic and non-cyclic ethers. The choice of solvent varies depending upon the method of vinylketene generation, with higher boiling, aromatic solvents usually chosen for vinylketene generation by cyclobutenone ring opening, and lower boiling chlorocarbons for acid chloride dehydrochlorinations.

EXPERIMENTAL PROCEDURES

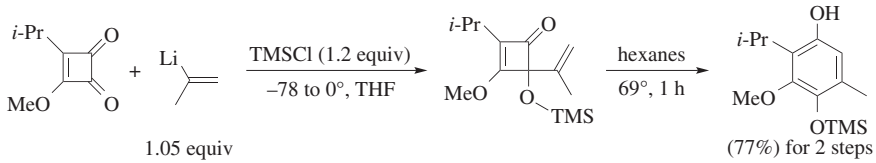


(*E*)-6-(5-Methyl-4-octen-4-yl)-3,4-di(1-propyl)-2-pyranone [Rhodium-Catalyzed Dimerization of a Cyclobutenone-Derived Vinylketene].[90] A mixture of 2,3-dipropyl-2-cyclobutenone (152 mg, 1.00 mmol), chlororhodium(I) dicarbonyl dimer (19.4 mg, 0.0500 mmol), and toluene (2.0 mL) was placed in a 20-mL Pyrex flask equipped with a magnetic stirring bar under a flow of argon and heated at 110° for 12 h with stirring. The reaction mixture was cooled, and the residue was subjected to Kugelrohr distillation to afford the title product (114 mg, 75%) as a pale-yellow oil: bp 170–180° (1.0 mm Hg); IR (neat) 1712, 1635, 1562 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.83 (s, 1H), 2.46 (t, $J = 7.81$ Hz, 2H), 2.41 (t, $J = 7.81$ Hz, 2H), 2.29 (t, $J = 7.81$ Hz, 2H), 2.11 (t, $J = 7.81$ Hz, 2H), 1.76 (s, 3H), 1.61–1.43 (m, 6H), 1.36–1.30 (m, 2H), 0.99 (t, $J = 7.32$ Hz, 3H), 0.98 (t, $J = 7.32$ Hz, 3H), 0.94 (t, $J = 7.32$ Hz, 3H), 0.88 (t, $J = 7.32$ Hz, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 164.3, 159.3, 153.2, 139.2, 128.6, 122.3, 108.3, 36.4, 34.5, 32.4, 28.6, 22.5, 22.1, 22.1, 21.3, 20.5, 14.3, 14.2, 14.0, 14.0; EIMS (*m/z*): M^+ 304. Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.80; H, 10.55.

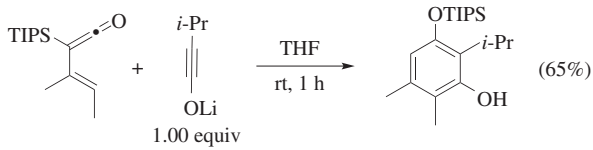


2-Bromo-6,6-dimethyl-5-(1-pyrrolidinyl)-2-cyclohexenone [Intermolecular [4+2] Cycloaddition of an Acid Chloride Derived Vinylketene to an Enamine].[50] A solution of 2-bromo-2-butenoyl chloride (1.83 g, 10.0 mmol) in CH_2Cl_2 (10 mL) was added over 1 h to a solution of 1-(2-methyl-1-propenyl)pyrrolidine (1.25 g, 10.0 mmol) and triethylamine (1.4 mL, 10 mmol) in CH_2Cl_2 (20 mL) at rt. The mixture was allowed to stand for 6 h at rt, after which time it was washed with H_2O (20 mL) and saturated, aqueous $NaHCO_3$. The amine was extracted from the organic phase with 5% aqueous HCl (2 × 20 mL) and the combined extracts were washed with Et_2O (2 × 10 mL), basified by addition of excess solid K_2CO_3, and extracted with CH_2C1_2. Drying and evaporation of the organic layer afforded crude title product (2.50 g, 92%) as a dark-colored oil: UV (EtOH) λ_{max} (log ε) 247 nm (4200); IR (film) 1680 (s) cm^{-1}; ^1H NMR ($CDC1_3$) δ 7.28 (t, $J = 4.5$ Hz, 1H), 3.15 (t, $J = 5$ Hz, 1H), 2.7–1.4 (m, 10H), 1.23 (s, 3H), 1.17 (s, 3H); LRMS-EI (*m/z*): M^+ 271. Hydrochloride: mp 186–188°. Anal. Calcd for $C_{12}H_{19}BrClNO$: C, 46.70; H, 6.21; N, 4.54. Found: C, 47.28; H, 5.89; N, 4.56.



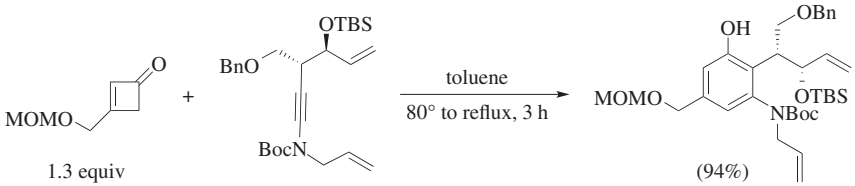
2-Isopropyl-3-methoxy-5-methyl-4-(trimethylsilyloxy)phenol [Electrocyclization of a Cyclobutenone-Derived Dienylketene].[185] *tert*-Butyllithium (1.7 M in pentane, 12.4 mL, 21.0 mmol) was added in a dropwise fashion to anhydrous THF (20 mL) at −78° under N_2. After 5 min, 2-bromopropene (0.93 mL, 10.5 mmol) was added dropwise over a 2-min period. After an additional 5 min, the resulting lithium reagent was added via cannula to a solution of 3-isopropyl-4-methoxy-3-cyclobutene-1,2-dione (1.54 g, 10.0 mmol) in anhydrous THF (50 mL) at −78°. Chlorotrimethylsilane (1.5 mL, 12 mmol) was then added via syringe. The solution was allowed to warm to 0°, re-cooled to −78°, and poured into 5% aqueous $NaHCO_3$ (50 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic phase was washed

with brine (50 mL), dried ($MgSO_4$), and concentrated under vacuum to afford crude 2-isopropyl-3-methoxy-4-(1-propen-2-yl)-4-trimethylsilyloxy-2-cyclobutenone: ^1H NMR ($CDCl_3$) δ 5.20 (s, 1H), 5.01 (s, 1H), 3.96 (s, 3H), 2.49 (hep, J = 7.1 Hz, 1H), 1.71 (s, 3H), 1.15 (d, J = 7.0 Hz, 6H), 0.14 (s, 9H). Hexanes (1000 mL) were added, and the resulting solution was heated at 69° for 1 h. After concentration, the product was purified by column chromatography (silica gel, hexanes/EtOAc, 9:1) to yield the title product (2.06 g, 77%). Recrystallization of a sample from hexanes provided a white solid: mp 82.0–83.0°; IR 3410 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.28 (s, 1H), 4.47 (s, 1H), 3.68 (s, 3H), 3.41 (hept, J = 7.2 Hz, 1H), 2.11 (s, 3H), 1.34 (d, J = 7.2 Hz, 6H), 0.22 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 148.3, 141.2, 127.3, 125.5, 113.1, 60.4, 25.3, 21.3 (2C), 16.5, 0.4 (3C); LRMS-CI (*m/z*) (% relative intensity): M^+ 268 (100); HRMS calcd for $C_{14}H_{24}O_3Si$, 268.1495; found, 268.1489.

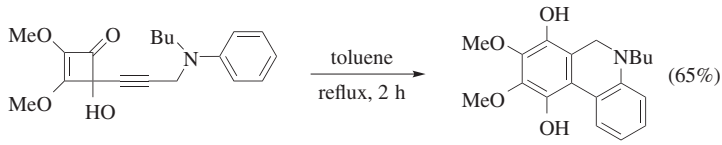


2-Isopropyl-5,6-dimethyl-3-(triisopropylsilyloxy)phenol [Electrocyclization of a Dienylketene with Silyl Group Migration].[103] A 25-mL, two-necked, round-bottomed flask equipped with a rubber septum and Ar inlet adapter was charged with 3-methyl-1-(triisopropylsilyloxy)-1-butyne (0.171 g, 0.711 mmol) and anhydrous THF (2 mL). Methyllithium (1.42 M in Et_2O, 0.50 mL, 0.71 mmol) was added dropwise via syringe over 2 min, and the resulting solution was stirred at rt for 4 h. A solution of (*E*)-2-(2-butenyl)-2-(triisopropylsilyl)ketene (0.179 g, 0.709 mmol) in THF (2 mL) was added via cannula in one portion (the flask was rinsed with 1 mL of THF), and the resulting solution was stirred for 1 h at rt. The reaction mixture was poured into saturated, aqueous NH_4Cl solution (10 mL), the aqueous phase was separated and was extracted with Et_2O (2 × 10 mL), and the combined organic phases were washed with 20 mL of water and 20 mL of brine. Drying over $MgSO_4$, filtration, and concentration of the organic layer provided 0.356 g of a yellow oil. This material was dissolved in 10 mL of CH_2Cl_2 and was concentrated onto 1.5 g of silica gel, which was transferred to the top of a column of 30 g of silica gel. Gradient elution with 0 to 2% EtOAc/hexanes provided the title product (0.165 g, 65%) as a yellow oil: IR (neat) 3621, 3573, 2946, 1615, 1574, 1493, 1464 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.24 (s, 1H), 4.68 (s, 1H), 3.62 (septet, J = 7.2 Hz, 1H), 2.18 (s, 3H), 2.07 (s, 3H), 1.34 (d, J = 7.2 Hz, 6H),

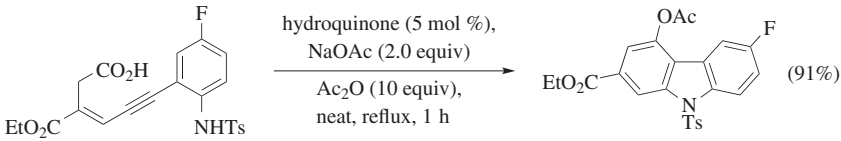
1.32 (septet, J = 7.2 Hz, 3H), 1.13 (d, J = 7.5 Hz, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 151.8, 134.5, 121.1, 114.5, 112.6, 24.7, 21.1, 20.5, 18.4, 13.4, 11.4; HRMS–ESI (*m/z*): $[M + Na]^+$ calcd for $C_{20}H_{36}NaO_2Si$, 359.2377; found, 359.2392.



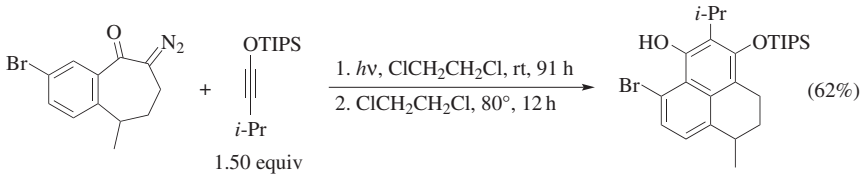
***tert*-Butyl Allyl[2-((2*R*,3*S*)-1-benzyloxy-3-(*tert*-butyldimethylsilyloxy)-4-penten-2-yl)-3-hydroxy-5-((methoxymethoxy)methyl)phenyl]carbamate [Pericyclic Reaction Cascade Including an Intermolecular [2+2] Cycloaddition of a Vinylketene with an Alkyne].**[18] A 25-mL pear-shaped flask, fitted with a rubber septum and an Ar inlet needle, was charged with a solution of *tert*-butyl allyl[(3*R*,4*S*)-3-(benzyloxymethyl)-4-(*tert*-butyldimethylsilyloxy)-5-hexen-1-ynyl]carbamate (0.108 g, 0.222 mmol) and 3-((methoxymethoxy)methyl)-2-cyclobutenone (0.041 g, 0.29 mmol) in toluene (0.7 mL). The septum was replaced with a cold finger reflux condenser with an Ar inlet, and the reaction mixture was heated at 80° for 1.5 h and then at reflux for 1.5 h. After being cooled to rt, the reaction mixture was concentrated to yield a viscous, orange oil (0.200 g). Purification by column chromatography on 14 g of silica gel (gradient elution with 0 to 15% EtOAc/hexanes) provided the title compound (0.125 g, 94%) as a viscous, pale-yellow oil: $[\alpha]^{21}_D$ – 6.3 (*c* 0.125, $CHCl_3$); IR (film) 3281, 2927, 2857, 1699, 1667, 1624, 1574, 1437, 1254, 1049, 922 cm^{-1}; ^{1}H NMR (500 MHz, 90°, DMSO-d_6) δ 9.20 (s, 1H), 9.13 (s, 1H minor rotamer), 7.30–7.22 (m, 3H), 7.16–7.15 (m, 2H), 6.73 (s, minor rotamer), 6.70 (s, 1H), 6.52 (s, minor rotamer), 6.43 (s, 1H), 5.97–5.93 (m, minor rotamer), 5.83–5.79 (m, 1H), 5.68–5.62 (m, 1H), 5.13–5.03 (m, minor rotamer), 4.99–4.97 (m, 2H), 4.87 (app d, J = 18.1 Hz, 1H), 4.80–4.73 (m, 2H), 4.61 (s, 2H), 4.41 (s, 4H), 4.37–4.31 (m, 1H), 4.14 (t, J = 9.0 Hz, 1H), 3.97–3.90 (m, 2H), 3.80 (dd, J = 6.8, 15.3 Hz, 1H), 3.64–3.61 (m, minor rotamer), 3.30 (s, 3H), 3.12 (br s, 1H), 1.38 (s, 9H), 1.32 (s, minor rotamer), 0.88 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (125 MHz, 90°, DMSO-d_6) δ 155.9, 153.8, 142.5, 140.1, 138.2, 136.4, 134.0, 127.6, 126.9, 126.8, 126.7, 123.6, 119.9, 116.0, 113.6, 113.4, 94.9, 78.5, 73.0, 72.2, 70.0, 67.8, 54.4, 52.2, 46.7, 27.7, 25.4, 17.4, −4.4, −4.9 (peaks corresponding to minor rotamer: δ 134.1, 116.4, 113.5, 95.0, 70.8, −4.5, −5.1). Anal. Calcd for $C_{35}H_{53}NO_7Si$: C, 66.95; H, 8.51; N, 2.23. Found: C, 66.91; H, 8.46; N, 2.40.



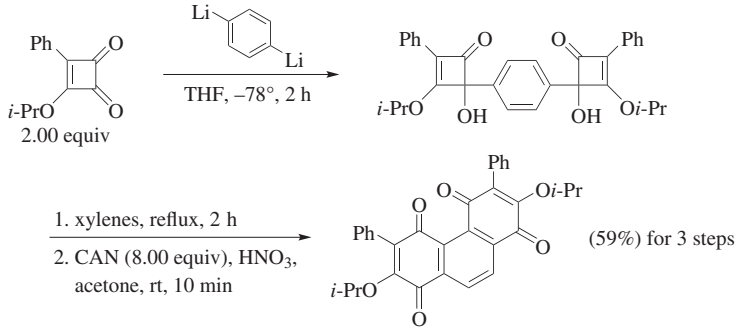
5-Butyl-5,6-dihydro-8,9-dimethoxy-7,10-phenanthridinediol [Electrocyclization of a Cyclobutenone-Derived Alkynylvinylketene with Further Cyclization].[121] A solution of 4-(3-(butyl(phenyl)amino)-1-propynyl)-4-hydroxy-2,3-dimethoxy-2-cyclobutenone (0.395 g, 1.20 mmol) in toluene (120 mL) was added dropwise over 100 min to refluxing toluene (250 mL) under N_2. The solution was refluxed for an additional 20 min, then was cooled to rt, and the solvent was removed under vacuum. Chromatography (hexanes/EtOAc, 3:1) afforded the title compound (0.255 g, 65%) as a purple oil: IR ($CDCl_3$) 3520, 1633, 1599 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.37 (dd, J = 1.4, 7.7 Hz, 1H), 7.17 (dt, J = 1.5, 8.0 Hz, 1H), 6.82 (dt, J = 1.1, 7.7 Hz, 1H), 6.76 (d, J = 8.01 Hz, 1H), 5.93 (br s, 1H), 5.40 (br s, 1H), 4.19 (s, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 3.28 (t, J = 7.7 Hz, 2H), 1.69 (quintet, J = 7.3 Hz, 2H), 1.41 (sextet, J = 7.7 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.2, 139.6, 138.3, 137.9, 136.8, 128.5, 127.9, 122.0, 117.4, 116.7, 114.6, 112.6, 60.9, 60.8, 50.7, 45.7, 27.4, 20.6, 13.9; HRMS (*m/z*): M^+ calcd for $C_{19}H_{23}NO_4$, 329.1627; found, 329.1634.



2-Ethoxycarbonyl-4-acetoxy-6-fluoro-9-(*p*-toluenesulfonyl)carbazole [Electrocyclization of an Acid-Derived Alkynylvinylketene with Further Cyclization].[55] 6-[2-(*p*-Toluenesulfonylamino)-5-fluorophenyl]-3-ethoxycarbonyl-3-hexen-5-ynoic acid (22.3 g, 50.0 mmol) was dissolved in Ac_2O (48 mL, 0.50 mol). To this solution, anhydrous sodium acetate (8.2 g, 0.10 mol) and hydroquinone (275 mg, 2.50 mmol) were added and the resulting heterogeneous mixture was heated at reflux for 1 h under a nitrogen atmosphere. After cooling to rt, the acetic anhydride was removed by evaporation under reduced pressure and the residue was treated with EtOAc (300 mL) and H_2O (100 mL). The organic phase was separated, was dried over Na_2SO_4, and then was concentrated under reduced pressure. The residue was purified by chromatography followed by recrystallization from hexane/$CHCl_3$ to provide the title product (21.4 g, 91%): mp 197–198°; FT-IR (nujol): 1763, 1722, 1591, 1472, 1417, 1369, 1299, 1207, 1175, 1087, 1027, 861, 666 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.31 (dd, J = 9.0, 4.3 Hz, 1H), 7.85 (s, 1H), 7.69 (d, J= 8.3 Hz, 2H), 7.54 (dd, J = 8.2, 2.5 Hz, 1H), 7.27 (dt, J = 9.0, 2.5 Hz, 1H), 7.13 (d, J = 8.3 Hz, 2H), 4.47 (q, J = 7.2 Hz, 2H), 2.49 (s, 3H), 2.27 (s, 3H), 1.46 (t, J = 7.2 Hz, 3H); MS-EI (*m/z*): [M^+ + 1] 470, M^+ 469, 427, 382, 354, 334, 315, 290, 272, 244, 227, 200, 171, 155, 139, 120, 91, 65. Anal. Calcd for $C_{24}H_{20}FNO_6S$: C, 61.40; H, 4.29. Found: C, 61.50; H, 4.30.

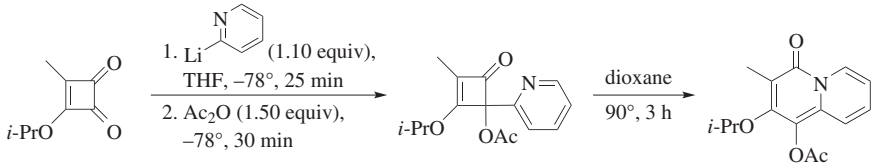


7-Bromo-2,3-dihydro-6-hydroxy-5-isopropyl-l-methyl-4-(triisopropylsilyloxy)-l*H*-phenalene [Pericyclic Reaction Cascade Including an Electrocyclization of a Cyclobutenone-Derived Vinylketene with an Arene].[136] A 28-cm vycor tube (16-mm o.d., 14-mm i.d.), fitted with a rubber septum, was charged with 3-bromo-6-diazo-9-methyl-7,8,9-trihydrobenzocyclohepten-5-one (1.63 g, 5.84 mmol), 3-methyl-l-(triisopropylsilyloxy)-l-butyne (2.04 g, 8.48 mmol), and 1,2-dichloroethane (20 mL). A second rubber septum (inverted) was secured with wire to the tube to ensure a good seal, and the solution was degassed with a stream of Ar for 20 min and was then irradiated at 254 nm for 91 h in a Rayonet photochemical reactor. The reaction mixture was transferred to a l00-mL round-bottomed flask fitted with a reflux condenser and an argon inlet adapter, was diluted with 1,2-dichloroethane (40 mL), and was heated at reflux. After 12 h, the reaction mixture was allowed to cool to rt and was concentrated to afford a red-brown oil (3.52 g). Column chromatography (120 g of silica gel, hexanes) provided the title product (1.79 g, 62%) as a viscous, colorless oil, which crystallized upon standing to a white solid: mp 85–87°; IR ($CDCl_3$) 3480, 2940, 2870, 1590, 1560, 1455, 1410, 1375, 1360, 1330, 1270, 1180, 1110, 1040, 1010, and 815 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.41 (d, J = 7.6 Hz, 1H), 6.97 (d, J = 7.5 Hz, 1H), 3.56 (septet, J = 7.2 Hz, 1H), 3.12–3.04 (m, 1H), 3.03–2.98 (m, 2H), 2.02–1.90 (m, 1H), 1.84–1.75 (m, 1H), 1.45 (d, J = 6.8 Hz, 3H), 1.43 (d, J = 7.4 Hz, 3H), 1.40–1.32 (m, 3H), 1.29 (d, J = 7.0 Hz, 3H), 1.16 (d, J = 6.9 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 150.5, 140.8, 131.4, 129.2, 124.9, 122.9, 116.7, 114.9, 112.1, 34.3, 28.9, 26.1, 22.5, 21.3, 20.3, 20.3, 18.2, 14.3. Anal. Calcd for $C_{26}H_{39}BrO_2Si$: C, 63.52; H, 8.00. Found: C, 63.08; H, 8.11.



2,7-Diisopropoxy-3,6-diphenyl-1,4,5,8-phenanthradiquinone [Double Electrocyclization of a Cyclobutenone-Derived Arylvinylketene].[130] To a

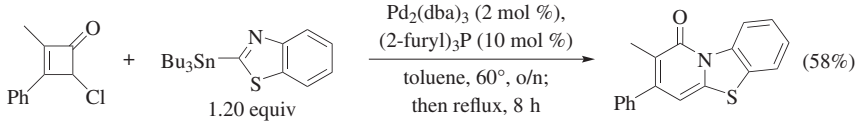
stirred solution of 1,4-dibromobenzene (0.436 g, 1.85 mmol) in THF (20 mL) at −78° was added a solution of *tert*-butyllithium (1.93 M, 3.83 mL, 7.40 mmol) in pentane. The resulting solution was stirred at −78° for 40 min, then the cold bath was removed. After stirring for an additional 20 min, the mixture was cooled again to −78° and transferred via cannula into a solution of 3-isopropoxy-4-phenyl-l,2-cyclobutenedione (0.800 g, 3.70 mmol) in THF (10 mL) at −78°. The reaction mixture was stirred for 2 h at −78°, then was quenched with saturated, aqueous NaCl (30 mL), was extracted with Et_2O (150 mL), and was washed with brine (2 × 30 mL). The aqueous layer was extracted again with EtOAc (2 × 70 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford a yellow solid (1.01 g). The crude product was suspended in xylenes (30 mL) and was heated for 2 h at reflux to provide a homogeneous solution. The solvent was removed under reduced pressure and the crude product (0. 986 g) was dissolved in acetone (50 mL). To this solution was added cerium(IV) ammonium nitrate (14.80 mmol, 8.11 g) and concentrated HNO_3 (4 mL). The mixture was stirred at rt for 10 min under air, then was extracted with Et_2O (200 mL), and was washed with brine (2 × 50 mL). The aqueous layer was extracted with CH_2C1_2 (100 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford an orange-colored solid (1.03 g). The crude product was purified by silica gel chromatography (3 × 15 cm, 20% EtOAc/hexanes) to afford the title product (0.519 g, 59%) as a bright-yellow solid. Triturating with Et_2O further purified the product: mp 219–222°; IR (CH_2C1_2) 1675 (s), 1594 (s), 1563 cm^{-1}; ^1H NMR (300 MHz, $CDC1_3$) δ 8.37 (s, 2H), 7.70–7.56 (m, 4H), 7.53–7.36 (m, 6H), 4.71 (hept, $J = 6.0$ Hz, 2H), 1.19 (d, $J = 6.3$ Hz, 12H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 185.4, 180.6, 153.9, 136.1, 135.5, 135.0, 131.0, 130.8, 129.1, 128.8, 127.8, 76.8, 22.7. Anal. Calcd for $C_{32}H_{26}O_6$: C, 75.88; H, 5.17. Found: C, 75.69; H, 5.06.



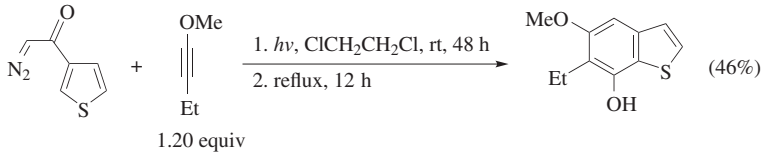
(50%) for 3 steps

l-Acetoxy-2-isopropoxy-3-methyl-4-quinolizinone [Electrocyclization of a Cyclobutenone-Derived Heteroarylvinylketene].[138] 2-Bromopyridine (0.204 mL, 2.14 mmol) in Et_2O (5 mL) was treated dropwise with *n*-BuLi in pentane (1.53 mL, 1.40 M, 2.14 mmol) at −78°. After 1.2 h, the solution was cannulated into a solution of 3-isopropoxy-4-methylcyclobutene-1,2-dione (0.300 g, 1.95 mmol) in THF (30 mL) at −78°. After 25 min, Ac_2O (0.275 mL, 2.92 mmol) was added, and after an additional 30 min the reaction mixture was quenched with saturated, aqueous $NaHCO_3$ and was extracted with EtOAc. The extract was dried ($MgSO_4$) and concentrated to provide a black oil that was dissolved in dry dioxane (8 mL), sparged with Ar, and heated at 90° for 3 h. Removal of solvent followed by silica gel chromatography (2 × 15 cm column, 30% hexanes/EtOAc) afforded the title

product as a dark green solid (0.267 g, 50%): mp 93–94°; IR (CH_2C1_2) 1778, 1653, 1627 cm^{-1}; ^1H NMR (300 MHz, $CDC1_3$) δ 9.00 (d, J = 7.5 Hz, 1H), 7.34 (d, J = 9.0 Hz, 1H), 7.22 (dd, J = 7.0, 9.0 Hz, 1H), 6.86 (ddd, J = 1.0, 7.0, 7.5 Hz, 1H), 4.49 (sept, J = 6.3 Hz, 1H), 2.41 (s, 3H), 2.28 (s, 3H), 1.32 (d, J = 6.3 Hz, 6 H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 168.7, 158.4, 156.2, 133.1, 128.4, 126.7, 122.1, 118.4, 113.5, 111.5, 77.4, 22.6 (2C), 20.4, 11.5. Anal. Calcd for $C_{15}H_{17}O_4N$: C, 65.44; H, 6.22. Found: C, 65.39; H, 6.19.

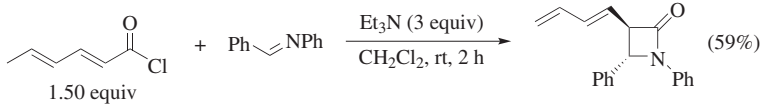


2-Methyl-3-phenyl-l-oxopyrido[2,l-*b*]benzothiazole [Electrocyclization of a Cyclobutenone-Derived Heteroarylvinylketene Using in Situ Generation of the Cyclobutenone].[138] A N_2-sparged solution of 4-chloro-2-methyl-3-phenyl-2-cyclobutenone (0.096 g, 0.50 mmol), 2-(tri-*n*-butylstannyl)benzothiazole (0.255 g, 0.600 mmol), $Pd_2(dba)_3$ (11.4 mg, 0.0100 mmol), and tris(2-fury1)phosphine (11.6 mg, 0.050 mmol) in toluene (8 mL) was heated at 60° overnight and then 8 h at reflux. The mixture was cooled and 5% aqueous KF was added to convert *n*-Bu_3SnCl to *n*-Bu_3SnF. The mixture was extracted with 2:l Et_2O/CH_2Cl_2 (3 × 35 mL) and the combined organic phases were washed with water (2 × 30 mL) and brine (30 mL), then were dried ($MgSO_4$) and concentrated. The resulting solid was purified by silica gel chromatography (2 × 20 cm column, CH_2Cl_2 followed by 14% EtOAc/hexanes) to afford the title compound (0.084 g, 58%) as a white solid: mp 152–154° (EtOAc/hexane); IR (CH_2Cl_2) 1644, 1592 cm^{-1}; ^1H NMR (300 MHz, $CDC1_3$) δ 9.34 (d, J = 8.1 Hz, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.47–7.32 (m, 7H), 6.56 (s, 1H), 2.18 (s, 3H); ^{13}C NMR ($CDC1_3$, 75.5 MHz) δ 163.3, 148.6, 141.4, 139.5, 138.6, 128.4 (4C), 128.1, 126.4, 126.2, 126.1, 121.3, 120.5, 119.6, 101.9,14.0. Anal. Calcd for $C_{18}H_{13}NSO$: C, 74.20; H, 4.50; N, 4.81. Found: C, 74.09; H, 4.51; N, 4.86.

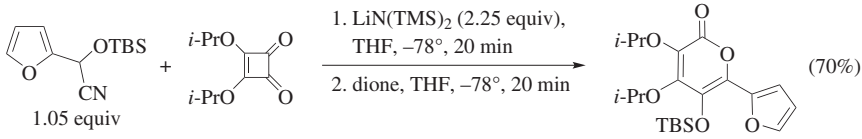


6-Ethyl-7-hydroxy-5-methoxybenzo[*b*]thiophene [Pericyclic Reaction Cascade Including an Electrocyclization of a Vinylketene with a Heteroarene].[221] A solution of 3-(diazoacetyl)thiophene (0.171 g, 1.12 mmol) and 1-methoxy-1-butyne (0.14 mL, 0.116 g, 1.35 mmol) in $ClCH_2CH_2Cl$ (8.2 mL) was distributed evenly between three 25-cm Vycor tubes fitted with rubber septa, and the reaction mixtures were degassed by three freeze–thaw cycles and then were irradiated for 48 h with 254 nm light. The samples were subsequently combined and heated at reflux for 12 h. Concentration afforded 0.25 g of a brown oil. Column chromatography on

silica gel (gradient elution with 0 to 50% benzene/petroleum ether) provided the title compound (0.107 g, 46%) as pale-yellow crystals: mp 54–56°; UV (MeCN) λ_{max}, nm (ε): 312 (2600), 302 (2600), 269 (7300), 261 (7400), 226 (23000), 209 (21000); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (d, J = 5.5 Hz, 1H), 7.22 (d, J = 5.5 Hz, 1H), 6.92 (s, 1H), 5.06 (s, 1H), 3.86 (s, 3H), 2.74 (q, J = 7.5 Hz, 2H), 1.17 (*t*, J = 7.5 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 156.7, 147.7, 138.9, 125.7, 124.1, 120.8, 114.7, 97.4, 55.8, 16.7, 13.9; HRMS (*m/z*): M^+ calcd for $C_{11}H_{I2}O_2S$, 208.0558; found, 208.0558.

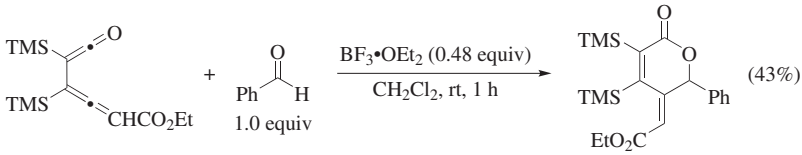


***trans*-3-((*E*)-1,3-Butadienyl)-1,4-diphenyl-2-azetidinone [Intermolecular [2+2] Cycloaddition of an Acid Chloride Derived Vinylketene to an Imine].[222]** A solution of (*E*,*E*)-2,4-hexadienoyl chloride (0.392 g, 3.00 mmol) in dry CH_2Cl_2 (30 mL) was added dropwise over ca. 1.5 h to a solution of *N*-benzylideneaniline (0.362 g, 2.00 mmol) and Et_3N (0.84 mL, 6.00 mmol) in CH_2Cl_2 with stirring at rt. After the addition was complete, the solution was stirred for an additional 15 min, was washed with H_2O (5 × 50 mL), and was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the crude product thus obtained was further purified by column chromatography (silica gel, hexane/EtOAc, 9:1) to afford the title product (0.325 g, 59%): mp 118–119°; IR (KBr) 1734, 1596, 1496 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.38–7.21 (m, 9H), 7.07–7.02 (m, 1H), 6.39–6.30 (m, 2H), 5.88 (dd, J = 14.3, 8.1 Hz, with fine splitting, 1H), 5.24 (d, J = 16.2 Hz, with fine splitting, 1H), 5.14 (d, J = 9.8 Hz, with fine splitting, 1H), 4.80 (d, J = 2.5 Hz, 1H), 3.77 (dd, J = 8.1, 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 165.4, 137.5, 137.2, 135.9, 135.5, 129.2, 129.1, 128.6, 125.8, 125.5, 124.0, 118.5, 117.1, 63.3, 61.7; LRMS (*m/z*): M^+ 275, [M^+ –PhN=C=O] 156. Anal. Calcd for $C_{19}H_{17}NO$: C, 82.88; H, 6.22; N, 5.08. Found: C, 82.83; H, 6.25; N, 5.15.

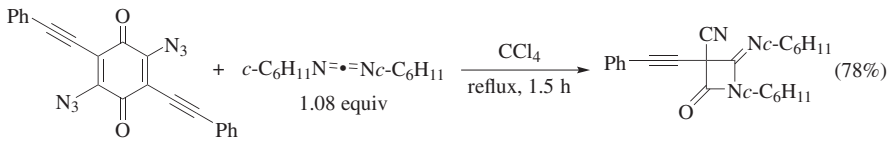


5-(*tert*-Butyldimethylsilyloxy)-6-(2-furyl)-3,4-diisopropoxy-2-pyranone [Intramolecular [4+2] Cycloaddition of a Cyclobutenone-Derived Vinylketene to an in Situ Generated Ketone].[160] Lithium hexamethyldisilazide in THF (1 M, 1.80 mL, 1.80 mmol) was added by syringe to a solution of 2-(*tert*-butyldimethylsilyloxy)-2-(2-furanyl)acetonitrile (0.200 g, 0.840 mmol) in THF (4 mL) at −78°. The solution was stirred for 20 min at −78° and was then added via cannula into a solution of diisopropyl squarate (0.159 g, 0.800 mmol) in THF (2 mL). After stirring for 20 min at −78°, the reaction was quenched with a saturated

solution of $NaHCO_3$ (2 mL) and the mixture was warmed to rt. The solution was extracted with Et_2O (3 × 5 mL), was dried over Na_2SO_4, and then was filtered and concentrated in vacuo. Silica gel chromatography (0 to 20% EtOAc in hexanes) provided the title product (0.231 g, 70%) as a white solid: mp 88–90°; IR (CH_2Cl_2) 1702, 1634 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.44 (s, 1H), 6.80 (d, J = 3.4 Hz, 1H), 6.47–6.46 (m, 1H), 5.25 (heptet, J = 6.2 Hz, 1H), 4.67 (heptet, J = 6.2 Hz, 1H), 1.30 (d, J = 6.2 Hz, 6H), 1.27 (d, J = 6.2 Hz, 6H), 0.95 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 159.8, 155.5, 145.4, 142.8, 136.8, 131.3, 129.3, 111.6, 111.4, 76.2, 74.1, 25.6, 22.4, 22.2, 18.3, −4.3. Anal. Calcd for $C_{21}H_{32}O_6Si$: C, 61.74; H, 7.89. Found: C, 61.93; H, 7.95.

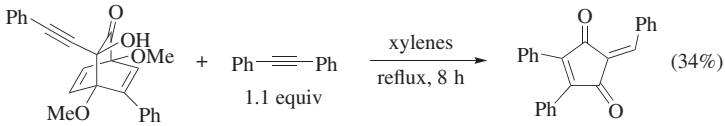


Ethyl (*Z*)-2-[2-Oxo-6-phenyl-3,4-bis(trimethylsilyl)-2*H*-pyran-5-ylidene] acetate [Intermolecular [4+2] Cycloaddition of a Stable Allenylketene to an Aldehyde].[169] A solution of ethyl 4,5-bis(trimethylsilyl)-6-oxo-2,3,5-hexatrienoate (0.198 g, 0.670 mmol), redistilled benzaldehyde (0.070 mL, 0.69 mmol), and BF_3•OEt_2 (0.040 mL, 0.32 mmol) in CH_2Cl_2 (5 mL) was stirred for 1 h at rt. After the addition of Et_2O (50 mL), the solution was washed with H_2O (3 × 20 mL) and the organic layer was dried ($MgSO_4$) and evaporated, and the residue was chromatographed to afford the title product (0.117 g, 43%) as a white solid: mp 89–90°; IR ($CDCl_3$) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.10 (m, 5H), 5.87 (br s, 1H), 5.78 (s, 1H), 4.19 (m, 2H), 1.29 (t, J = 7.2 Hz, 3H), 0.34 (s, 9H), 0.08 (br s, 9H); ^{13}C NMR ($CDCl_3$) δ 165.5, 164.0, 153.0, 145.9, 135.7, 128.5, 128.2, 125.5, 119.0, 81.4, 60.7, 14.2, 2.0, 1.7; HRMS (*m*/*z*): M^+ calcd for $C_{21}H_{30}O_4Si_2$, 402.1683; found, 402.1672.



1-Cyclohexyl-4-cyclohexylimino-3-cyano-3-phenylethynyl-2-azetidinone [Intermolecular [2+2] Cycloaddition of an Azidoquinone-Derived Alkynylketene to a Carbodiimide].[178] A solution of 2,5-diazido-3,6-bis(phenylethynyl)-1,4-benzoquinone (0.946 g, 0.200 mmol) in dry CCl_4 (75 mL) was added dropwise to a refluxing solution of *N*,*N*′-dicyclohexylcarbodiimide (0.088 g, 0.430 mmol) in dry CCl_4 (250 mL) under an Ar atmosphere. The solution was heated at reflux for 1.5 h. The reaction mixture was concentrated and the residue was absorbed onto silica gel and subjected to chromatography (hexanes/EtOAc, 7:3) to afford the title product (0.30 g, 78%) as yellow crystals: mp 116° dec; IR 3050 (w), 2920, 2860, 2220, 1835,

1710, 1440, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.46–7.32 (m, 5H), 3.71–3.59 (m, 2H), 2.05–1.23 (m, 20H); HRMS-CI (*m/z*): M^+ calcd for $C_{24}H_{27}N_3O$, 373.2154; found, 373.2148.



4,5-Diphenyl-2-(phenylmethylene)-4-cyclopentene-1,3-dione [Pericyclic Reaction Cascade Including an Intermolecular [2+2] Cycloaddition of a Retro Diels–Alder Derived Alkynylketene with an Alkyne].[182] A solution of 3-hydroxy-1,4-dimethoxy-5-phenyl-3-(phenylethynyl)bicyclo[2.2.2]-5,7-octadiene-2-one (0.10 g, 0.26 mmol) and diphenylacetylene (0.052 g, 0.29 mmol) in xylenes (20 mL) was refluxed under argon for 8 h. The solvent was evaporated, and the residue was subjected to preparative plate chromatography (silica gel, hexanes/EtOAc 7:3) to provide a yellow oil which crystallized upon addition of diisopropyl ether to afford the title product (0.030 g, 34%) as yellow crystals: mp 159–160°; IR 1690, 1638, 1610, 1355, 1158, 1125 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.40 (d, J = 3.0 Hz, 2H), 7.77 (s, 1H), 7.6–7.2 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 192.6, 191.25, 152.5, 148.8, 143.7, 133.9, 133.8, 133.1, 132.8, 130.6, 129.7, 122.7, 76.94; EIMS (*m/z*): M^+ 336. Anal. Calcd for $C_{24}H_{16}O_2$: C, 85.69; H, 4.79. Found: C, 85.50; H, 4.49.

TABULAR SURVEY

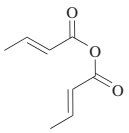
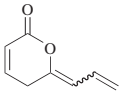
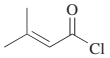
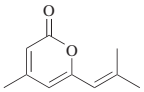
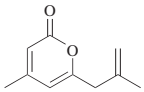
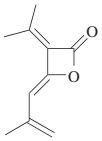
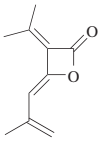
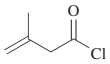
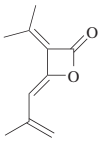
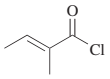
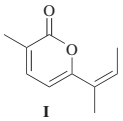
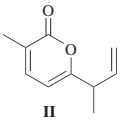
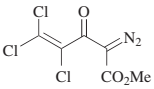
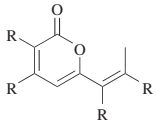
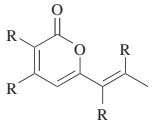
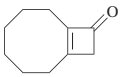
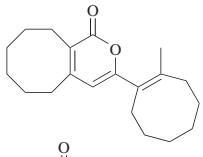
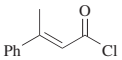
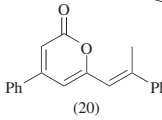
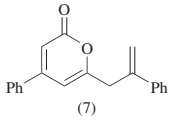
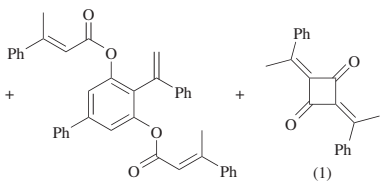
Entries within the tables are arranged according to increasing carbon count of the substrate (the ketene or ketene precursor). With respect to those cases where a precursor molecule loses a carbon-containing fragment in the process of vinylketene generation, the carbon count used is that of the derived vinylketene. Counts for protecting groups on oxygen, nitrogen, and sulfur and also counts for alkyl or aryl groups on those heteroatoms are not included, unless the group is altered during the reaction. In the interest of grouping like reactions together wherever possible, the carbon counts for heteroatomic substituents such as trimethylsilyl that are located on acetylenic and olefinic carbons are also excluded from the count, irrespective of whether these groups undergo relocation without structural alteration in the reaction. A small number of reactions that form acyclic products are included, since their formation proceeds through a cyclic process that is analogous to other reactions within the table.

In addition to the standard abbreviations used in *The Journal of Organic Chemistry*, the following abbreviations are used in the tables:

BHT	butylated hydroxytoluene; 2,6-di-*tert*-butyl-4-methylphenol
dba	dibenzylideneacetone
eq	equivalent(s)
FVP	flash vacuum pyrolysis
hv	irradiation by ultraviolet light
o/n	overnight

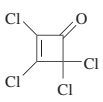
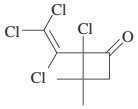
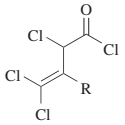
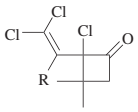
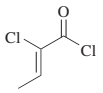
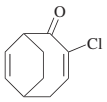
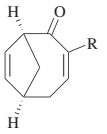
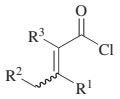
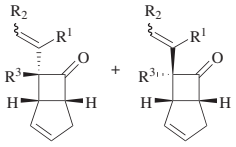
Phth	phthaloyl
PMP	4-methoxyphenyl
PNB	4-nitrobenzyl
quant	quantitative
SEM	(2-trimethylsilyl)ethoxymethyl
SM	starting material
TES	triethylsilyl
TFE	2,2,2-trifluoroethanol
TMSE	2-(trimethylsilyl)ethyl

TABLE 1. DIMERIZATION OF VINYLKETENES

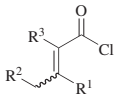
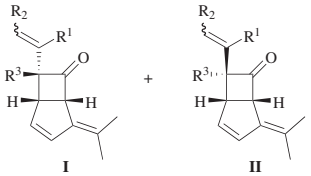
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	1. FVP, 0.1 Torr, 560° 2. –70° to rt	 (15)	53
C_5 	Et_3N, $CHCl_3$, rt, 30 h	 +  **I** **II**	89
		+  **III** **I + II + III** (65), **I/II/III** = 40:52:8	
	1. Me_3N, hexane, 10–12° 2. NaI, acetone, rt, 15 h	 (62)	223
	1. Me_3N, hexane, 10–12° 2. NaI, acetone, rt, 15 h	 (20)	223
	Et_3N, $CHCl_3$, rt, 30 h	 +  **I** **II** **I + II** (72), **I/II** = 1:1	89
	*hν*, benzene, 10–15°	$C_{12}H_6Cl_6O_6$[a] (20)	224
$C_{8–14}$ 	Catalyst, toluene, 110°, 12 h	 +  **I** **II** R = Et, Catalyst = $[RuCl_2(CO)_3]_2$: **I + II** (79), **I/II** 41:59 R = Et, Catalyst = $[RhCl(CO)_2]_2$: **I + II** (86), **I/II** 100:0 R = *n*-Pr, Catalyst = $[RuCl_2(CO)_3]_2$: **I + II** (81), **I/II** 22:78 R = *n*-Pr, Catalyst = $[RhCl(CO)_2]_2$: **I + II** (75), **I/II** 100:0 R = *n*-C_5H_{11}, Catalyst = $[RuCl_2(CO)_3]_2$: **I + II** (85), **I/II** 24:76 R = *n*-C_5H_{11}, Catalyst = $[RhCl(CO)_2]_2$: **I + II** (86), **I/II** 100:0	90
C_{10} 	Catalyst, toluene, 110°, 12 h	 Catalyst: $[RuCl_2(CO)_3]_2$ (93); $[RhCl(CO)_2]_2$ (84)	90
	Et_3N, $CHCl_3$, rt, 30 h	 +  (20) (7)  (17) (1)	89

[a] The dimer was shown to have the composition $C_{12}H_6Cl_6O_6$ but the structure was not established.

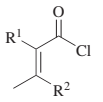
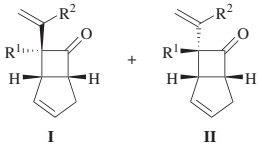
TABLE 2. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKENES

Ketene or Ketene Source	Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 		Cyclohexane, autoclave, 120°, 12 h	 (46)	67
		Et_3N, cyclohexane, autoclave, 70°, 7 h	 R: H (17); Cl (26)	67
		Et_3N, cyclohexane, sealed tube, 80°, 21 h; 140°, 2 h	 (44)	92
$C_{4–5}$ 		1. Et_3N, cyclohexane, 80° 2. Benzene, sealed tube, 120°, 18 h	 R: H (18); Me (40)	92
$C_{4–8}$ 		Et_3N, $CHCl_3$, 0° to rt, 15 h	 **I** + **II**	21

R^1	R^2	R^3	**I + II**	**I/II**
H	H	Cl	(84)	5:5
H	Me	Cl	(80)	5:5
Me	H	Cl	(73)	10:0
H	H	Me	(77)	3:7
–$(CH_2)_4$–		Cl	(76)	10:0

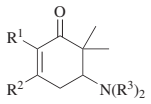
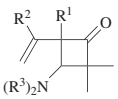
$C_{4–6}$ 		Et_3N, $CHCl_3$, 0° to rt, 15 h	 **I** + **II**	21

R^1	R^2	R^3	**I + II**	**I/II**
H	H	Cl	(57)	5:5
H	H	Me	(69)	3:7
Et	H	Cl	(66)	10:0

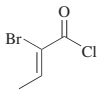
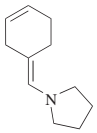
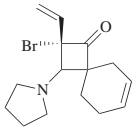
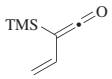
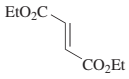
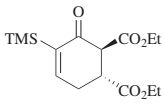
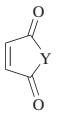
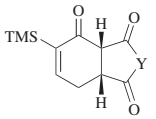
$C_{4–8}$ 		Et_3N, $CHCl_3$	 **I** + **II**	

R^1	R^2	Temp	Time (h)	**I + II**	**I/II**	
H	H	35°	72	(38)	18:82	95
Cl	H	rt	12	(84)	50:50	21
Me	H	65°	2	(76)	70:30	95
Me	H	rt	12	(77)	70:30	21
Me	H	20°	16	(78)	65:35	225
Cl	Me	rt	12	(73)	0:100	225
n-Bu	H	65°	72	(59)	92:8	95

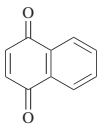
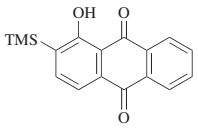
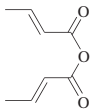
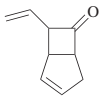
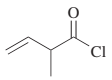
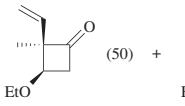
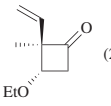
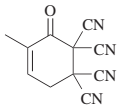
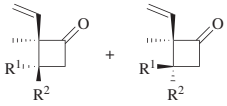
TABLE 2. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKENES (*Continued*)

Ketene or Ketene Source	Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-5} 		Et_3N, solvent	 +  **I** **II**	50

R^1	R^2	$N(R^3)_2$	Solvent	Temp	Time (h)	**I + II**	**I/II**
H	H	4-morpholinyl	hexane	rt	28	(46)	0:100
Br	H	1-pyrrolidinyl	CH_2Cl_2	rt	6	(92)	100:0
Br	H	4-morpholinyl	CH_2Cl_2	rt	6	(69)	100:0
Br	Me	4-morpholinyl	CH_2Cl_2	rt	36	(63)	100:0
H	Me	4-morpholinyl	CH_2Cl_2	rt	28	(67)	0:100
Me	H	1-pyrrolidinyl	CH_2Cl_2	rt	24	(53)	100:0
Me	H	4-morpholinyl	CH_2Cl_2	rt	24	(26)	64:36
Me	H	1-pyrrolidinyl	hexane	70°	24	(56)	50:50
Me	H	4-morpholinyl	hexane	70°	48	(26)	9:91

C_4 		Et_3N, CH_2Cl_2, rt, 6 h	 (69)	50
		Toluene, 95°, 38 h	 (62)	24
		$CHCl_3$		24

Y	Temp	Time (h)	
O	rt	12	(89)
PhN	40°	24	(74)

		1. $CHCl_3$, 60°, 41 h 2. KOH, EtOH, air, rt, 1 h	 (28)	24
		1. 550°, gas phase 2. Alkene, –196° to rt	 (23)	53
C_5 		Et_3N, neat alkene, rt, 8 h	 (50) +  (22)	20
		1. Et_3N, CCl_4, 0°, 5 min 2. TCNE, THF, –30 to 20°, 3 h	 (35)	20
		Et_3N, neat, sealed tube, 150°	 **I** **II**	96 97 97

R^1	R^2	Time	**I + II**	**I/II**
Et	Et	4 h	(12)	—
n-Bu	Me	—	(11)	1:1
n-C_5H_{11}	H	—	(40)	2.3:1

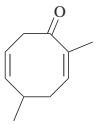
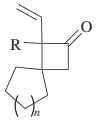
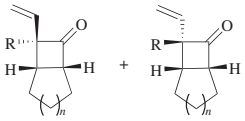
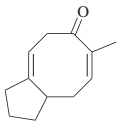
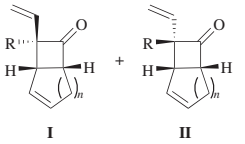
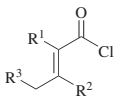
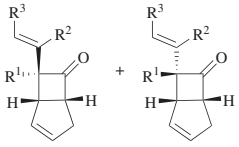
		$CHCl_3$, sealed tube, 137°, 2 h	 (30)	92

TABLE 2. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKENES (*Continued*)

Ketene or Ketene Source	Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-6} 		Et_3N, neat alkene, sealed tube, 150°, 4 h	 R = Me, n = 2 (79); R = Me, n = 3 (67); R = Et, n = 1 (67); R = Et, n = 2 (42)	97 97 96 97
		Et_3N, neat alkene, sealed tube, 150°, 4 h	 **I** + **II**; R = Me, n = 1, I + II = (28), I/II = 2.3:1; R = Me, n = 4, (60), 3:1; R = Et, n = 4, (52), 5.7:1	97
C_5 		Et_3N, cyclohexane, sealed tube, 100°, 41 h	 (19)	92
C_{5-8} 		Et_3N, $CHCl_3$, reflux, 18 h	 **I** + **II**; R = Me, n = 1, I + II = (76), I/II = 70:30; R = Me, n = 2, (57), 65:35; R = *n*-Bu, n = 1, (59), 92:8; R = *n*-Bu, n = 2, (42), 97:3	95
		Et_3N, CH_2Cl_2 or $CHCl_3$, rt	 **I** + **II**	226

R^1	R^2	R^3	I + II	I/II
Me	H	H	(77)	30:70
Me	H	Me	(33)	40:60
Me	Me	H	(28)	100:0
Et	Me	H	(10)	91:9
Me	$–(CH_2)_3–$		(74)	100:0
Cl	$–(CH_2)_4–$		(76)	91:9

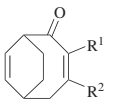
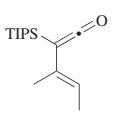
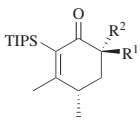
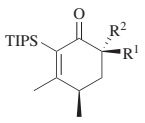
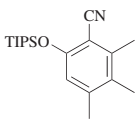
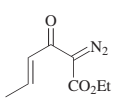
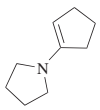
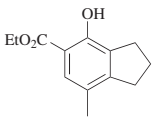
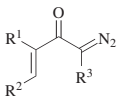
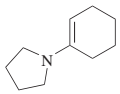
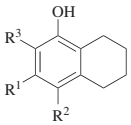
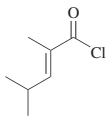
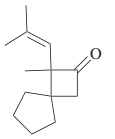
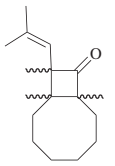
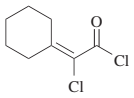
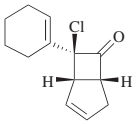
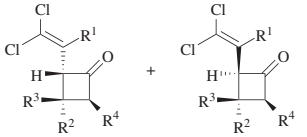
		Solvent, sealed tube	 R^1 = H, R^2 = Me, solvent = benzene, temp = 80°, time = 65 h, (49); R^1 = Me, R^2 = Me, benzene, 120°, 4 d, (91); R^1 = H, R^2 = *n*-Bu, toluene, 160°, 20 h, (33)	92
C_6 		Solvent	 **I** +  **II**; R^1 = H, R^2 = O_2N, benzene, rt, 39, (85), —; R^1 = Me, R^2 = O_2N, toluene, 110°, 116, (35), —; R^1 = EtO_2C, R^2 = NC–, toluene, rt, 24, (98), 2:1	91
		Toluene, sealed tube, 150°, 31 h	 (67)	91
		$Rh_2(OAc)_4$, benzene, reflux, 5–20 min	 (47)	93

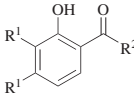
TABLE 2. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKENES (*Continued*)

Ketene or Ketene Source	Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-11} 		$Rh_2(OAc)_4$, benzene, reflux, 5–20 min		93

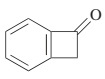
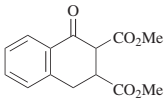
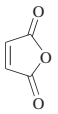
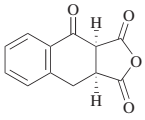
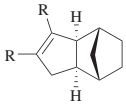
R^1	R^2	R^3	Solvent	
H	Me	EtO_2C	benzene	(64)
Me	H	EtO_2C	CH_2Cl_2	(75)
H	Ph	$(MeO)_2PO$	benzene	(84)
H	Ph	EtO_2C	benzene	(73)

C_7 		Et_3N, neat alkene, sealed tube, 150°, 4 h	 (20)	96
		Et_3N, neat alkene, sealed tube, 165°, 44 h	 (33) 3 isomers, ratio = 20:7:3	96
C_8 		Et_3N, $CHCl_3$, 0° to rt, 15 h	 (76)	21
C_{8-10} 		*hν*, benzene, 3–24 h	 **I** + **II**	227, 228

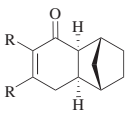
R^1	R^2	R^3	R^4	**I + II**	**I/II**
n-Bu	EtO	H	H	(50)	—
Ph	EtO	H	H	(80)	33:67
Ph	Me	H	Me	(30)	—
Ph	Me	Me	H	(40)	—
Ph	CH_2=CH	TMSO	H	(50)	100:0
Ph	CH_2=CH	Me	H	(70)	83:17
Ph	Ph	H	H	(90)	100:0

		$[RhCl(C_2H_4)_2]_2$, (c-$C_6H_{11})_3P$ toluene, 130°, 12 h		94

R^1	R^2	
Et	Et	(60)
n-Pr	Et	(65)
n-Pr	*n*-Pr	(41)
n-Pr	MeO	(40)

C_8 		Neat, sealed tube, 160°	 (30)	69
		Neat, sealed tube, 160°	 (30)	69
C_{8-14} 		$[RhCl(CO)_2]_2$, toluene, 110°, 12 h		90

R	
Et	(76)
n-Pr	(79)
n-C_5H_{11}	(84)

		$[RhCl(CO)_2]_2$, CO (30 atm), toluene, 110°, 12 h		90

R	
Et	(78)
n-Pr	(83)
n-C_5H_{11}	(94)

TABLE 2. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKENES (*Continued*)

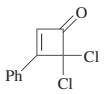
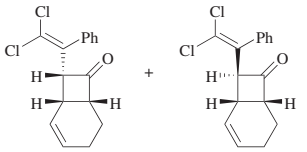
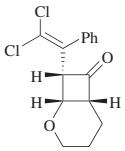
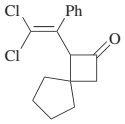
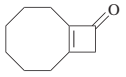
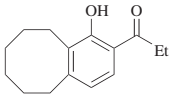
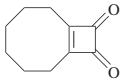
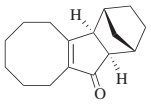
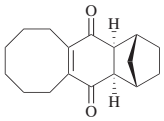
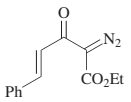
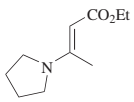
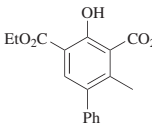
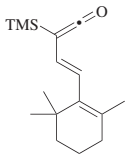
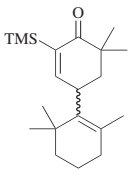
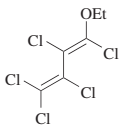
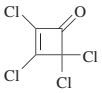
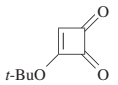
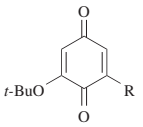
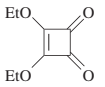
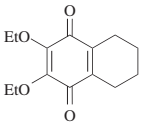
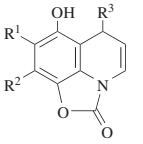
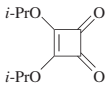
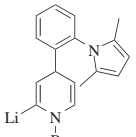
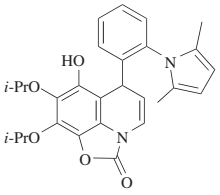
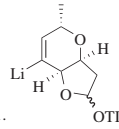
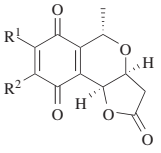
Ketene or Ketene Source	Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
		Benzene	 **I** + **II**	227, 228
			Cond: *h*ν, rt, 3–24 h, (75), I + II 1:0; heating, 130°, 18, (70), I/II 1:3	
		*h*ν, benzene, 3–24 h	 (80)	227, 228
		*h*ν, benzene, 3–24 h	 (50)	227, 228
		$[RhCl(C_2H_4)_2]_2$, (*c*-$C_6H_{11})_3P$, toluene, 130°, 12 h	 (43)	94
		$[RhCl(CO)_2]_2$, toluene, 110°, 12 h	 (67)	90
		$[RhCl(CO)_2]_2$, CO (30 atm), toluene, 110°, 12 h	 (84)	90
C_{11}				
		$Rh_2(OAc)_4$, benzene, reflux, 5–20 min	 (64)	93
C_{13}				
		Toluene, rt, 93 h	 (43)	91

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	Neat, 160–180°, 40 min; 5 Torr distillation	 (89)	67, 68
	1. Li, THF, hexane, –78° 2. *p*-Xylene, reflux, 30 min 3. Ag_2O, K_2CO_3, rt, 1.75 h	 R: Me (66); *n*-Bu (58)	229
	1. Li, THF, –78°, 15 min 2. *p*-Xylene, reflux, 2 h 3. CAN, CH_2Cl_2, 20 min	 (55)	106
$C_{4–10}$ 	1.  Boc, THF, –78°, 2 h 2. Neat, 160–165°, 1 h		230

R^1	R^2	R^3	
i-PrO	*i*-PrO	H	(53)
i-PrO	*i*-PrO	Me	(55)
i-PrO	*i*-PrO	*n*-Bu	(65)
i-PrO	*i*-PrO	Ph	(60)
i-PrO	*i*-PrO	2-FC_6H_4	(53)
i-PrO	*i*-PrO	2-$MeOC_6H_4$	(57)
Me	*i*-PrO	Me	(42)
Me	*i*-PrO	*n*-Bu	(55)
Me	*i*-PrO	Ph	(41)
Et	Et	Me	(65)
Et	Et	4-$(allyl)_2NC_6H_4$	(62)
4-FC_6H_4	*i*-PrO	H	(44)
4-FC_6H_4	*i*-PrO	Me	(74)

C_4 	1.  Boc, THF, –78°, 2 h 2. Neat, 160–165°, 45 min	 (66)	230
$C_{4–10}$ 	1.  OTIPS, Et_2O, –78° 2. Solvent, reflux 3. HCl 4. PCC		186

R^1	R^2	Solvent	
MeO	MeO	toluene	(38)
i-PrO	*i*-PrO	toluene	(61)
Ph	MeO	toluene	(50)
Ph	*i*-PrO	toluene	(72)
i-PrO	Ph	xylene	(68)

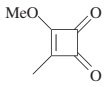
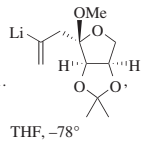
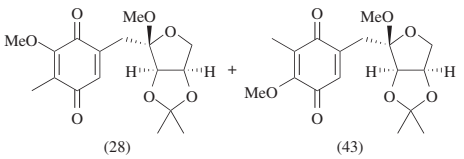
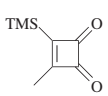
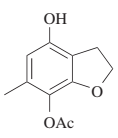
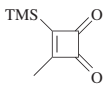
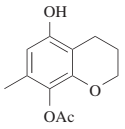
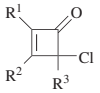
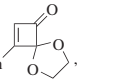
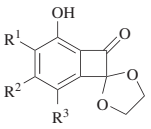
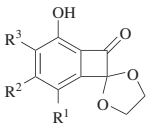
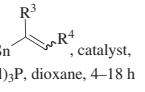
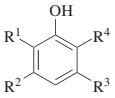
C_5 	1.  THF, –78° 2. *p*-Xylene, 138° 3. CAN, CH_2Cl_2	 (28) + (43)	231
	1.  , THF, –78°, 2 h 2. Ac_2O, –78°, 1.5 h 3. Toluene, 90°, 1.5 h	 (67)	232

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

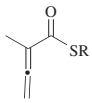
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	1. Li  , THF, –78°, 3 h 2. Ac_2O, –78°, 1.5 h 3. Toluene, reflux, 2 h	 (59)	232
$C_{5–12}$ 	 , $PdCl_2(PhCN)_2$, $(2\text{-furyl})_3P$, THF, 40–70°	 +  **I** **II**	110

R^1	R^2	R^3	Time (h)	**I + II**	**I/II**
Me	*i*-PrO	H	2–4	(95)	1:0
n-Bu	*i*-PrO	H	2–4	(99)	1:0
s-Bu	*i*-PrO	H	2–4	(91)	1:0
t-Bu	*i*-PrO	H	16–18	(69)	1:0
Et	Et	H	2–4	(61)	1:0
Me	*n*-Bu	H	2–4	(72)	1:0
n-Bu	Me	H	2–4	(71)	1:0
Ph	*i*-PrO	H	2–4	(90)	1:0
Me	Ph	H	2–4	(56)	1:0
Ph	Me	H	2–4	(75)	1:0
Me	*i*-PrO	Ph	2–4	(57)	2:1
n-Bu	*i*-PrO	*n*-Bu	2–4	(79)	1:0

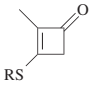
 , catalyst,
$(2\text{-furyl})_3P$, dioxane, 4–18 h

 233

R^1	R^2	R^3	R^4	Catalyst	Temp (°)	
Me	*i*-PrO	H	H	$Pd(dba)_2$	60	(67)
Me	*i*-PrO	EtO	H	$PdCl_2(PhCN)_2$	100	(55)
Me	Bn_2N	H	H	$PdCl_2(PhCN)_2$	100	(62)
Me	Bn_2N	EtO	H	$PdCl_2(PhCN)_2$	100	(74)
Me	Ph	H	H	$PdCl_2(PhCN)_2$	100	(75)
Me	Ph	EtO	Ac	$PdCl_2(PhCN)_2$	100	(50)
Ph	Me	H	H	$PdCl_2(PhCN)_2$	100	(75)
n-Bu	*n*-Bu	H	H	$PdCl_2(PhCN)_2$	100	(74)
n-Bu	*n*-Bu	EtO	H	$PdCl_2(PhCN)_2$	100	(54)

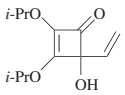
C_5 

Xylene, reflux, 2 h

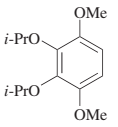


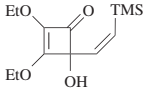
R	
Et	(67)
Ph	(84)
Bn	(58)
4-MeC_6H_4	(77)

87

C_6 

1. Neat, 160°, 15 min
2. MeI, KOH, DMSO, rt, 2 h

 (87) 25



1. *p*-Xylene, reflux, 4 h
2. CAN, CH_2Cl_2, 15 min

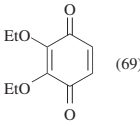
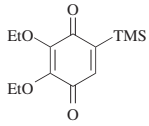
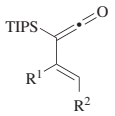
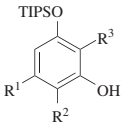
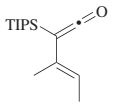
 (69) +  (27) 106

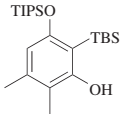
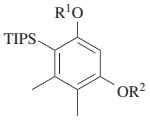
TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-11} 	R^3—≡—OLi, THF, rt, 0.5–1 h		102, 103

R^1	R^2	R^3		
Me	Me	Ph	(30)	102
Me	Me	*i*-Pr	(65)	102, 103
Me	Me	*n*-Bu	(62)	102, 103
Me	Me	*t*-Bu	(55)	102
Me	Et	$EtOCH_2CH_2$	(46)	102, 103
Me	Et	CH_2=$CHCH_2CH_2$	(68–70)	102, 103
Me	Et	(*E*)-PhCH=CH	(37)	102
Me	*c*-C_6H_{11}	$EtOCH_2CH_2$	(44–46)	102, 103

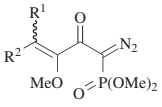
C_6 

LiO—≡—TBS, 70 min

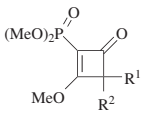
 (20) +  (30)

R^1 = H, R^2 = TBS
or R^1 = TBS, R^2 = H

102

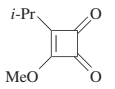
C_{6-7} 

Benzene, reflux

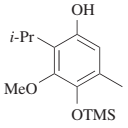


R^1	R^2	Time (h)	
Me	Me	22	(75)
H	*n*-Pr	48	(49)

98

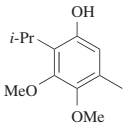
C_7 

1.  Li, THF, –78°
2. TMSCl, –78 to 0°
3. Hexanes, 69°, 1 h

 (77)

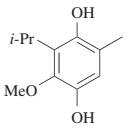
185

1.  Li, THF, –78°
2. MeOTf, –78 to 0°
3. Hexanes, 69°, 2 h

 (70)

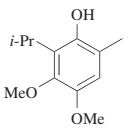
185

1.  Li, THF, –78°
2. Ac_2O, –78 to 0°, 10 min
3. Hexanes, 69°, 2 h
4. NaH, THF, –78 to 0°
5. MeOTf, –78 to 0°
6. NaOH, $(n\text{-Bu})_4NI$

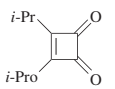
 (44)

185

1.  Li , THF, –78°
2. MeOTf, –78 to 0°
3. Hexanes, 69°, 2 h

 (70)

185



1.  Li, THF, –78°
2. MeOTf, –78°
3. *n*-BuLi, THF
4. TFAA, –78°
5. *o*-Xylene, 100°, 20 min
6. CAN, MeCN, H_2O

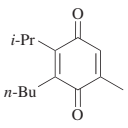
 (22)

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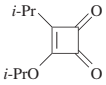
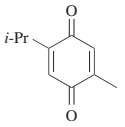
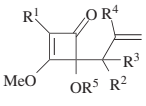
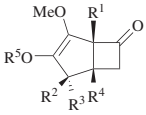
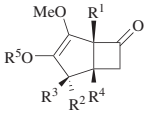
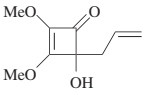
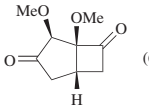
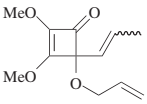
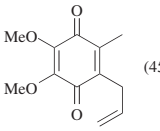
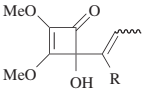
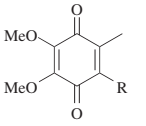
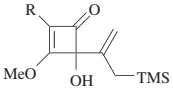
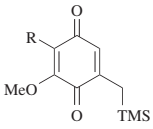
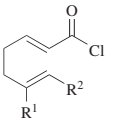
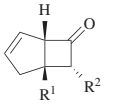
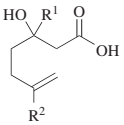
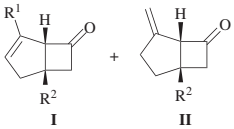
TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	1. Li, THF, –78° 2. MeOTf, –78° 3. $LiAlH_4$, Et_2O, –23°, 0.5 h 4. TFAA, pyridine, Et_2O, 0°, 0.5 h 5. *o*-Xylene, 100°, 20 min 6. CAN, MeCN, H_2O	 (17)	234
$C_{7–13}$ 	A: Solvent, reflux; or B: Solvent, sealed tube, 150°	 +  **I** **II**	115

R^1	R^2	R^3	R^4	R^5	Cond	Solvent	Time (h)	**I + II**	**I/II**
MeO	H	H	H	Me	A	*p*-xylene	50	(83)	100:0
MeO	Me	H	H	Me	B	toluene	36	(90)	6:1
MeO	H	H	Me	Me	B	toluene	26	(86)	100:0
MeO	Me	Me	H	Me	B	toluene	22	(85)	100:0
CH_2=CH	H	H	H	Me	A	toluene	6	(90)	100:0
n-Bu	H	H	H	Me	A	*p*-xylene	5	(85)	100:0
n-Bu—≡	H	H	H	Me	A	*p*-xylene	7	(72)	100:0
Ph	H	H	H	Me	A	THF	14	(86)	100:0
MeO	Ph	H	H	Me	B	*p*-xylene	15	(76)[b]	12:1
Ph	H	H	H	TMS	A	toluene	5	(89)	100:0

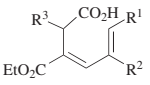
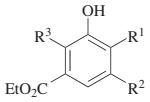
C_7 	Toluene, reflux, 10 h	 (65)	235
	Xylene, reflux, 29 h	 (45)	106
$C_{7–8}$ 	1. Xylene, reflux, 75–95 min 2. CAN, CH_2Cl_2, 20 min, rt	 R: H (84), Me (81)	106
$C_{7–11}$ 	1. *p*-Xylene, reflux 2. Ag_2O, *p*-xylene, rt	 R: MeO (89–92), *n*-Bu (89–92)	236
$C_{7–9}$ 	Et_3N, solvent, reflux		237 237 244

R^1	R^2	Solvent	Time	
H	H	benzene	8 h	(38)
Me	H	benzene	15 h	(43)
H	Et	toluene	20 min	(46)

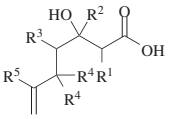
	Ac_2O, KOAc, rt, 2 h; rt to reflux, 4 h	 **I** **II**	238

R^1	R^2	**I + II**	**I/II**
H	H	(57)	—
Me	H	(79)	100:0
H	Me	(75)	100:0
Me	Me	(82)	98:2

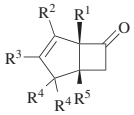
TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{7-13} 	A: 1. $ClCO_2Et$, Et_3N, THF, <20° to rt, 15 min 2. NaOH, EtOH; or B: 1. TFAA, Et_3N, THF, rt, 2 h 2. $NaBH_4$, EtOH, 1 h		239

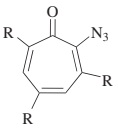
R^1	R^2	R^3	Cond		
H	I	H	A	(60)	
H	I	H	B	(91)	
MeO	H	H	A	(70)[a]	
H	EtO	H	A	(90)	
H	TMS	H	A	(50)	
H	TMS	H	B	(60)	
H	PhS	H	A	(70)	
Me	Br	H	A	(89)	
Me	PhS	H	B	(86)	
Me	PhS	Me	B	(95)	
Br	*n*-Pr	H	A	(72)	
MeO	*n*-Pr	H	B	(89)	
H	TMS[c]	allyl	B	(80)	
MeO	Ph	H	A	(88)	
Br	Ph	H	A	(78)	

C_{7-9} 

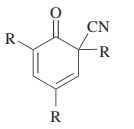
Ac_2O, KOAc, rt, 2 h; rt to reflux, 4 h



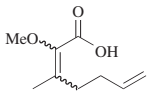
R^1	R^2	R^3	R^4	R^5		
H	H	H	H	H	(62)	
Me	H	H	H	H	(63)	240
H	Me	H	H	H	(79)	
H	H	Me	H	H	(63)	
H	H	H	H	Me	(78)	
H	H	H	Me	H	(48)	
H	H	Me	H	Me	(55)	
H	Me	H	H	Me	(82)	

C_{7-10} 

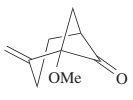
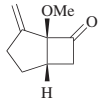
hv, hexane, 22°

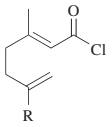


R		
H	(90)	241, 242, 16
Me	(—)	

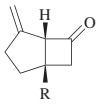
C_8 

1. $(COCl)_2$, THF, 78°, 1.5 h
2. Et_3N, toluene, reflux, 4 h

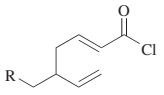
 (28) +  (22) — 243

C_{8-9} 

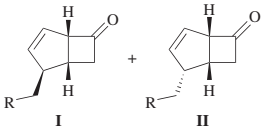
Et_3N, toluene, reflux, 1 h



R		
H	(41)	244, 245
Me	(43)	

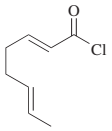
C_8 

Et_3N, benzene, rt, 1 h; reflux, 5–15 h

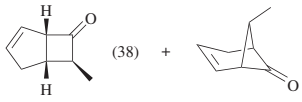


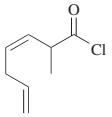
I + **II**

R	I + II	I/II	
H	(30)	3:1[d]	237
MeO	(40)	5:1	
TBDPSO	(39)	5:1	

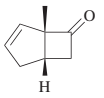


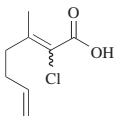
Et_3N, benzene, reflux, 1.5 h

 (38) + (9) — 237



Et_3N, benzene, reflux, 1.5 h

 (48) — 237



1. $(COCl)_2$, THF, reflux, 2 h
2. Et_3N, toluene, reflux, 3 h; rt, 14 h

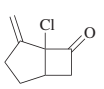
 (35) — 112

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

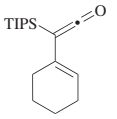
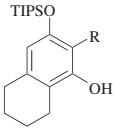
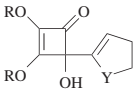
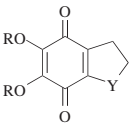
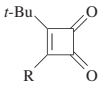
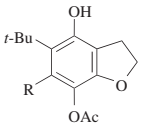
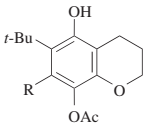
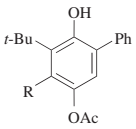
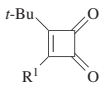
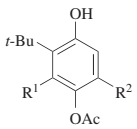
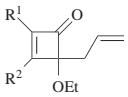
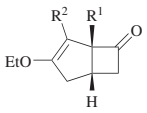
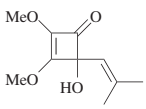
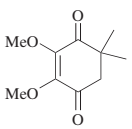
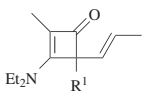
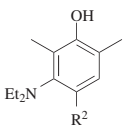
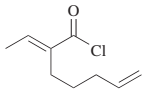
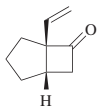
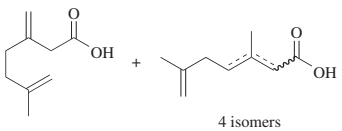
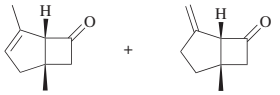
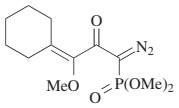
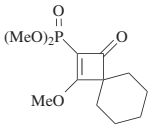
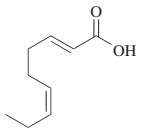
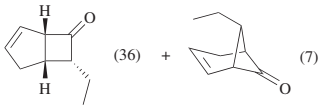
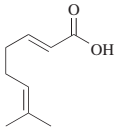
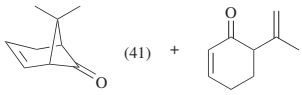
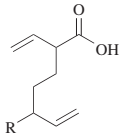
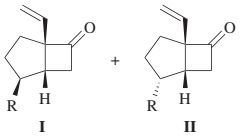
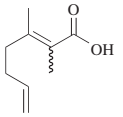
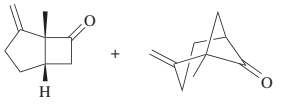
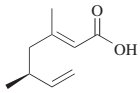
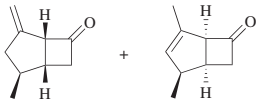
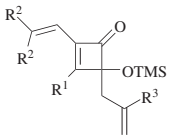
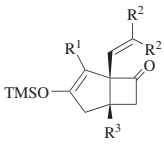
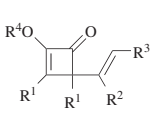
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	R—≡—OLi, THF, rt, 0.5–1 h	 R: allyl (44–48); 1-cyclohexenyl (43); cyclohexyl (67–71)	102, 103
C_{8-9}			
	1. *p*-Xylene, reflux, 2 h 2. Ag_2O, K_2CO_3, Et_2O, 2 h	 R, Y: Et, O (82); Me, CH_2 (71)	106
	1. Li-, THF, –78°, 1 h 2. Ac_2O, –78°, 10 min 3. Neat, 140°, 40 min	 R: *i*-PrO (71); Me (62)	232
	1. Li-, THF, –78° 2. Ac_2O, –78°, 10 min 3. Neat, 140°, 40 min	 R: *i*-PrO (55); Me (61)	232
	1. Ph-≡-Li, THF, –78°, 1 h 2. Ac_2O, –78°, 10 min 3. Neat, 120°, 40 min	 R: *i*-PrO (73); Me (50)	232
	1. R^2-≡-Li, THF, –78°, 1 h 2. Ac_2O, –78°, 10 min 3. Neat, 120°, 40 min	 R^1, R^2: *i*-PrO, EtO (58); Me, EtO (48); Me, Me (52)	232
C_{8-15}			
	Xylene, reflux, 2 h	 R^1, R^2: Me, EtO (98); CH_2=CH, EtO (98); BnO_2CCH_2, EtO (83); Ph, EtO (73); Ph, Me (97); Me, Ph (99); Ph-≡-, EtO (94)	246
C_8			
	THF, microwave, 120°, 0.5 h	 (73)	107
C_{8-9}			
	Neat, 140°	 R^1, R^2: TMS, H (60); Me, Me (—)	247
C_9			
	Et_3N, toluene, reflux, 1.25 h	 (51)	244

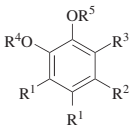
TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9  4 isomers	Ac_2O, NaOAc, reflux, 4 h	 **I** + **II** (62), **I/II** = 2:1	248
	Benzene, reflux, 48 h	 (62)	98
	1. $(COCl)_2$, benzene, 0° to rt, 2 h 2. Et_3N, benzene, reflux, 1 h	 (36) + (7)	237
	1. $(COCl)_2$, benzene, 0° to rt, 2 h 2. Et_3N, benzene, reflux, 12 h	 (41) + (16)	237
$C_{9–10}$ 	1. NaH, toluene, 0° to rt, 1 h; 55°, 0.5 h (for R = H only) 2. $(COCl)_2$, toluene, 0° to rt, 2 h 3. Et_3N, toluene, reflux, 1.25–3.25 h	 **I** + **II** R = H: **I** + **II** (50), — R = Me: **I** + **II** (52), **I/II** = 2.5:1	99
C_9 	1. NaH, benzene, 0°, 10 min 2. $(COCl)_2$, benzene, 55–60°, 1 h 3. Et_3N, toluene, reflux, 3 h	 **I** + **II** (36), **I/II** = 4:1	249
	1. $(COCl)_2$, benzene, 78°, 0.5 h 2. Et_3N, toluene, reflux, 7.5 h	 **I** + **II** (52), **I/II** = 2.5:1	245
$C_{9–12}$ 	Toluene, reflux, 4–5 h		114, 250

R^1	R^2	R^3		
MeO	H	H	(97)	114
Me	H	H	(98)	114
MeO	H	Me	(98)	114
Me	H	Me	(97)	114
MeO	Me	H	(92)	114
Me	Me	H	(98)	114
Me	Me	H	(98)	250

$C_{9–20}$ 

1. Solvent, temp 1, time 1, then chromatography
2. A: Ac_2O, Et_3N, Et_2O, rt, 4.5 h; or
   B: $NaHCO_3$, MeOH, H_2O, rt, 5 min



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R^1	R^2	R^3	R^4	R^5	Solvent	Temp 1 (°)	Time 1 (h)	Cond	
Me	Me	H	MEM	H	*m*-xylene	140	19	A	(95)
Me	Me	Me	MEM	H	dioxane	100	38	A	(64)
n-Bu	H	H	Ac	Ac	dioxane	100	24	A	(79)[e]
n-Bu	H	Ph	H	H	*m*-xylene	140	20	B	(62)[e]

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

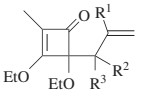
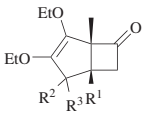
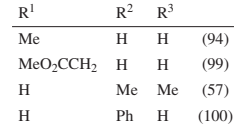
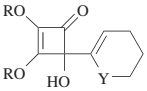
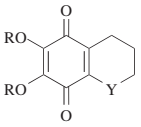
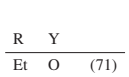
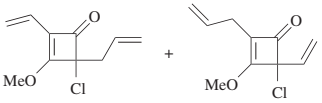
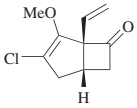
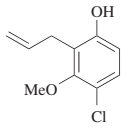
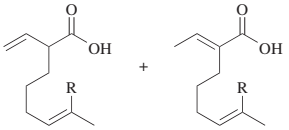
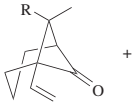
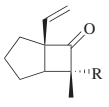
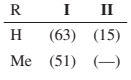
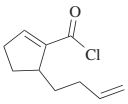
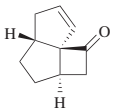
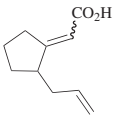
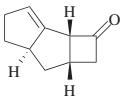
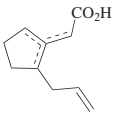
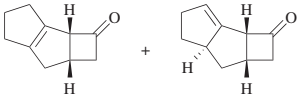
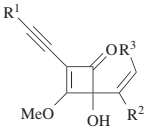
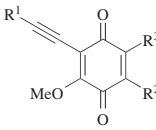
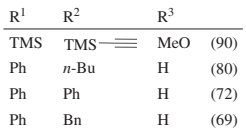
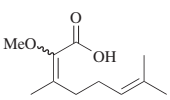
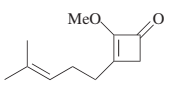
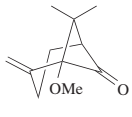
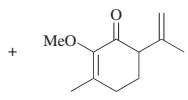
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{9–14}$ 	Xylene, reflux, 2 h	 	246
$C_{9–10}$ 	1. *p*-Xylene, reflux, 2 h 2. Ag_2O, K_2CO_3, Et_2O, 2 h	 	106
C_9 	Toluene, reflux, 4 h	 (27) +  (51)	115
$C_{10–11}$ 	1. NaH, $(COCl)_2$, benzene, 0° to rt, 1 h 2. Et_3N, toluene, reflux, 5 h	 +  **I** **II** 	252
C_{10} 	*i*-Pr_2NEt, DMAP, toluene, 108°, 16 h	 (78)	253
 (*Z*)/(*E*) = 67:33	1. $Me_2C{=}C(Cl)NMe_2$, $CHCl_3$, 0° 2. Et_3N, $CHCl_3$, rt	 (62)	254
 mixture of diene isomers	1. $Me_2C{=}C(Cl)NMe_2$, $CHCl_3$, 0° 2. Et_3N, $CHCl_3$, rt	 **I** **II** **I** + **II** (75), **I**/**II** = 3:1	254
$C_{10–21}$ 	1. Xylene, reflux, 2 h 2. CAN, CH_2Cl_2, rt, 0.5 h	 	106
C_{10} 	1. $(COCl)_2$, THF, reflux, 1.5 h 2. Et_3N, toluene, reflux, 5 h	 (22) +  (17) +  (10)	243

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

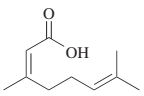
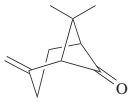
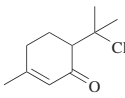
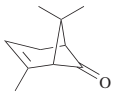
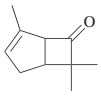
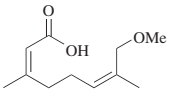
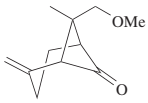
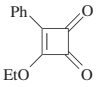
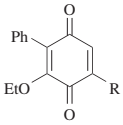
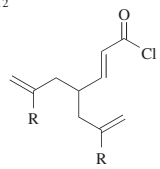
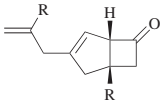
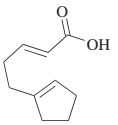
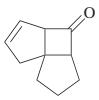
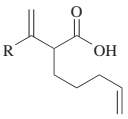
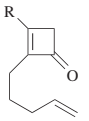
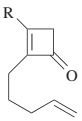
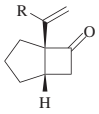
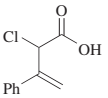
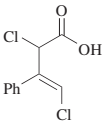
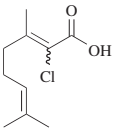
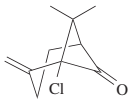
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	1. $(COCl)_2$, benzene, rt to 45°, 2.5 h 2. Et_3N, toluene, reflux, 3 h	 (43) +  (7) +  (2)	255, 256
	NaOAc, Ac_2O, reflux, 16 h	 (28)	257, 258
	1. NaH, benzene, rt, 0.25 h 2. $(COCl)_2$, benzene, rt, 1.5 h; 40°, 0.5 h 3. Et_3N, toluene, reflux, 1 h	 (30)	256
	1.  2. *p*-Xylene, reflux 3. CAN, CH_2Cl_2	 R: Ph (71); Bn (76)	231
C_{10-12}			
	Et_3N, CH_2Cl_2, reflux	 R: H (83); Me (84)	259
C_{10}			
	1. NaH, $(COCl)_2$, benzene, 0° to rt, 1 h; reflux, 2 h 2. Et_3N, benzene, reflux, 12 h	 (50)	237
	1. NaH, benzene, 0°, 10 min 2. $(COCl)_2$, benzene, 55–60°, 1 h 3. Et_3N, toluene, reflux, 2–3 h	 R: Me (56); Et (87)	99
C_{10-11}			
	A: Toluene, sealed tube, 125–140°, 4 d B: Benzene, sealed tube, 135°, 6 d	 R: Me (A) (76); Et (B) (75)	99
C_{10}			
	Ac_2O, reflux, 30 min	 (20–30)	260
	Ac_2O, 140°, 10 min	 (11)	12
	1. $(COCl)_2$, THF, reflux, 2 h 2. Et_3N, toluene, reflux	 (42)	112

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

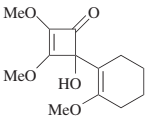
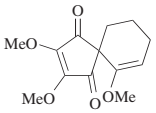
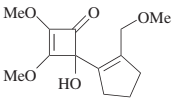
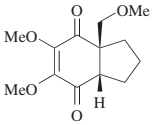
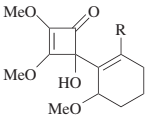
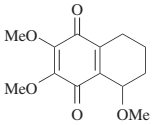
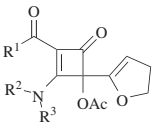
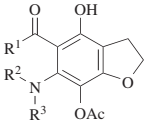
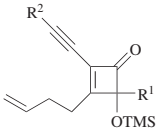
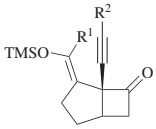
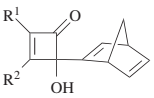
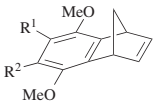
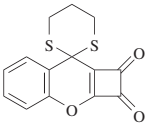
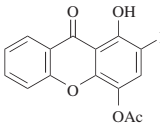
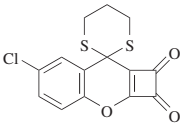
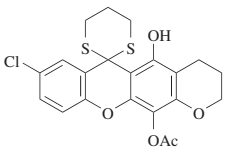
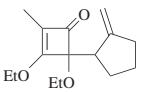
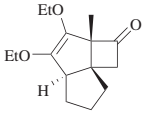
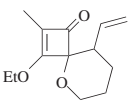
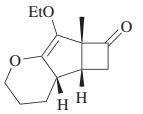
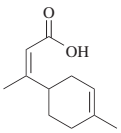
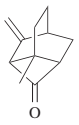
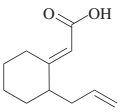
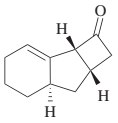
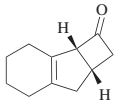
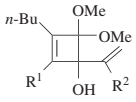
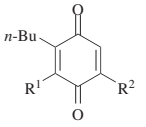
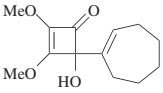
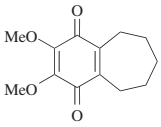
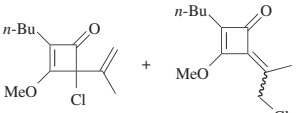
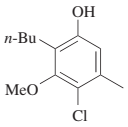
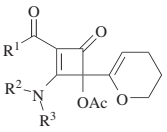
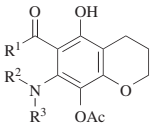
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	1. THF, microwave, 120°, 30 min 2.  , CH_2Cl_2, 0°, 1 h	 (60)	107
	THF, microwave, 120°, 0.5 h	 (64)	107
	THF, microwave, 120°, 0.5 h	 R: PhO (74); PhS (72)	107
C_{10-15}			
	Mesitylene, reflux, 5 min	 R^1 R^2 R^3: Me Bn Bn (92); Ph H *t*-Bu (82)	131
C_{11-15}			
	*p*-Xylene, reflux, 1 h	 R^1 R^2: Me TMS (91); Me $MeOCH_2$ (92); Me *n*-Bu (95); CD_3 *n*-Bu (—)	113
C_{11-23}			
	1. Toluene, 110°, 1 h 2. $Bn(n\text{-}Bu)_3N^+OH^-$, Me_2SO_4, 10 h	 R^1 R^2: MeO MeO (60); EtO EtO (72); *i*-PrO *i*-PrO (73); *n*-BuO *n*-BuO (70); *t*-Bu *i*-PrO (50); Ph *i*-PrO (80); Ph Me (31); Ph *t*-Bu (21); Ph Ph (75)	261
C_{11}			
	1. (*E*)-PhCH=CHLi, THF, –78°, 10 min 2. Ac_2O, –78° to rt 3. THF, reflux, 1 h 4. $HgCl_2$, $CaCO_3$, acetone, H_2O	 (21)	145
	1.  , THF, –78°, 10 min 2. Ac_2O, –78° to rt 3. THF, reflux, 1 h	 (66)	145
	Xylene, reflux, 2 h	 (94)	246
	Xylene, reflux, 2 h	 (94)	246

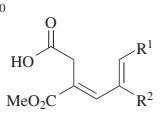
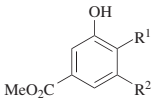
TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	1. $(COCl)_2$, benzene, rt, 3 h; 55°, 1 h 2. Et_3N, toluene, reflux, 3 h	 (59)	192
	1. NaH, THF, toluene, 0°, 5 min 2. $(COCl)_2$, toluene, pyridine, 60° 3. Et_3N, toluene, reflux, 2.5 h	 (33) +  (25)	245
C_{11-16} 	1. HCl, H_2O, $CHCl_3$, 0°, 0.25 h 2. A: $CHCl_3$, rt, 1–3 h; or B: Benzene, reflux, 1.75 h 3. Ag_2O, K_2CO_3, benzene or toluene, rt, 30 min		135

R^1	R^2	Cond	
H	Me	A	(50)
Ph	H	B	(75)

C_{11} 	1. *p*-Xylene, reflux, 2 h 2. CAN, CH_2Cl_2, 30 min	 (72)	106
 **I** + **II** **I/II** = 3.5:1	Xylene, reflux, 20 h	 (82)	100
C_{11-16} 	Solvent, reflux		131

R^1	R^2	R^3	Solvent	Time (min)	
Me	Bn	Bn	xylene	10	(86)
Ph	H	*t*-Bu	mesitylene	5	(97)

C_{11-20} 	1. $ClCO_2Et$, CH_2Cl_2, 0° 2. Et_3N, CH_2Cl_2, <20°, 0.25 h		262

R^1	R^2	
2-furyl	H	(80)
2-thienyl	H	(82)
2-furyl	Me	(87)
Ph	H	(77)
4-FC_6H_4	H	(90)
Ph	Me	(81)
3-MeO-4-Ph-5-MeC_6H_2	H	(67)

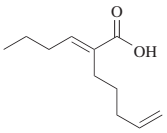
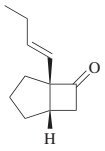
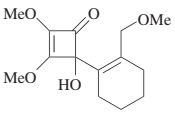
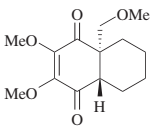
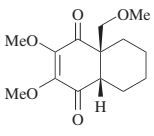
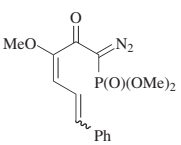
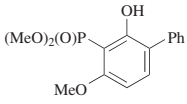
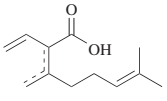
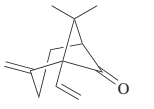
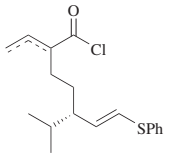
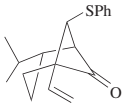
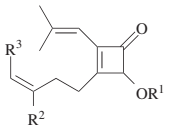
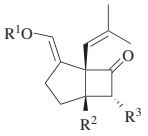
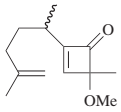
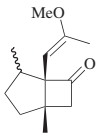
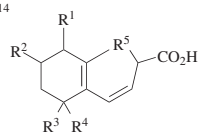
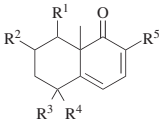
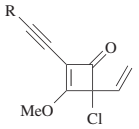
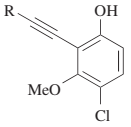
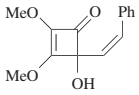
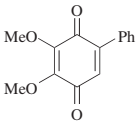
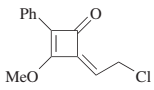
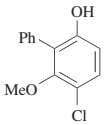
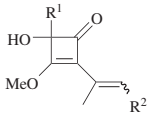
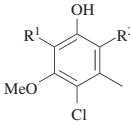
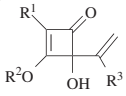
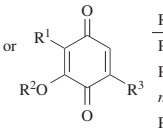
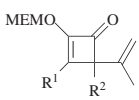
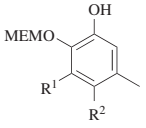
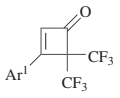
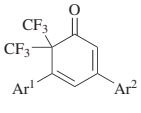
C_{11} 	1. NaH, benzene, 0°, 10 min 2. $(COCl)_2$, benzene, 0–60°, 1 h 3. Et_3N, toluene, reflux, 4 h	 (52)	99
	THF, microwave, 120°, 0.5 h	 +  **I** + **II** (86), **I/II** = 2:1	107
C_{12} 	Benzene, reflux, 30 h	 (63)	98
 mixture of isomeric trienes	1. NaH, benzene 2. $(COCl)_2$, benzene, rt, 1 h 3. Et_3N, benzene, reflux, 5 h	 (29)	252

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}  mixture of isomeric dienes	Et_3N, benzene, reflux	 (57)	263
C_{12-13} 	Xylene, reflux		264
C_{12} 	1. MeCN, 70°, 15 h 2. HOAc	 (26)	265
C_{12-14} 	Ac_2O, pyridine	 (—)	266
	*p*-Xylene, reflux, 3 h		267, 100
C_{12} 	1. *p*-Xylene, reflux, 2 h 2. Ag_2O, K_2CO_3, Et_2O, 2 h	 (71)	106
	*p*-Xylene, reflux, 24 h	 (80)	267, 100
C_{12-13} 	1. $SOCl_2$, pyridine, CH_2Cl_2, 0° [g] 2. *p*-Xylene, reflux, 20–24 h		100
C_{12-19} 	1. Xylene, reflux, 2 h 2. A. AgO, K_2CO_3, Et_2O, rt, 2 h; or B. CAN, CH_2Cl_2, rt, 0.5 h		106
C_{12} 	*m*-Xylene, 140°, 20 h		251
	Ar^2—≡, neat, 100°, 50–185 h		268

R^1	R^2	R^3	Time (h)	
Me	H	H	1	(90)[f]
TMS	H	H	1.5	(95)
Me	Me	H	1	(94)
Me	H	Me	17	(69)

R^1	R^2	R^3	R^4	R^5
H	H	Me	H	H
Me	H	H	H	H
H	AcO	Me	Me	H
TBSO	H	Me	Me	Me
AcO	H	Me	Me	Me
H	H	Me	Me	Me

R	
n-Bu	(48)
Ph	(45)

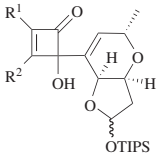
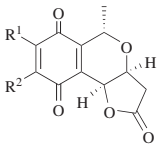
R^1	R^2	
n-Bu	Me	(59)
Ph	H	(65)

R^1	R^2	R^3	Cond	
Ph	Me	EtO	A	(55)
Ph	Me	Me	A	(68)
n-Bu	Me	*n*-Bu	B	(83)
Ph	Me	*n*-Bu	B	(87)
Ph	Et	*n*-Bu	B	(82)
n-Bu	Me	Bn	B	(86)
Ph	Et	Ph	B	(71)
Ph	Et	Bn	B	(76)

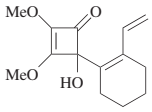
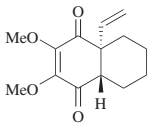
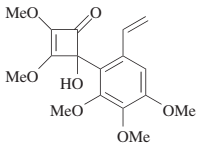
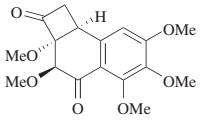
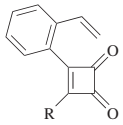
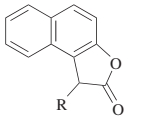
R^1	R^2	
Me	*n*-Bu	(94)
n-Bu	Me	(86)

Ar^1	Ar^2	
Ph	Ph	(73)
Ph	4-ClC_6H_4	(20)
4-ClC_6H_4	Ph	(38)

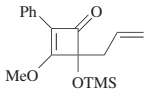
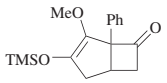
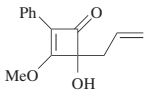
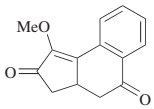
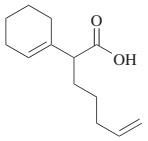
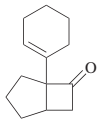
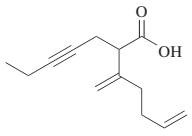
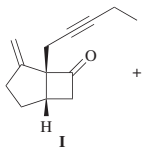
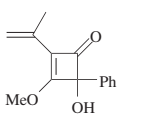
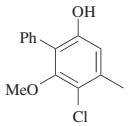
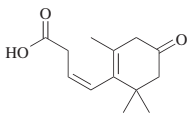
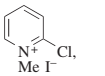
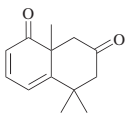
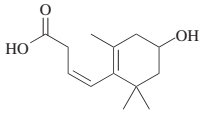
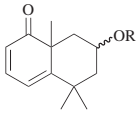
TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12-18} 	1. Solvent, reflux 2. HCl 3. PCC		186

R^1	R^2	Solvent	Time (h)	
MeO	MeO	toluene	1	(38)
i-PrO	*i*-PrO	toluene	1	(61)
Ph	MeO	toluene	1	(50)
Ph	*i*-PrO	toluene	1	(72)
i-PrO	Ph	*p*-xylene	4	(68)

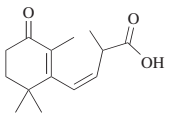
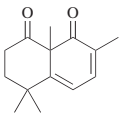
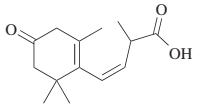
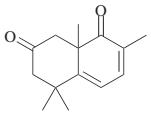
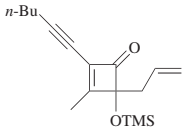
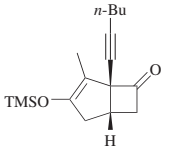
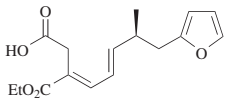
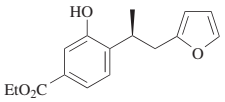
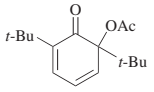
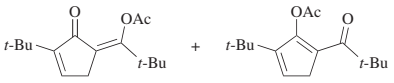
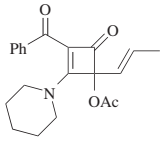
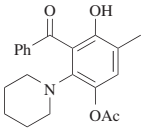
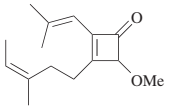
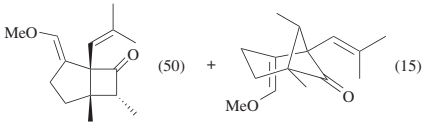
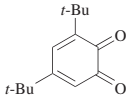
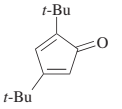
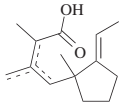
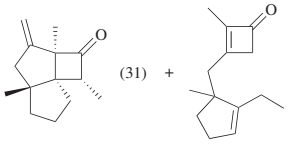
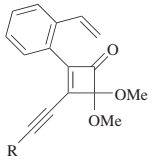
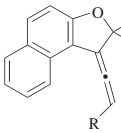
C_{12} 	THF, microwave, 120°, 0.5 h	 (50) dr 9:1	107
	THF, microwave, 120°, 1 h	 (73)	107
C_{13-24} 	*p*-Xylene, reflux		109

R	
Me	(60)
Ph	(76)
2-PhC_6H_4	(69)

C_{13} 	Toluene, reflux, 5 h	 (89)	115, 235
	Toluene, reflux, 1.5 h	 (42)	115, 235
	1. NaH, benzene, 0°, 10 min 2. $(COCl)_2$, benzene, 0–60°, 1 h 3. Et_3N, toluene, reflux, 3 h	 (68)	99
	1. NaH, benzene, 0°, 10 min 2. $(COCl)_2$, benzene, 0–60°, 1 h 3. Et_3N, toluene, reflux, 3 h	 + unidentified product **II** **I** + **II** (45), **I**/**II** = 5:1	249
	1. $SOCl_2$, pyridine, CH_2Cl_2, 0° [g] 2. Xylene, reflux, 24 h	 (65)	100
	 Me I^- Et_3N, CH_2Cl_2, reflux, 4 h	 (60)	105
	A: Ac_2O, DMAP, pyridine, 0° to rt, 3 h; or B: Et_3N, MsCl, pyridine, 0° to rt, 3 h		105

R	Cond	
Ac	A	(68)
Ms	B	(50)

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			
	Ac_2O, pyridine	 (—)	266
	Ac_2O, pyridine	 (—)	266
	Toluene, reflux, 1.5 h	 (98)	113
	1. $ClCO_2Et$, Et_3N, THF, <20° to rt, 20 min 2. NaOH, EtOH, rt, 10 min	 (90)	269
	*h*ν, TFE, rt, 2 h	 **I** **I + II** (41) **II**	71
	Mesitylene, reflux, 1.5 h	 (87)	131
	*m*-Xylene, reflux, 4 h	 (50) + (15)	264
	*h*ν, MeCN, rt, 6 h	 (quant)	270
 mixture of alkene isomers	1. $(COCl)_2$, benzene, 7° to rt, 2 h; 55°, 1 h 2. Et_3N, toluene, reflux, 3 h	 (31) + (6)	192
C_{14-22}			
	Toluene, reflux, 8 h		108

R	
TMS	(83)
Me	(25)
n-Bu	(38)
Ph	(81)
Bn	(45)
$Ph(CH_2)_2$	(61)

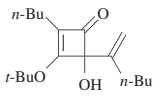
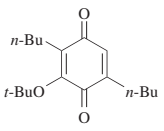
C_{14}			
	1. Xylene, reflux, 0.25 h 2. Ag_2O, K_2CO_3, benzene, rt, 2 h	 (96)	134

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

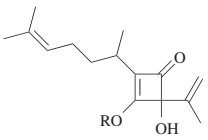
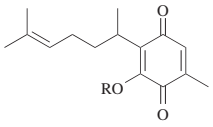
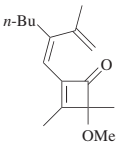
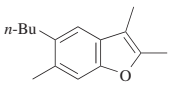
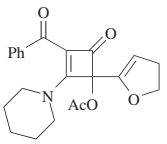
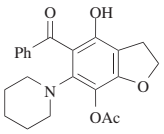
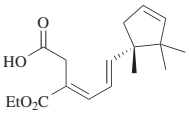
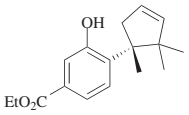
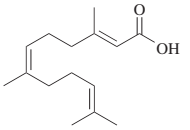
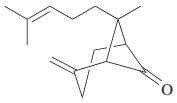
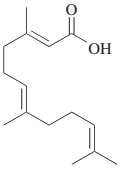
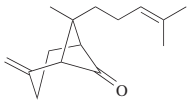
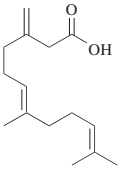
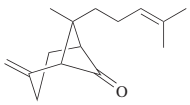
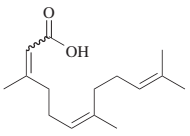
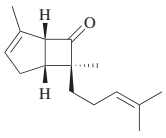
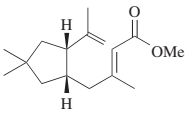
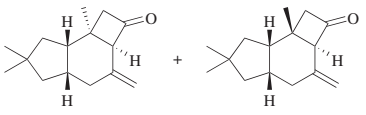
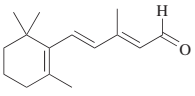
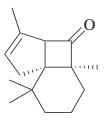
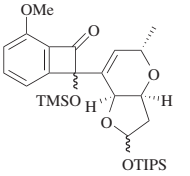
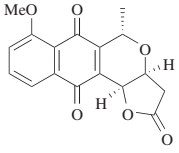
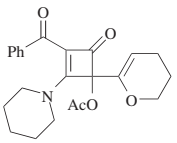
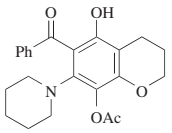
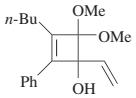
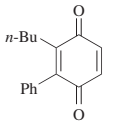
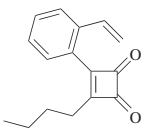
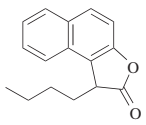
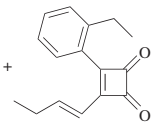
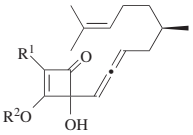
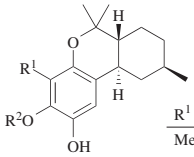
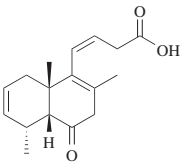
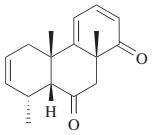
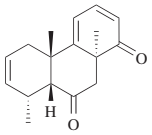
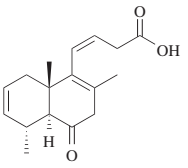
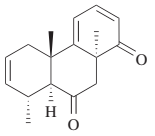
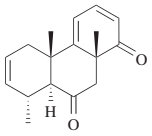
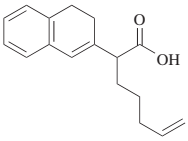
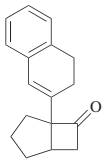
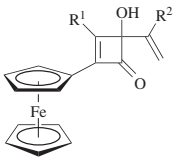
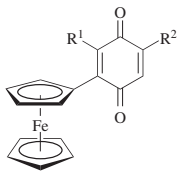
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	1. Benzene, reflux, 2 h 2. A: CAN, CH_2Cl_2, rt, 0.5 h; or B: Ag_2O, K_2CO_3, benzene, rt, 1.5 h	 R Cond Me A (74) *t*-Bu B (55)	106, 231, 134
	1. *p*-Xylene, reflux, 0.75 h 2. TFA, rt, 20 min	 (55)	129
	Mesitylene, reflux, 10 min	 (94)	131
	TFAA, Et_3N, THF, rt, 2 h	 (91)	204
	1. NaH, benzene, rt, 0.25 h 2. $(COCl)_2$, benzene, rt, 1.5 h; 40°, 0.5 h 3. Et_3N, toluene, reflux, 1 h	 (39)	256, 255, 271
	1. NaH, benzene, rt, 0.25 h 2. $(COCl)_2$, benzene, rt, 1.5 h; 40°, 0.5 h 3. Et_3N, toluene, reflux, 1 h	 (38)	256, 255
	1. $(COCl)_2$, benzene, rt, 2 h 2. $(i\text{-Pr})_2NEt$, toluene, reflux, 6 h	 (43)	271
	Ac_2O, NaOAc, reflux	 (40)	272
	1. NaOH, MeOH/H_2O (5:1), 65°, 3 h 2. $(COCl)_2$, toluene, rt, 3 h 3. $(i\text{-Pr})_2NEt$, toluene, reflux	 **I** + **II** (57), **I**/**II** = 3:1	273
	"distillation in vacuo"	 (50)	274
C_{16}			
	1. *p*-Xylene, reflux 2. PCC	 (66)	186

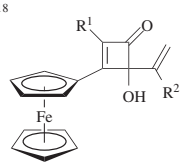
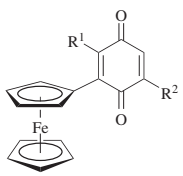
TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16} 	Mesitylene, reflux, 10 min	 (100)	131
	1. $CHCl_3$, HCl, 0°, 0.25 h 2. Benzene, reflux, 1.75 h 3. Ag_2O, K_2CO_3, benzene, rt, 0.5 h	 (75)	135
	*p*-Xylene, reflux	 (47) +  (26)	109
C_{16-22} 	Benzene		196

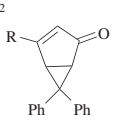
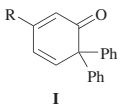
R^1	R^2	Temp (°)	Time (h)	
MeO	Me	50	36	(86)
Ph	*i*-Pr	40	7	(79)

C_{17} 	1. $(COCl)_2$ 2. Et_3N, CH_2Cl_2	 +  **I** **II** **I** + **II** (81), **I/II** = 2:1	275
	1. $(COCl)_2$ 2. Et_3N, CH_2Cl_2	 +  **I** **II** **I** + **II** (75), **I/II** = 2:1	275
	1. NaH, benzene, 0°, 10 min 2. $(COCl)_2$, benzene, 0°; 55–60°, 1 h 3. Et_3N, toluene, reflux, 2 h	 (81)	99
C_{17-32} 	1. Dioxane, reflux, 5 h 2. PbO_2, CH_2Cl_2		101

R^1	R^2	
i-PrO	Me	(85)
Me	Me	(71)
i-PrO	Ph	(61)
1-ferrocenyl	Me	(56)
1-ferrocenyl	Ph	(75)

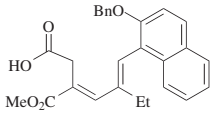
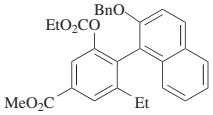
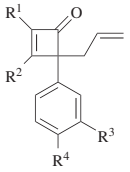
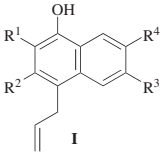
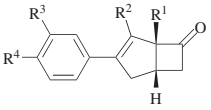
C_{17-18} 	1. Dioxane, reflux, 5 h 2. PbO_2, CH_2Cl_2		101

R^1	R^2	
i-PrO	Me	(77)
Me	Me	(70)

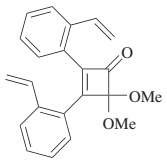
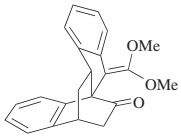
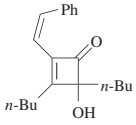
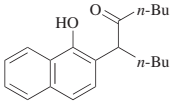
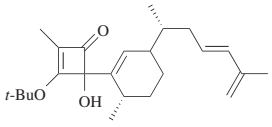
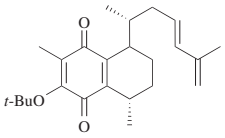
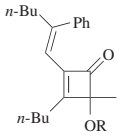
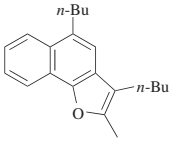
C_{18-22} 	A: *h*ν, benzene, rt, 25–40 min B: *h*ν, crystalline state, 15–20°, 1.5 h	 + SM (—) **I**	276

R	Cond	**I**
H	A	(25)
MeO	A	(4)
Ph_2CHO	B	(27)
Me	A	(12)
t-Bu	A	(9)

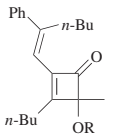
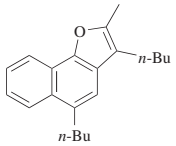
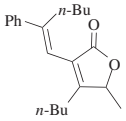
TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{19} 	$ClCO_2Et$, Et_3N, THF, <20°, 0.5 h	 (78)	262
$C_{19–23}$ 	Toluene, reflux, 3 h	 **I** +  **II**	111

R^1	R^2	R^3	R^4	**I + II**	**I/II**
n-Bu—≡	*i*-PrO	H	H	(88)	2:1
n-Bu—≡	*i*-PrO	H	MeO	(90)	1.5:1
n-Bu—≡	*i*-PrO	MeO	MeO	(84)	3:1
Ph	MeO	H	H	(83)	1:2.6
Ph	*i*-PrO	H	H	(92)	1:2.1
4-$MeOC_6H_4$	*i*-PrO	H	MeO	(92)	1:2
Ph	Me	H	H	(96)	2:1
Ph	*i*-Bu	H	H	(97)	1.3:1

C_{20} 	*p*-Xylene, 138°, 9 h	 (72)	109
	Toluene, reflux, 16 min	 (67)	129
	1. THF, microwave, 110°, 30 min 2. Air, rt, 24 h	 (80)	104
C_{21} 	1. *p*-Xylene, reflux, 0.75 h 2. TFA, 20 min		129

R	
H	(86)
Me	(75)

	1. *p*-Xylene, reflux, 1.5 h 2. TFA, 20 min	 **I** +  **II**	129

R	**I**	**II**	**I/II**
H	(—)	(46)	1:2
Me	(45)	(0)	—

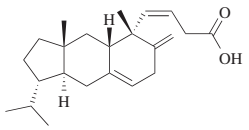
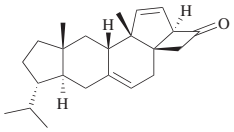
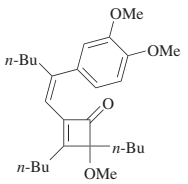
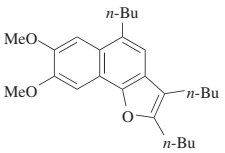
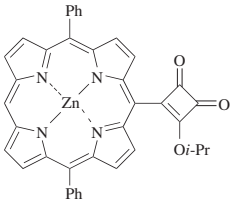
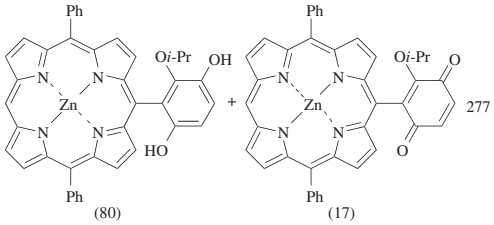
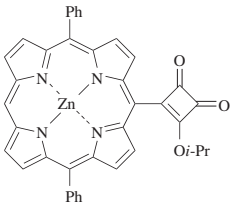
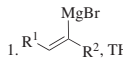
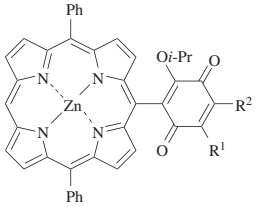
C_{23} 	1. $(COCl)_2$, benzene, rt, 2 h 2. Et_3N, benzene, rt, 5 min	 (80)	191
C_{24} 	1. *p*-Xylene, reflux, 0.75 h 2. TFA, 20 min	 (74)	129

TABLE 3. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKENYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{36}			
	1. CH_2=CHMgBr, THF, –78° to rt 2. DDQ, THF, rt, 5 min	 (80) + (17)	277
	1.  R^2, THF, –78° to rt 2. DDQ, THF, rt, 5 min		277

R^1	R^2	
H	Me	(86)
Me	Me	(87)

[a] The product was isolated as the carboxylic acid after hydrolysis.

[b] Upon separation of the diastereomers, the isolated yield was 61% for product **I** and 5% for product **II**.

[c] The C–TMS group was replaced by H in this product.

[d] Compounds **I** and **II** were separated.

[e] The initial, isolated, but not fully characterized, product was a 1:1 isomer mixture of the monoacetoxy compounds. The indicated yield is for the two-step sequence.

[f] This product was a 4:1 mixture of (*E*)/(*Z*) isomers.

[g] This step produced a mixture of regio- and geometrically isomeric allylic chlorides, which was used without purification in the next step.

TABLE 4. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKYNES

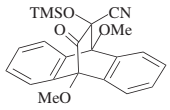
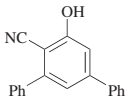
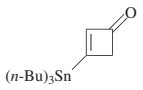
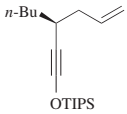
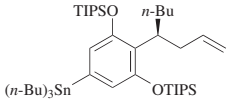
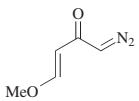
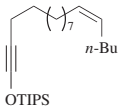
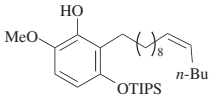
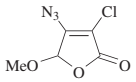
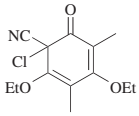
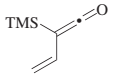
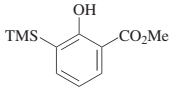
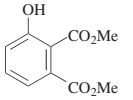
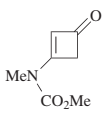
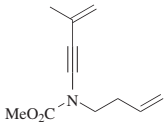
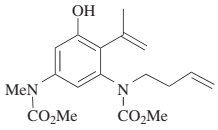
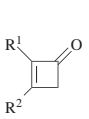
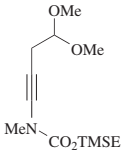
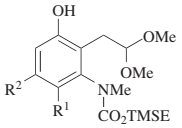
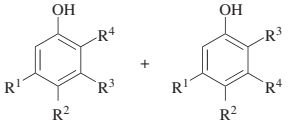
Ketene or Ketene Source	Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 		1,2-$Cl_2C_6H_4$, sealed tube, 220°, 48 h	 (27)	177
C_4 		1. Benzene, 95°, 2 h 2. Et_3N, TIPSOTf, DMF, 55°, 1.5 h	 (70)	70
		*hv*, $ClCH_2CH_2Cl$, rt, 9.5 h	 (54)	116
		Toluene, 103°, 1.75 h	 (56)	155
		Toluene, 95°, 63 h	 (45)	24
		1. $CHCl_3$, 40°, 25 h 2. TFA, $CHCl_3$, 55°, 23 h	 (60)	24
		Toluene, 110°, 10 h	 (53)[a]	18

TABLE 4. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKYNES (*Continued*)

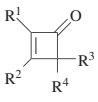
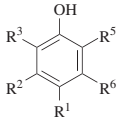
Ketene or Ketene Source	Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-10} 		Toluene, 80°, 1.5–2 h; 110°, 1.5–3 h		19

R^1	R^2	
H	EtO	(53–61)
H	$(n\text{-Bu})_3$Sn	(87)
H	*n*-Bu	(84)
H	Ph	(79)
Me	Me	(63)

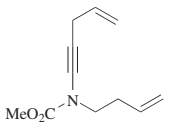
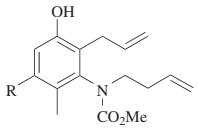
C_{4-11} 		$Ni(COD)_2$, solvent, 0°, 0.5–3 h		66

I **II**

R^1	R^2	R^3	R^4	Solvent	**I + II**	**I/II**
$(n\text{-Bu})_3$Sn	H	Et	Et	hexanes	(43)	—
n-Bu	H	Et	Et	hexanes	(76)	—
n-Bu	H	Me	$THPO(CH_2)_2$	hexanes	(47)	65:35
n-Bu	H	Me	$TBSO(CH_2)_2$	hexanes	(59)	75:25
n-Bu	H	Me	$TBSO(CH_2)_3$	hexanes	(67)	50:50
Ph	H	Me	TMS	Et_2O	(58)	45:55
Ph	H	Et	Et	Et_2O	(75)	—
Ph	H	Me	*i*-Pr	Et_2O	(81)	50:50
Ph	H	Et	$Cl(CH_2)_2$	Et_2O	(64)	72:28
Ph	H	Et	allyl	Et_2O	(60)	50:50
Ph	H	Et	$Cl(CH_2)_3$	Et_2O	(57)	58:42
Ph	Me	Et	Et	Et_2O	(60)	—
Ph	Me	Me	$TBSO(CH_2)_2$	Et_2O	(63)	75:25

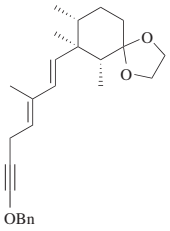
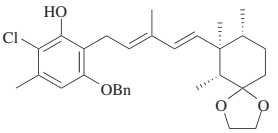
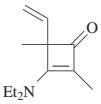
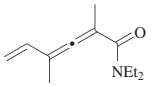
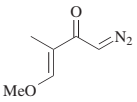
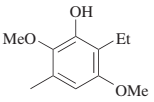
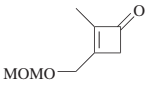
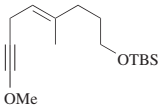
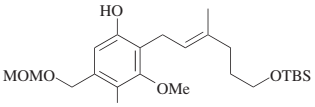
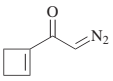
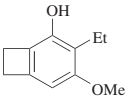
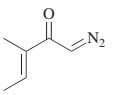
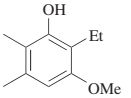
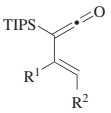
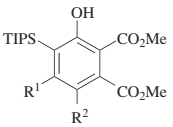
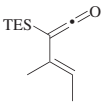
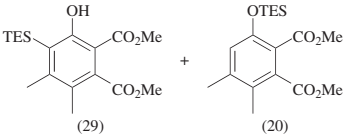
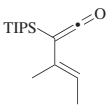
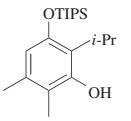
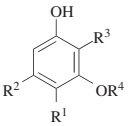
C_{5-8} 		2,4,6-$(t\text{-Bu})_3C_6H_2OH$ (*x* eq), solvent, sealed tube		278

R^1	R^2	R^3	R^4	R^5	R^6	*x*	Solvent	Temp (°)	Time (h)		
H	Me	H	H	H	MeO	1.1	benzene[a]	80	26	(71)	278
H	Me	H	H	Me	MeO	0	benzene	80	21	(92)	278
H	Me	H	H	*n*-C_6H_{13}	Me_2N	0	benzene	150	2	(74)	278
H	Me	H	H	farnesyl	MeO	0	benzene	80	4	(65–68)	278
Me	EtO	H	H	*n*-C_6H_{13}	MeO	0	benzene	125	96	(71)	278
H	Me	Cl	Cl	Me	MeO	1.1	toluene[a]	135	2.5	(65)	278
Me	Me	H	H	Me	MeO	0	$CHCl_3$	120	71	(61)	278
Me	Me	H	H	Me	MeS	0	$CHCl_3$	135	73	(86)	278
Me	*n*-Pr	H	H	*n*-C_6H_{13}	MeO	0	benzene	80	22	(69–82)	278
Me	Et	Me	H	*n*-C_6H_{13}	MeO	0	benzene	160	48	(33)	278
Me	Et	Me	H	*n*-C_6H_{13}	Me_2N	0	benzene	160	2	(83)	278
H	*n*-Bu	Cl	Cl	*n*-C_7H_{15}	TIPS	1.1	xylene[a]	135	1.5	(77)	197
H	*n*-Bu	H	H	Me	MeS	0	$CHCl_3$	80	24	(82)	278

C_{5-6} 		$CHCl_3$, 60°, 16.5 h		18

R		
MeO	(62)	
$MOMOCH_2$	(60)	

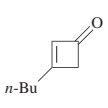
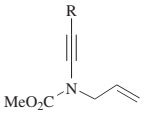
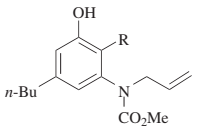
TABLE 4. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKYNES (*Continued*)

Ketene or Ketene Source	Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
		1. *hν*, benzene, rt, 40 h 2. Toluene, reflux, 4 h	 (65)	279
		1. Et_3N, CCl_4, 0° 2. Add alkyne, 3 h	 (35) +  (8)	20
		$ClCH_2CH_2Cl$, rt, 10 h; reflux, 4 h	 (31)	221
C_6				
		Benzene, sealed tube, 120°, 14 h	 (73)	195
		*hν*, $ClCH_2CH_2Cl$, rt, 5 h	 (56)	221
		*hν*, $ClCH_2CH_2Cl$, rt, 6 h; reflux, 3.5 h	 (46)	221
C_{6-12}				
		Toluene, sealed tube, 150°		91
C_6				
		Toluene, sealed tube, 150°, 16 h		91
		THF, rt, 1 h	 (65)	279
C_{6-8}				
		A: Toluene, sealed tube, 140° B: Benzene, 95°		280

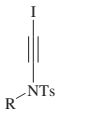
R^1	R^2	R^3	R^4	Cond	Time (h)	
Me	$MOMOCH_2$	Me	TIPS	A	44	(59)
Me	$MOMOCH_2$	Me	TBDPS	A	65	(58)
H	*n*-Bu	*i*-Pr	TIPS	B	18	(96)
H	*n*-Bu	cyclohexyl	TIPS	B	20	(92)
H	*n*-Bu	$PhCH_2CH_2$	TIPS	B	18	(98)

R^1	R^2	Time (h)	
Me	Me	24	(95)
H	$PhCH_2CH_2$	3	(61)

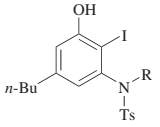
TABLE 4. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKYNES (*Continued*)

Ketene or Ketene Source	Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 		See table.		

R	Cond		
Me	toluene, 80–90°, 1.5–2 h; 110°, 1.5–3 h	(78)	19
$TBSOCH_2$	toluene, 80–90°, 1.5–2 h; 110°, 1.5–3 h	(85)	19
$TBSOCH_2CH_2$	toluene, 80–90°, 1.5–2 h; 110°, 1.5–3 h	(94)	19
allyl	toluene, 80°, 1.5 h; 110°, 1.5 h	(84)	18
CH_2=C(Me)	benzene, 80°, 3 h	(67–69)[a]	18
TMS—≡—CH_2	toluene, 80°, 1.5 h; 110°, 1.5 h	(70)	18

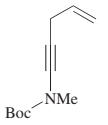


Toluene, 110°, 1.5 h

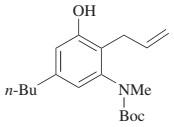


R	[a]
allyl	(41–49)
2-(C_4H_3O)CH_2	(49)
PMB	(59–77)

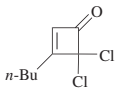
19

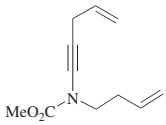


Toluene, 110°, 1.5 h

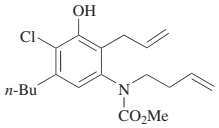


(70–90)[a] 19

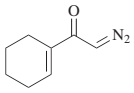


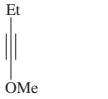


Toluene

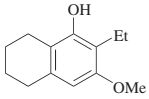


(45)[b] 18

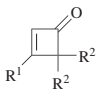


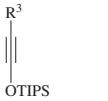


1. *hv*, $ClCH_2CH_2Cl$, rt, 10 h
2. Reflux, 4 h

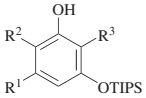


(50) 221

$C_{8–9}$ 

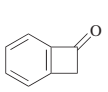


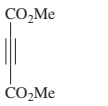
A: Xylene, 135°, 1.5 h
B: Toluene, 80°, 1–1.5 h



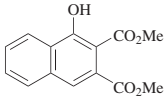
197

R^1	R^2	R^3	Cond	
n-Bu	Cl	cyclohexyl	A	(80)
n-Bu	Cl	*n*-C_7H_{15}	A	(77)
n-C_5H_{11}	H	Ph	B	(76)
n-C_5H_{11}	H	*n*-C_7H_{15}	B	(88)
n-C_5H_{11}	H	$PhCH_2CMe_2$	B	(86)

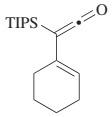
C_8 

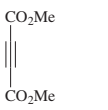


Neat, sealed tube, 160°

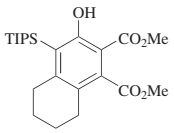


(22) 69

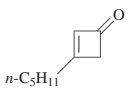


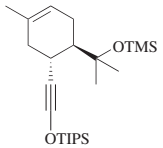


Toluene, sealed tube, 150°, 22 h

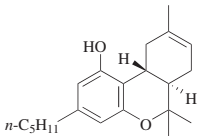


(73) 91

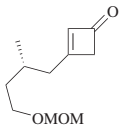
C_9 

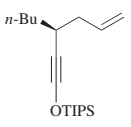


1. Toluene, 80°, 1 h
2. HCl, EtOH, reflux

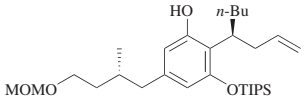


(61) 197



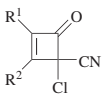


Toluene, 80°, 1.5 h

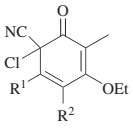


(78)

70, 355

$C_{9–17}$ 

Benzene, rt, 2 h; 40°, 3–11 h



R^1	R^2	
Et	Et	(85)
Ph	Me	(33)
Ph	Ph	(69)

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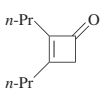
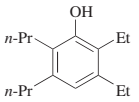
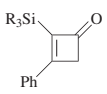
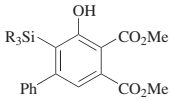
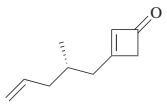
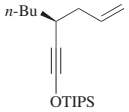
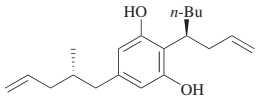
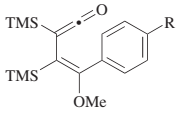
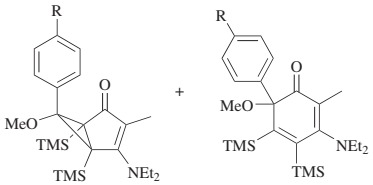
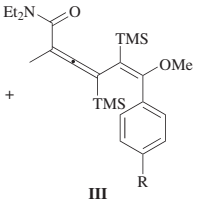
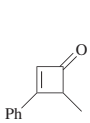
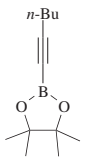
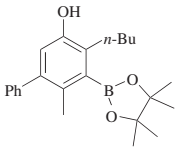
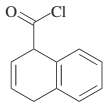
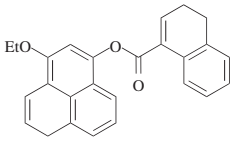
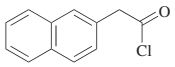
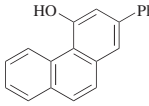
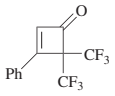
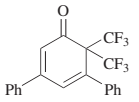
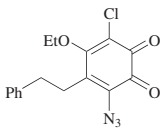
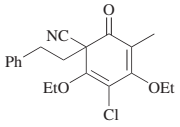
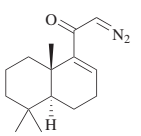
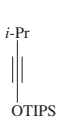
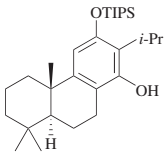
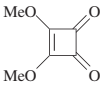
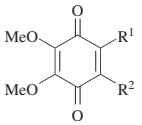
TABLE 4. INTERMOLECULAR CYCLOADDITIONS OF VINYLKETENES WITH ALKYNES (*Continued*)

Ketene or Ketene Source	Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 		$[RhCl(CO)_2]_2$, toluene, 130° (bath temp), 12 h	 (51)	94
		Toluene, 110°, 42–55 h	 R: Me (63); Et (55)	91
		1. Toluene, 100°, 2 h 2. TBAF, THF, rt, 15 min	 (69)	70
C_{10-11} 		Hexane, rt, 3 h	 **I** + **II**  **III** **I** + **II** + **III** (41–51) R: H 3:1:1; Me 3:1:1; CF_3 3:1:1	281, 282
C_{11} 		$Ni(COD)_2$, Et_2O, 0° to rt, 16 h	 (68)	117
		Et_3N, Et_2O, reflux, 50 min	 (29)	52
C_{12} 		1. Neat, 185°, 36 h 3. KOH, H_2O, MeOH, rt	 (54)	283
		Neat, sealed tube, 100°, 185 h	 (73)	268
C_{14} 		Benzene, reflux, 2 h	 (49)	77
C_{15} 		*hν*, $ClCH_2CH_2Cl$, rt, 5 h	 (64–67)	194

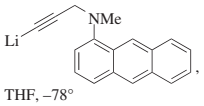
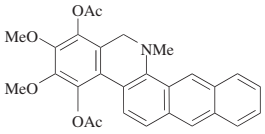
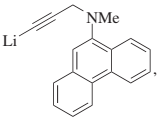
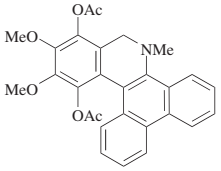
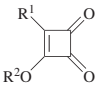
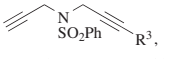
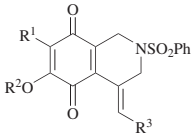
[a] The crude product was heated for 2.5–3 h with 5 M KOH in MeOH prior to workup and chromatographic isolation.

[b] The reaction was performed in the presence of 2.0 equiv of BHT.

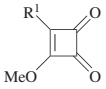
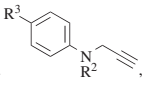
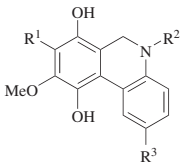
TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	1. R^1—≡—Li, THF, –78°, 0.5 h 2. Reagent 3. *p*-Xylene, reflux, 40 min		26

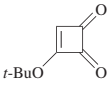
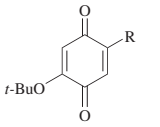
R^1	R^2	Reagent	
$TMSOCH_2$	TMS	TMSCl	(54)
THPOCH(Me)	H	NH_4Cl	(46)
≡—CH_2CH_2	TMS	TMSCl	(42)

	1.  THF, –78° 2. Chlorobenzene, reflux, 140 min 3. Ac_2O, pyridine, rt, 1 h	 (34)	190
	1.  THF, –78° 2. Chlorobenzene, reflux, 140 min 3. Ac_2O, pyridine, rt, 1 h	 (41)	190
$C_{4–10}$ 	1.  *n*-BuLi, THF, –78°, 0.5 h 2. Toluene, reflux, 1 h		121

R^1	R^2	R^3	
MeO	Me	TMS	(40)
MeO	Me	$Me_2C(OH)$	(50)
MeO	Me	Ph	(55)
n-Bu	*i*-Pr	TMS	(60)
n-Bu	*i*-Pr	Ph	(57)
Ph	*i*-Pr	TMS	(44)

	1.  *n*-BuLi, THF, –78°, 0.5 h 2. Toluene, reflux, 80 min		121

R^1	R^2	R^3	
MeO	*n*-Bu	MeO	(42)
Ph	allyl	H	(48)

C_4 	1. R—≡—Li, THF, hexane, –78°, 0.5 h 2. MeCN, reflux, 0.5 h		229

R	
Me	(63)
n-Bu	(56)

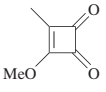
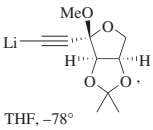
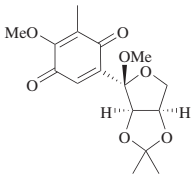
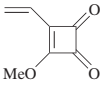
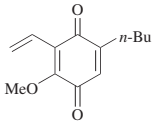
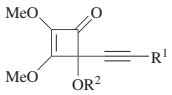
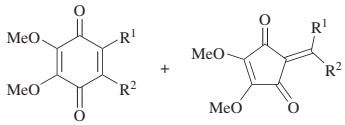
C_5 	1. Li—≡—  THF, –78° 2. *p*-Xylene, reflux	 (43)	231
C_6 	1. *n*-Bu—≡—Li, THF, hexane 2. MeCN, reflux, 1.5 h	 (49)	284, 285

TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{6–13}$ 	A: *p*-Xylene, reflux, 0.25–2 h B: 1. *p*-Xylene, reflux, 0.5 h 2. $Na_2S_2O_4$, H_2O 3. Ag_2O, K_2CO_3, benzene	 **I** + **II**	

R^1	R^2	Cond	**I**	**II**	Refs.
H	H	A	(48)	(—)	26
H	TMS	A	(75)	(—)	26
TMS	TMS	A	(55)	(—)	26
EtO	H	B	(25)	(50)	26
EtO	TMS	B	(23)	(55)	26
Me	H	A	(55–73)	(—)	286
$TMSOCH_2$	TMS	A	(80)	(—)	46
$THPOCH_2$	H	A	(47)	(—)	26
$THPOCH_2$	TMS	A	(41)	(—)	26
EtO_2C	H	A	(0)	(66)	26
EtO_2C	TMS	A	(0)	(33)	26, 46
TMSOCH(Me)	H	A	(64)	(—)	26
THPOCH(Me)	TMS	A	(36)	(—)	26
(*Z*)-MeOCH=CH	H	A	(0)	(49)	26
CH_2=C(Me)	TMS	A	(16)	(69)	26
n-Bu	H	A	(78)	(—)	26
n-Bu	TMS	A	(75)	(—)	26
Ph	H	A	(21)	(46)	26
Ph	TMS	A	(13)	(52)	26, 46
Bn	H	A	(71)	(—)	26
Bn	TMS	A	(74)	(—)	26

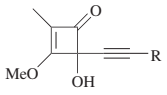
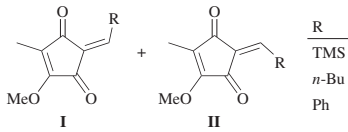
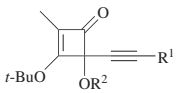
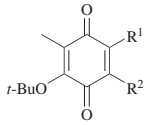
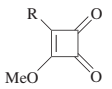
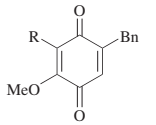
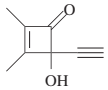
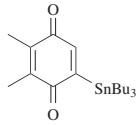
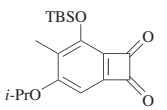
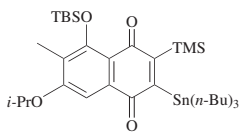
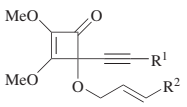
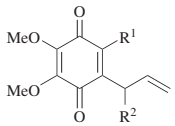
$C_{7–13}$ 	$Pd(OTf)_2$, THF, 40°, 5 h or 60°, 1 h	 **I** + **II**	R	**I + II**	**I/II**	356
			TMS	(49)	11:1	
			n-Bu	(45)	12:1	
			Ph	(40)	15:1	
C_7 	Solvent, reflux, 2 h		R^1	R^2	Solvent		134
			H	H	MeCN	(79)	
			TMS	H	MeCN	(69)	
			H	TMS	benzene	(68)	
$C_{8–12}$ 	1. Bn—≡—Li, THF, –78°, 0.5 h 2. *p*-Xylene, reflux, 40 min		R			26
			n-Bu	(84)		
			Ph—≡—	(50)		
C_8 	Bu_3SnOMe, $ClCH_2CH_2Cl$, reflux, 10 min	 (78)				125
C_9 	1. TMS—≡—Li, THF, –78° 2. HCl, THF 3. $(n\text{-Bu})_3SnOMe$, $ClCH_2CH_2Cl$, reflux, 0.25 h	 (75–80)				126
$C_{9–17}$ 	*p*-Xylene, reflux, 17 min		R^1	R^2			26
			H	H	(60)		
			Bn	H	(76)		
			Bn	Me	(54)		

TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS (*Continued*)

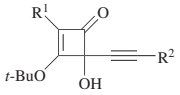
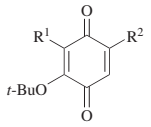
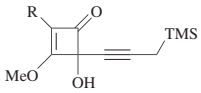
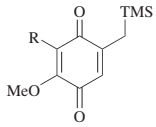
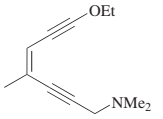
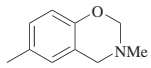
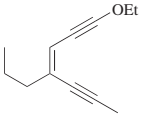
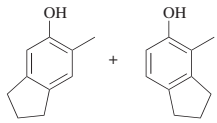
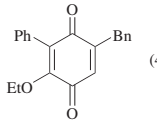
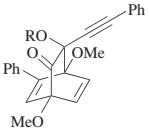
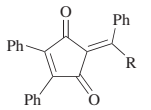
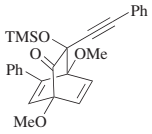
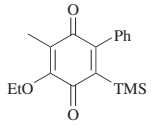
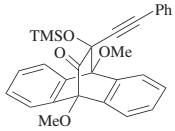
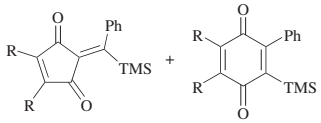
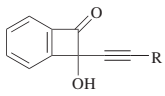
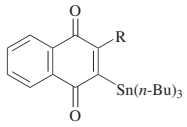
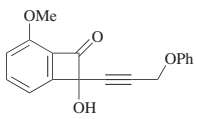
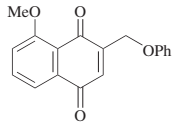
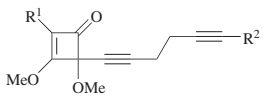
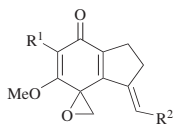
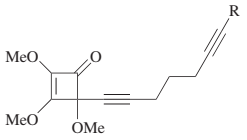
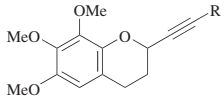
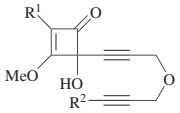
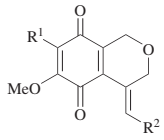
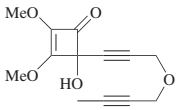
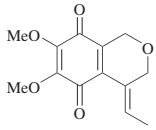
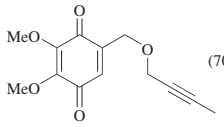
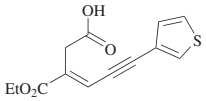
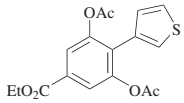
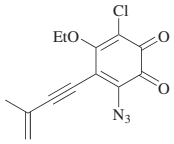
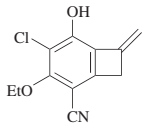
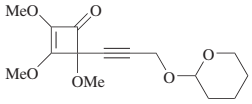
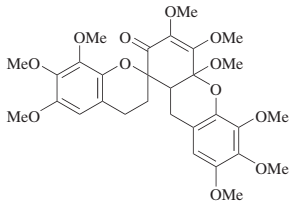
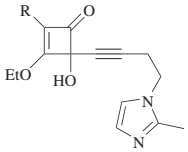
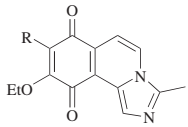
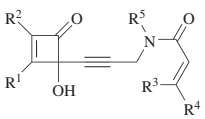
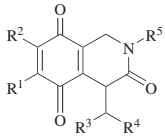
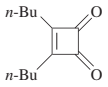
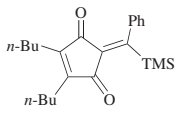
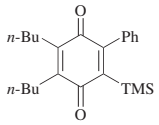
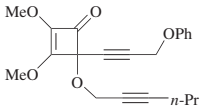
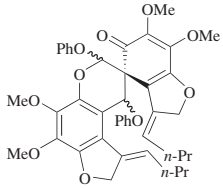
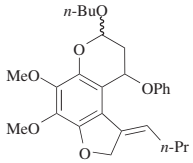
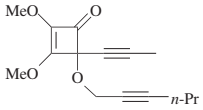
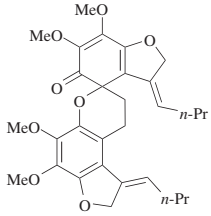
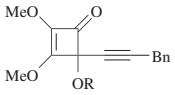
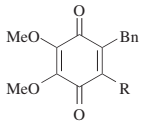
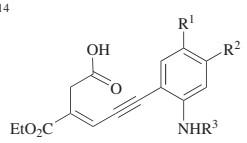
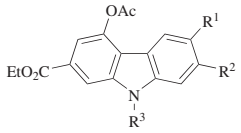
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{10–17}$ 	Xylene, reflux		134
		R^1 R^2 Time *t*-BuO *n*-Bu 1.5 h (80) *t*-BuO Bn 3 h (77) *n*-Bu *n*-Bu 5 min (89) *n*-Bu Bn 5 min (82)	
$C_{10–14}$ 	*p*-Xylene, reflux		236
		R (69–75) MeO (69–75) *n*-Bu (69–75)	
C_{10} 	Chlorobenzene, reflux, 3 h	 (37)	74
	Chlorobenzene, reflux, 3 h	 **I** + **II** (4), **I**/**II** = 8:1	74
	1. Bn—≡—Li, THF, –78° 2. *p*-Xylene, reflux	 (46)	231
	Ph—≡—Ph, *p*-xylene, reflux, 8 h		124
		R H (34) TMS (55)	
	EtO—≡—, *p*-xylene, reflux, 8 h	 (45)	124
	R—≡—R, *p*-xylene, sealed tube, 220°, 48 h		177
		R **I** **II** *n*-Bu (54) (12) Ph (70) (—)	
$C_{10–14}$ 	$(n\text{-Bu})_3SnOMe$, $ClCH_2CH_2Cl$, reflux, 2–4 h		125
		R TMS (76) Me (79) *n*-Bu (59)	
C_{11} 	*p*-Xylene, reflux, 1 h	 (84)	287
$C_{11–23}$ 	Toluene, reflux		119
		R^1 R^2 MeO H (54) MeO $BnOC(Me)_2$ (62) MeO *n*-Bu (87) MeO CH_2=$CH(CH_2)_3$ (70) MeO Ph (91) Ph Ph (71)	

TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11-17} 	Toluene, reflux	 R: H (87); Ph (76)	119
C_{11-20} 	Toluene, reflux, 0.75–2 h[a]	 R^1 / R^2: MeO / Me (61); MeO / *n*-Bu (67); MeO / Ph (75); *n*-Bu / Ph (52)[b]	120
C_{11} 	Toluene, reflux, 2 h	 (9) +  (70)	120
	NaOAc, Ac_2O, reflux, 2 h	 (83)	288
	Benzene, reflux, 1 h	 (33)	289, 123
C_{12} 	Toluene, reflux, 2 h	 (49)	120
C_{12-13} 	1. Solvent, temp 1 2. Pd/C, 80–90°, 4–15 h	 R: EtO, Solvent: PhOMe, Temp 1: 120° (18); Me, MeCN, reflux (26)	122
C_{12-17} 	Xylenes, reflux, 20 min to 1 h		290

R^1	R^2	R^3	R^4	R^5	
MeO	MeO	Me	Me	Bn	(54)
i-PrO	*i*-PrO	Me	Me	Boc	(56)
i-PrO	Me	Me	Me	Bn	(45)
i-PrO	*i*-PrO	H	Ph	*t*-Bu	(62)
i-PrO	*i*-PrO	H	Ph	Ph_2CH	(67)
i-PrO	*i*-PrO	H	4-$MeOC_6H_4$	Bn	(55)
EtO	EtO	H	4-MeC_6H_4	Bn	(33)
i-PrO	Me	H	Ph	Bn	(51)

TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}			
	1. Ph—≡—Li, THF, –78°, 0.5 h 2. TMSCl, –78° to rt, 10 min 3. Et_2O, reflux, 1 h	 (35) +  (12)	177
C_{13}			
	Toluene, reflux, 2.5 h	 (38)	291
	n-BuOCH=CH_2, THF, reflux, 3 h	 (98)	291
	*p*-Xylene, reflux, 20 min	 (37)	291
$C_{13–16}$			
	*p*-Xylene, reflux, 1 h	 R: H (71); allyl (76)	287
$C_{13–14}$			
	NaOAc, Ac_2O, hydroquinone, reflux, 1–3 h		55

R^1	R^2	R^3	
F	H	Ts	(91)
O_2N	H	Ts	(77)
H	MeO	Ts	(82)
H	H	Ts	(89)
H	Me	Ac	(35)
H	Me	Ms	(65)
H	Me	Ts	(91)
Me	H	Ts	(90)
EtO_2C	H	Ts	(87)

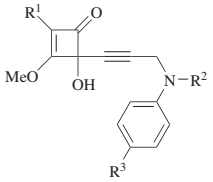
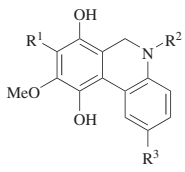
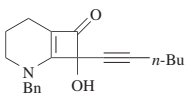
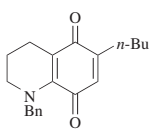
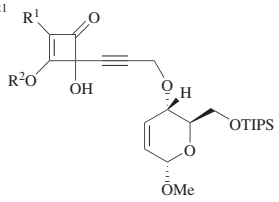
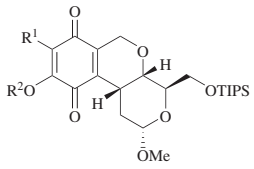
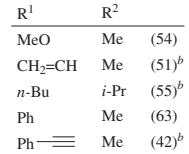
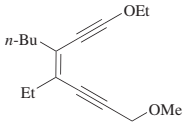
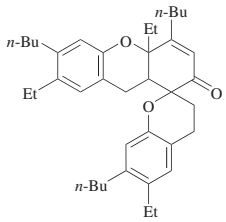
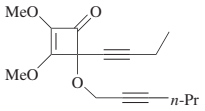
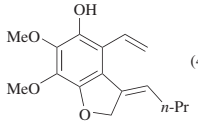
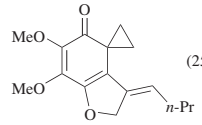
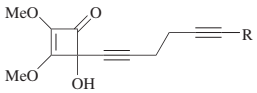
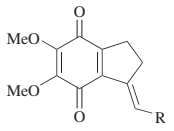
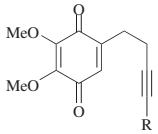
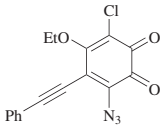
$C_{13–19}$					
	Toluene, reflux, 1.5–3 h		R^1	R^2	R^3		
			MeO	*n*-Bu	H	(65)	
			MeO	*n*-Bu	MeO	(42)	
			MeO	*t*-Boc	H	(70)	121
			MeO	allyl	H	(63)	
			MeO	4-pentenyl	H	(70)	
			Ph	allyl	H	(48)[b]	
C_{13}							
	THF, air, 75°, 3.5 h	 (87)					292

TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS (*Continued*)

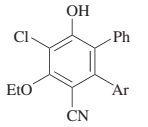
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13-21} 	Toluene, reflux, 0.75–1.5 h	 	120
C_{13} 	Chlorobenzene, reflux, 3 h	 (34)	74
C_{14} 	*p*-Xylene, reflux, 0.5 h	 (49) +  (25)	291
	Substrate (*x* M), toluene, reflux, 2 h	 + 	119

I **II**

R	*x*	I	II	I + II	I/II
n-Bu	0.00386	(—)	(—)	(80)	23:1
n-Bu	1.20	(8)	(62)	(70)	—
CH_2=$CH(CH_2)_2$	0.00243	(57)	(—)	(57)	—
CH_2=$CH(CH_2)_2$	0.1	(—)	(—)	(77)	1:1

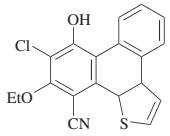
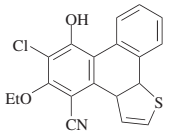


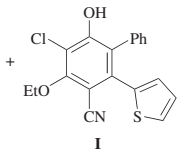
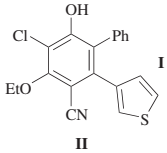
Solvent, reflux, 3.5 h



Solvent	Ar		
benzene	C_6H_5	(84)	
chlorobenzene	ClC_6H_4 [c]	(31–56)[d]	123
toluene	MeC_6H_4 [c]	(31–56)[d]	
p-xylene	$2,5\text{-}Me_2C_6H_3$	(56)	
m-xylene	$Me_2C_6H_3$ [c]	(31–56)[d]	

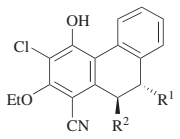
Thiophene, reflux, 3 h

 (22) +  (12) 123

 +  **I + II** (12)

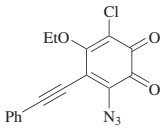
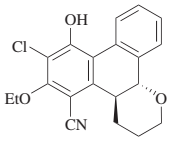
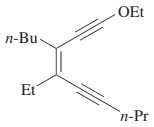
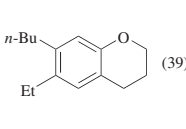
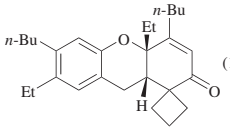
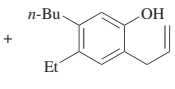
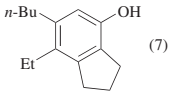
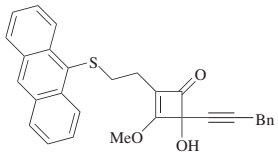
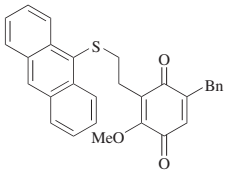
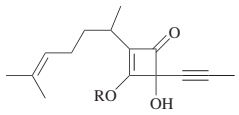
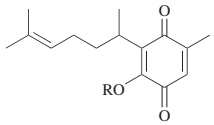
I **II**

R^1–⟨⟩–R^2, CCl_4, reflux, 4 h

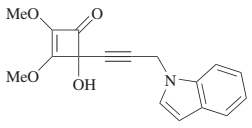
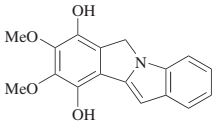
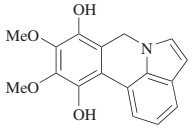
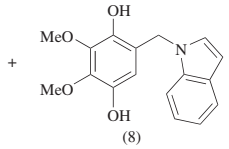
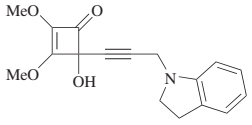
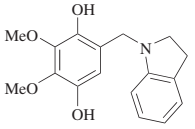
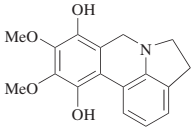
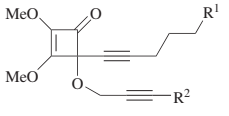
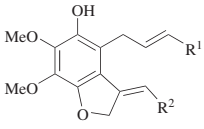


R^1	R^2		
Ph	H	(63)	123
Ph	Ph	(54)	

TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS (*Continued*)

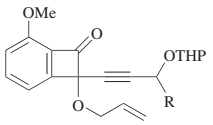
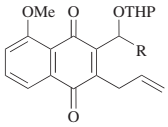
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			
	 , cyclohexane, reflux, 4 h	 (37)	289, 123
C_{15}			
	Chlorobenzene, reflux, 3 h	 (39) +  (14) +  (8) +  (7)	74
	MeCN, reflux, ~1.5 h	 (71)	118
	Solvent, reflux		231, 236

R	Solvent	Time (h)	
Me	MeCN	—	(76)
t-Bu	C_6H_6	1.5	(70)

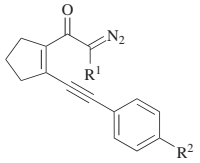
	Chlorobenzene, reflux, 2 h	 (57) +  (12) +  (8)	121
	*p*-Xylene, reflux, 2 h	 (50) +  (40)	121
C_{15-17}			
	*p*-Xylene, reflux, 0.5–2 h		291

R^1	R^2	
H	*n*-Pr	(69)
Me	*n*-Pr	(75)
Me	*n*-Bu	(73)

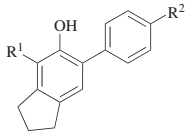
TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15-17} 	*p*-Xylene, reflux, 1–3 h		293

R	
Me	(71)
n-Pr	(74)

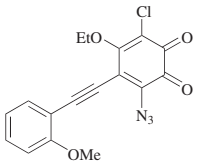


A: 1,4-Cyclohexadiene, toluene, sealed tube, 0.5 h; or
B: *h*ν, toluene, 2 h

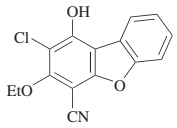


127, 294

R^1	R^2	Cond	Temp	
H	H	A	170°	(38)
Me	H	B	rt	(36)
Me	H	A	140°	(58)
CHO	Me	A	140°	(56)
CHO	Me	B	rt	(21)
$Me_2N(CH_2)_2NHC(O)OCH_2$	Me	A	140°	(67)
$Me_2N(CH_2)_2NHC(O)OCH_2$	Me	B	rt	(29)

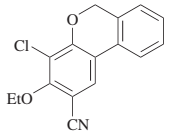
C_{15} 

TMSCl, CCl_4, reflux, 1.5 h

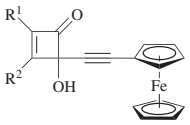
 (76)

123

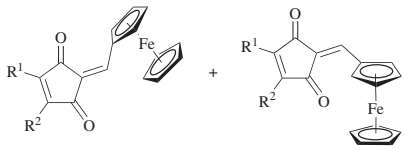
CCl_4, reflux, 1.5 h

 (16)

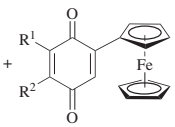
123

C_{16-28} 

A: Dioxane, reflux, 4 h; or
B: Neat, SiO_2, 125°, 0.25 h; or
C: EtOAc, SiO_2, rt, 24 h



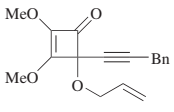
I **II**



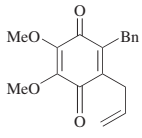
III

R^1	R^2	Cond	**I**	**II**	**III**
i-PrO	*i*-PrO	A	(70)	(0)	(2)
i-PrO	*i*-PrO	B	(67)	(0)	(0)
i-PrO	*i*-PrO	C	(34)	(0)	(0)
Me	*i*-PrO	A	(61)	(3)	(4)
Me	*i*-PrO	B	(45)	(32)	(0)
Me	*i*-PrO	C	(51)	(6)	(0)
Me	Me	A	(55)	(0)	(8)
Me	Me	B	(71)	(0)	(5)
Me	Me	C	(74)	(0)	(8)
Ph	*i*-PrO	A	(53)	(0)	(0)
Ph	*i*-PrO	C	(56)	(0)	(0)
Ph	Ph	A	(58)	(0)	(0)
Ph	Ph	C	(45)	(0)	(0)

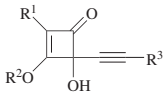
295

C_{16} 

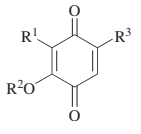
p-Xylene, reflux, 17 min

 (76)

26

C_{16-23} 

p-Xylene, reflux, 20 min



R^1	R^2	R^3	
Ph	Me	*n*-Bu	(57)
n-Bu	Et	Bn	(47)
Ph—≡	Me	*n*-Bu	(57)
Ph	Et	Bn	(46)
1-$C_{10}H_7$	Et	Bn	(65)

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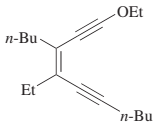
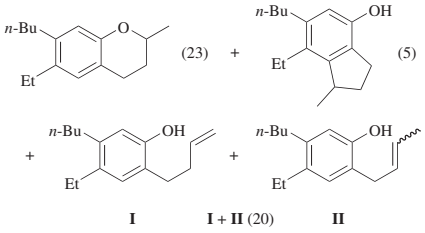
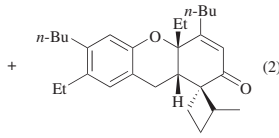
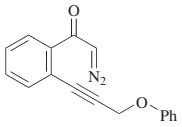
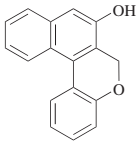
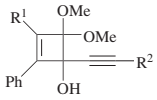
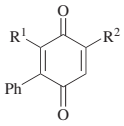
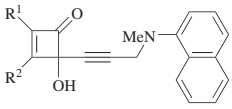
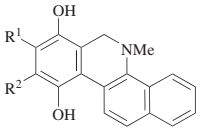
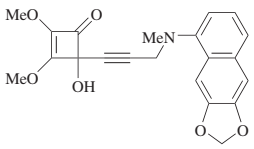
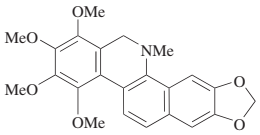
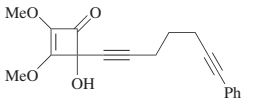
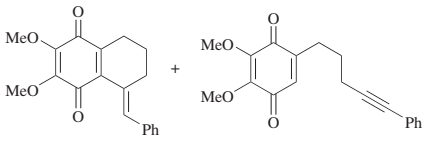
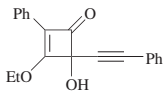
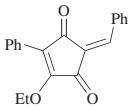
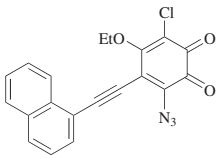
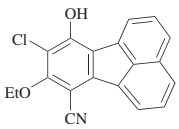
TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS (*Continued*)

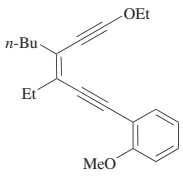
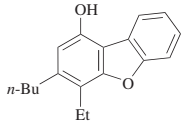
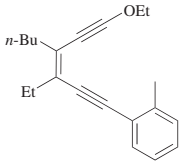
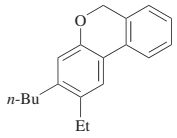
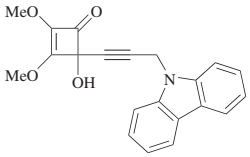
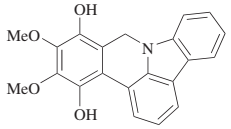
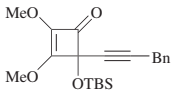
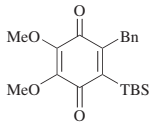
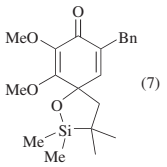
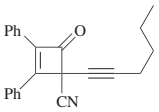
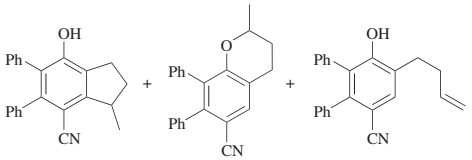
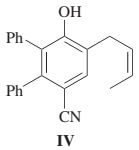
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16} 	Chlorobenzene, reflux, 3 h	 **I** (23) **I + II** (20) **II** (5)  (2)	74
C_{17} 	*hν* (Vycor), CH_2Cl_2	 (70)	357
C_{17-23} 	1. HCl, $CHCl_3$, 0°, 0.25 h 2. Benzene, reflux, 1.75 h		135
	Chlorobenzene, reflux, 2–3 h		190
C_{17} 	1. Chlorobenzene, reflux, 2.3 h 2. NaH, MeI, THF, rt, 18 h	 (30)	190
	Substrate (*x* M), toluene, reflux, 2 h		119
C_{18} 	Benzene, reflux, 4 h	 (46)	26
	CCl_4, reflux, 2 h	 (24)	123

R¹	R²	
Me	*n*-Bu	(80)
n-Bu	*n*-Bu	(79)
n-Bu	Bn	(61)

R¹	R²	
MeO	MeO	(66)
i-PrO	*i*-PrO	(71)
n-Bu	*i*-PrO	(61)
Ph	*i*-PrO	(42)

x	I	II
0.00215	(63)	(0)
0.7	(4)	(66)

TABLE 5. INTRAMOLECULAR CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH ALKYNYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{19}			
	Chlorobenzene, reflux, 3 h	 (28)	74
	Chlorobenzene, reflux, 3 h	 (55)	74
	Chlorobenzene, reflux, 1.75 h	 (83)	121
	*p*-Xylene, reflux, 0.5 h	 (49) +  (7)	26
C_{23}			
	Ph, benzene, reflux	 **I** **II** **III**	289
		+  **IV** **I + II + III + IV** (54), **I/II/III/IV** = 10:10:2:3	

[a] The substrate concentration was 0.001 M.

[b] This value represents the overall yield for the two-step sequence from the cyclobutenedione precursor.

[c] A mixture of isomers was obtained.

[d] The individual yields were not specified for these examples.

TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS

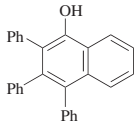
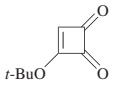
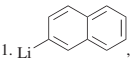
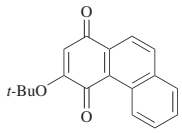
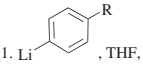
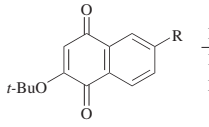
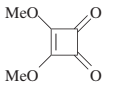
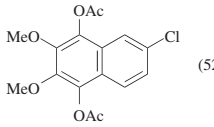
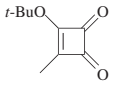
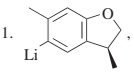
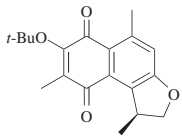
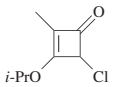
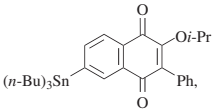
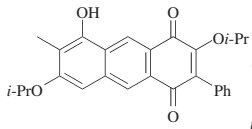
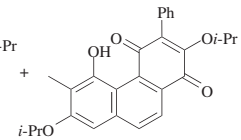
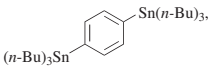
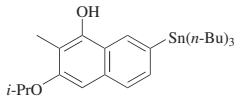
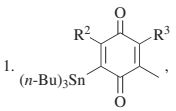
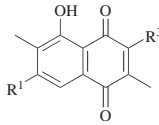
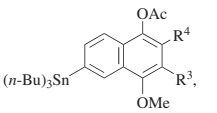
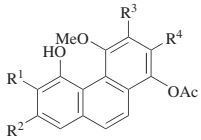
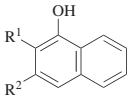
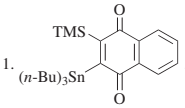
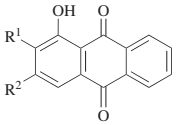
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4			
	$AlCl_3$, benzene, 20° to reflux, 20 h	 (7)	296
	1. Li  , THF, hexane, –78° 2. *p*-Xylene, reflux, 25 min 3. Ag_2O, K_2CO_3, *p*-xylene, rt, 1.75 h	 (48)	229
	1. Li  , THF, hexane, –78° 2. *p*-Xylene, reflux, 30 min 3. Ag_2O, K_2CO_3, *p*-xylene, rt		229
		R: H (63); Me (48)	
	1. 4-ClC_6H_4Li, THF, –78° 2. *p*-Xylene, reflux, 3 h 3. H_2, Pd/C, DMAP, Ac_2O, pyridine	 (52)	133
C_5			
	1.  , THF, –78°, 1.5 h 2. Toluene, reflux, 2 h 3. Air, o/n	 (57)	297
	 $Pd_2(dba)_3$, (2-furyl)$_3$P, dioxane, reflux, 17 h	 (46) +  (18)	130
	 $Pd_2(dba)_3$, (2-furyl)$_3$P, dioxane, reflux, 2 h	 (28)	130
C_{5-11}			
	1.  $Pd_2(dba)_3$, (2-furyl)$_3$P, dioxane, 80–110°, 3–6 h 2. KF/H_2O when R^2 = TMS		126
		R^1 / R^2 / R^3: *i*-PrO / H / *i*-PrO (77); *i*-PrO / TMS / Me (81); Ph / H / *i*-PrO (81); Ph / TMS / Me (74)	
C_{5-10}			
	 $Pd_2(dba)_3$, (2-furyl)$_3$P, dioxane, reflux, 15–24 h		130
		R^1 / R^2 / R^3 / R^4: Me / *i*-PrO / Me / *i*-PrO (41); Me / *i*-PrO / Me / Me (51); Me / *i*-PrO / Ph / *i*-PrO (63); Et / Et / Me / *i*-PrO (68); Et / Et / Me / Me (77); Et / Et / Ph / *i*-PrO (81); Ph / *i*-PrO / Ph / *i*-PrO (17)	

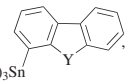
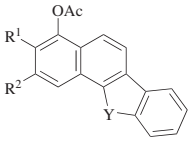
TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-13} 	$PhSnMe_3$, $PdCl_2(PhCN)_2$, (2-furyl)$_3$P, dioxane, sealed tube		233

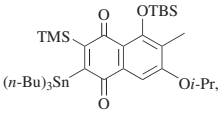
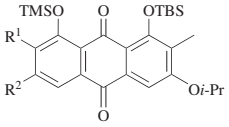
R^1	R^2	Temp (°)	Time (h)	
Me	*i*-PrO	100	6	(53)
n-Bu	*n*-Bu	110	5	(77)

				Refs.
C_{5-11} 	1.  $Pd_2(dba)_3$, (2-furyl)$_3$P, dioxane, 80–110° 2. KF/H_2O		126

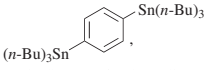
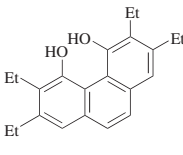
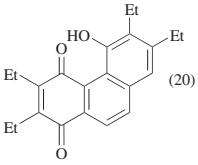
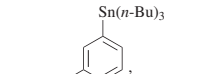
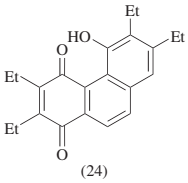
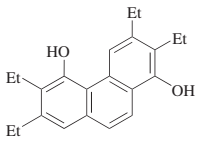
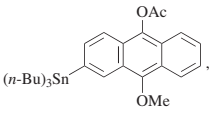
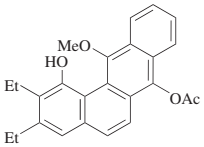
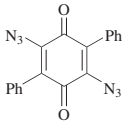
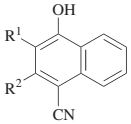
R^1	R^2	Time (h)	
Me	*i*-PrO	8	(75)
t-Bu	*i*-PrO	16	(77)
Et	Et	8	(95)
Ph	*i*-PrO	8	(76)
Ph	Me	8	(94)
Me	Ph	8	(82)

				Refs.
C_{8-11} 	1.  $PdCl_2(PhCN)_2$, (2-furyl)$_3$P, dioxane, 50°, 12 h; 100°, 4 h 2. Ac_2O, pyridine, 100°, 4 h		140

R^1	R^2	Y	
Et	Et	O	(76)
Et	Et	S	(78)
Me	Ph	O	(60)
Me	Ph	S	(62)

				Refs.
	 $Pd_2(dba)_3$, (2-furyl)$_3$P, dioxane, 80–110°		126

R^1	R^2	Time (h)	
s-Bu	*i*-PrO	18	(62)
Me	Ph	1–2	(83)

				Refs.
C_8 	 $Pd_2(dba)_3$, (2-furyl)$_3$P, dioxane, reflux, 20 h	 (27) +  (20)	130
	 $Pd_2(dba)_3$, (2-furyl)$_3$P, dioxane, reflux, 16 h	 (24) +  (15)	130
	 $Pd_2(dba)_3$, (2-furyl)$_3$P, dioxane, reflux, 15–24 h	 (80)	130
C_9 	$R^1{-}{\equiv}{-}R^2$, CCl_4, reflux		143

R^1	R^2	
Me	EtO	(30)
Et	Et	(33)
H	Ph	(67)
Ph	Ph	(41)

TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

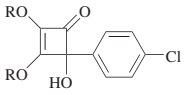
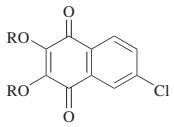
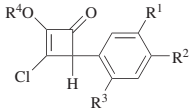
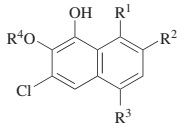
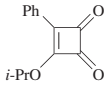
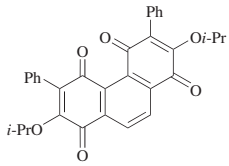
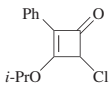
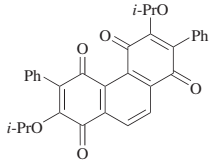
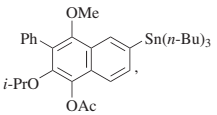
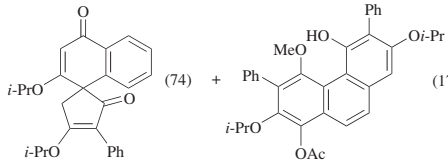
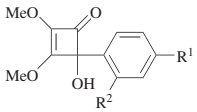
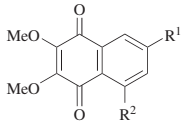
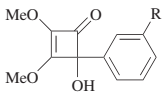
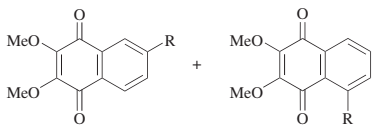
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	A: 1. *p*-Xylene, reflux, 2 h 2. Ag_2O, K_2CO_3, benzene, rt, 20 min; or B: 1. 1,8-bis(Dimethylamino)-naphthalene, *p*-xylene, reflux, 9.5 h 2. Ag_2O, K_2CO_3, benzene, rt, 2 h	 R Cond Me A (85) *t*-Bu B (57)	133, 298 134
C_{10-14} 	*m*-Xylene, reflux, 3 h	 R^1 R^2 R^3 R^4 H H H H (82) H I H H (66) Cl H Cl H (79) H Cl H H (71) H I H Me (81) H MeO H Me (75) Cl H Cl Me (71) H H H Me (64) H Me H H (80) H Me H Me (81) Me H Me H (56) H *t*-Bu H Me (75)	299
C_{10} 	1.  THF, –78°, 2 h 2. Xylenes, reflux, 2 h 3. CAN, HNO_3, acetone, air	 (59)	130
	1.  THF, –78°, 2 h 2. Xylenes, reflux, 2 h 3. CAN, HNO_3, acetone, air, rt	 (60)	130
	 $Pd_2(dba)_2$, $(2\text{-furyl})_3P$, dioxane, reflux, 22 h	 (74) + (17)	130
C_{10-11} 	1. *p*-Xylene, reflux, 2 h 2. A: CAN, CH_2Cl_2, 10 min; or B: Ag_2O, K_2CO_3, benzene, 1 h	 R^1 R^2 Cond H H A (73) MeO H B (80) H MeO B (80) MeO MeO B (80) Me H A (87) H Me A (76)	287, 133
	1. *p*-Xylene, reflux, 2 h 2. Ag_2O, K_2CO_3, benzene, 1 h	 **I** + **II** R **I + II** **I/II** MeO (80) 10:1 Me (83) 1:1	287, 133

TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

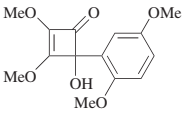
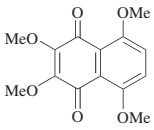
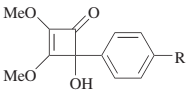
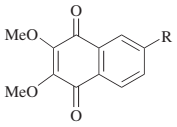
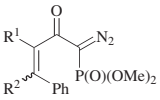
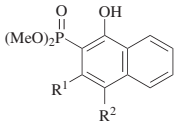
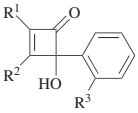
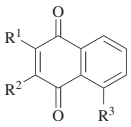
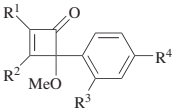
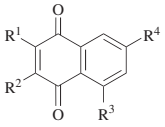
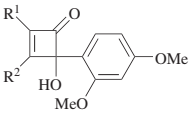
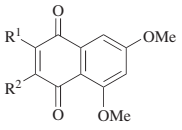
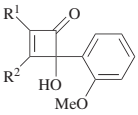
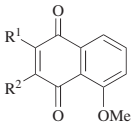
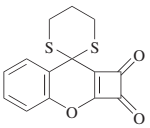
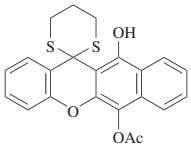
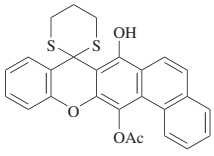
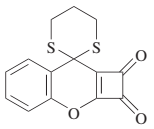
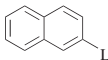
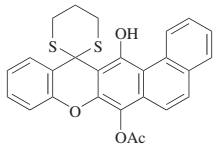
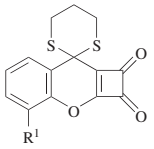
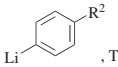
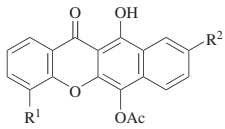
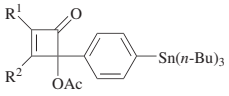
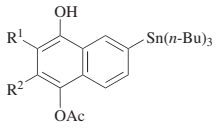
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	1. *p*-Xylene, reflux, 2 h 2. Ag_2O, K_2CO_3, benzene, 1 h	 (80)	287
C_{10-16} 	1. Dioxane, 150°, flow reactor, time 2. air		48
C_{10-11} 	Toluene, reflux, 1.5–4 h		98, 300
C_{11-12} 	1. Xylenes, 160°, 5 min to 4 h 2. Oxidant		139
C_{11-20} 	1. *o*-Xylene, 140°, 0.25–1 h 2. CAN, MeCN, 0° to rt		234
C_{11-12} 	1. Solvent, reflux, time 1 2. Ag_2O, K_2CO_3, rt, 20 min to 2 h		301
C_{11} 	1. Toluene, 110°, 3 h 2. Ag_2O, K_2CO_3, toluene, rt, 0.5 h		302
	1.  THF, cyclohexane, Et_2O, –78° 2. Ac_2O, –78° to rt 3. THF, reflux, 1 h	 (81)	145
	1.  , THF, –78° 2. Ac_2O, –78° to rt 3. THF, reflux, 1 h	 (75)	145

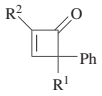
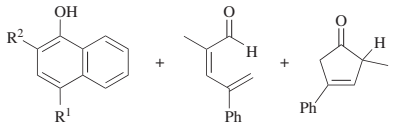
TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
	1.  Li, THF, –78° 2. Ac_2O, –78° to rt 3. Neat, rt, o/n	 (89)	145
	1. Li  , THF, –78° 2. Ac_2O, –78° to rt 3. THF, reflux, 1 h 4. $HgCl_2$, $CaCO_3$, acetone, H_2O, reflux		145

R^1	R^2	
H	MeO	(33)
MeO	Me_2N	(41)

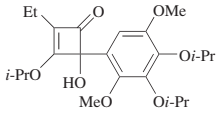
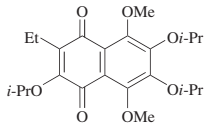
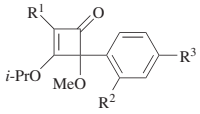
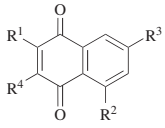
$C_{11–16}$			
	Xylenes, reflux, 0.5–1.5 h		130

R^1	R^2	
Me	*i*-PrO	(94)
Me	Me	(96)
Ph	*i*-PrO	(91)

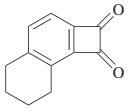
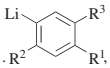
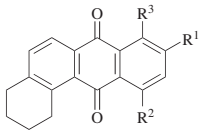
$C_{12–18}$			
	Cyclohexane, reflux, 1 h		303

I **II** **III**

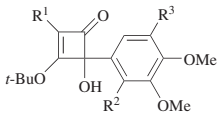
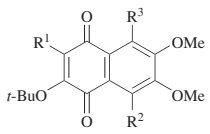
R^1	R^2	**I**[a]	**II**[a]	**III**[a]
Me	Me	(31)	(14)	(19)
Ph	H	(quant)	(0)	(0)
Ph	Me	(quant)	(0)	(0)
Ph	Et	(quant)	(0)	(0)

C_{12}			
	1. Neat, 150°, 0.25 h 2. CAN, Et_2O, H_2O 3. Air, 7 h	 (91)	25
$C_{12–14}$			
	1. R^4M, THF, –78° 2. TFAA, –78° 3. *o*-Xylene, 140°, 0.25–1 h 4. CAN, MeCN, H_2O, 0° to rt		234

R^1	R^2	R^3	R^4M	R^4	
Me	H	Me	PhLi	Ph	(31)
n-Bu	MeO	H	$LiAlH_4$	H	(40)
n-Bu	H	Me	$MeCeCl_2$	Me	(66)

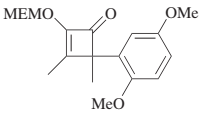
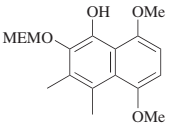
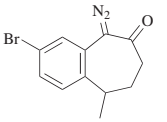
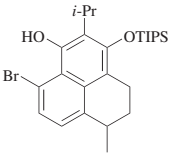
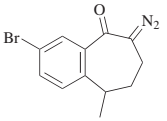
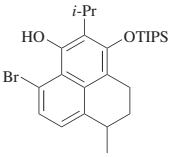
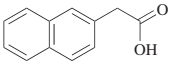
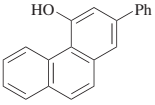
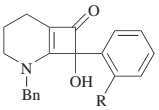
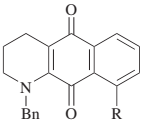
C_{12}			
	 1. R^2  R^1, THF, –78° 2. HCl, THF 3. *p*-Xylene, reflux 4. Ag_2O, K_2CO_3		304

R^1	R^2	R^3	Time (h)	
H	H	H	36	(81)
H	MeO	H	24	(88)
MeO	H	H	36	(70)
H	MeO	MeO	36	(84)

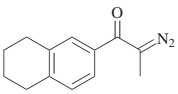
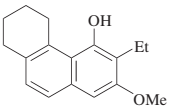
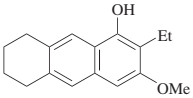
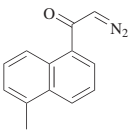
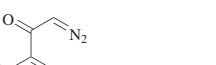
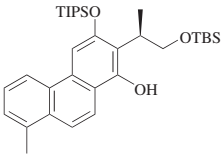
$C_{12–13}$			
	1. Toluene, reflux, 2 h 2. Ag_2O		305

R^1	R^2	R^3	
Et	H	MeO	(93)
n-Pr	MeO	H	(92)

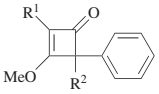
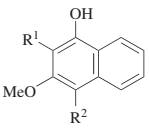
TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}			
	*m*-Xylene, 140°, 20 h	 (82)	251
	1. *i*-Pr—≡—OTIPS, *h*ν, $ClCH_2CH_2Cl$, rt, 19.5 h 2. $ClCH_2CH_2Cl$, reflux, 16.5 h	 (68)	136
	1. *i*-Pr—≡—OTIPS, *h*ν, $ClCH_2CH_2Cl$, rt, 91 h 2. $ClCH_2CH_2Cl$, reflux, 12 h	 (62)	136
	1. $SOCl_2$, reflux 2. Ph—≡, neat, 185°, 36 h 3. KOH, H_2O, MeOH, rt	 (54)	283
C_{13}			
	*o*-Xylene, air, heat, 2 h		292

R	Temp (°)	
H	160	(89)
MeO	140	(71)

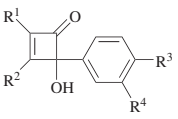
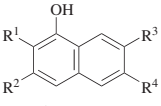
	Et—≡—OMe, *h*ν, $ClCH_2CH_2Cl$, rt, 6 h	 (43) +  (14)	221
	1.  *h*ν, $ClCH_2CH_2Cl$, rt, 8 h 2. 90º, 12 h	 (70–75)	36

$C_{14–16}$

	*p*-Xylene, reflux		267

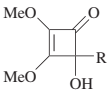
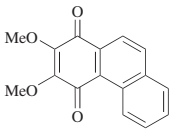
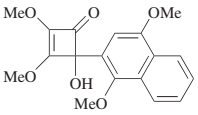
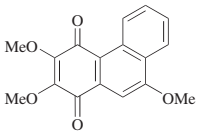
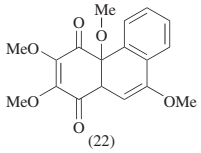
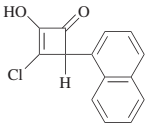
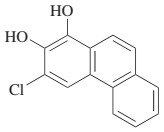
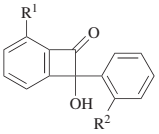
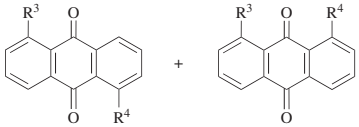
R^1	R^2	
n-Bu	Cl	(62)
n-Bu—≡	Cl	(78)
Ph	*i*-PrO	(74)
Ph	PhS	(86)

$C_{14–16}$

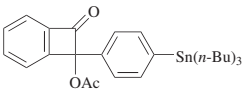
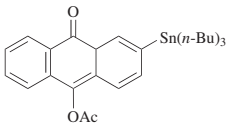
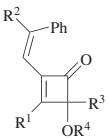
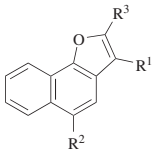
	1. Et_3SiH, BF_3•Et_2O, CH_2Cl_2, rt, 5 h 2. Toluene, reflux, 1–2 h	 306

R^1	R^2	R^3	R^4	
n-Bu	*i*-PrO	H	H	(72)
2-Bu	*i*-PrO	H	H	(73)
Ph	*i*-PrO	MeO	H	(64)
3,4-$(MeO)_2C_6H_3$	MeO	MeO	MeO	(85)
3,4-$(MeO)_2C_6H_3$	4-$MeOC_6H_4(CH_2)_2NH$	MeO	MeO	(73)

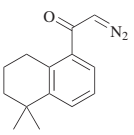
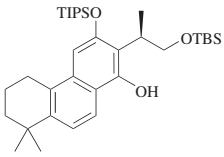
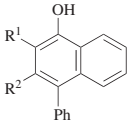
TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			
	1. *p*-Xylene, reflux, 2 h 2. Ag_2O, K_2CO_3, benzene, rt, 1 h	 R: 1-$C_{10}H_7$ (87); 2-$C_{10}H_7$ (90)	133
	1. *p*-Xylene, reflux, 3.5 h 2. Ag_2O, K_2CO_3, benzene, 1 h	 (23) +  (22)	133
	*m*-Xylene, 139°, 3 h	 (64)	299
	1. *p*-Xylene, 160°, 20 min to 4 h 2. Air	 **I** + **II**	139

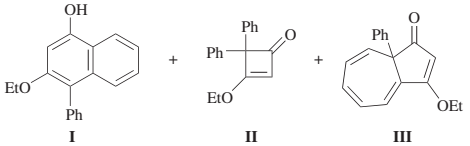
R^1	R^2	R^3	R^4	**I + II**	**I/II**
H	H	H	H	(83)	—
MeO	H	MeO	H	(81)	—
MeO	MeO	MeO	MeO	(96)	3.5:1
TBSO	H	HO	H	(76)[b]	—
TBSO	MeO	HO	MeO	(89)[b]	—

	Xylenes, reflux, 8 h	 (64)	130
C_{14-21}			
	1. A: Toluene, reflux, 0.5 h; or B: *p*-Xylene, reflux, 0.5–2 h 2. TFA, toluene or xylene, rt, 5 min		129

R^1	R^2	R^3	R^4	Cond	
Me	PhS	Me	Me	B	(88)
Me	H	*n*-Bu	H	A	(86)
n-Bu	H	*n*-Bu	H	A	(88)
n-Bu	*n*-Bu	Me	H	B	(75)
n-Bu	*n*-Bu	Me	Me	B	(86)

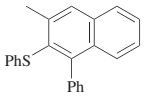
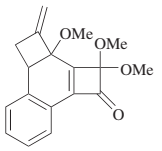
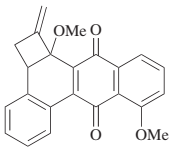
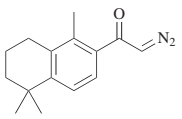
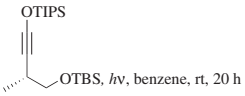
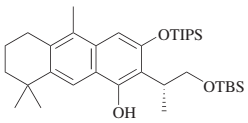
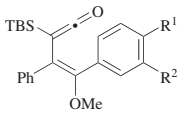
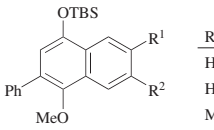
C_{14}			
	 OTBS, *hν*, benzene, rt, 24 h	 (58–65)	194
	A: $R^1{-}{\equiv}{-}R^2$, neat; or B: 1. $R^1{-}{\equiv}{-}R^2$, neat 2. KOH, MeOH, H_2O, rt, 36 h		9, 307, 10

R^1	R^2	Cond	Temp	Time	
H	Ph	A	rt	3 d	(81)
H	4-MeC_6H_4	A	rt	24 h	(77)
Ph	Ph	B	70–80°	3 d	(82)

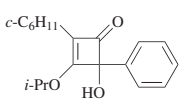
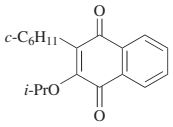
	A: EtO—≡, benzene, rt to 35°, 6 h; or B: EtO—≡, pentane or $MeNO_2$, –35 to –20°, 9 d	 **I** + **II** + **III**	308, 11, 309

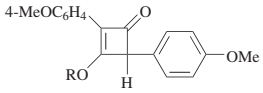
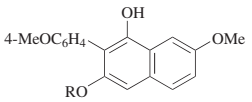
Cond	**I**	**II**	**III**
A	(23)	(—)	(14)
B	(—)	(30)	(32)

TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

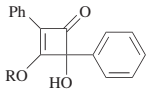
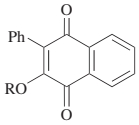
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	PhS—≡—, benzene, reflux, 16 h	 (26)	87
C_{15} 	1. 2-$MeOC_6H_4Li$, THF, –78°, 1 h 2. HCl, H_2O, –78° to rt, 1 h 3. Benzene, reflux, 1 h 4. Ag_2O, K_2CO_3, benzene, rt, 1 h	 (60)	108
		 (58–70)	310
C_{16} 	Benzene, 80°, 2–8 h		128

R^1	R^2	
H	H	(96)
H	MeO	(92)
MeO	H	(94)

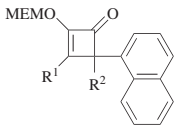
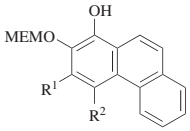
	1. Neat, 135°, 0.75 h 2. Air, Et_2O, rt, 4 h	 (77)	311

	Xylene, reflux		358

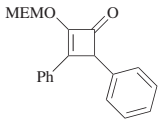
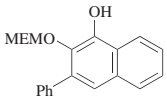
R	
H	(88)
Me	(88)
$PhCH_2CO$	(42)

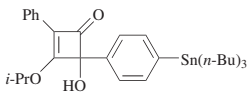
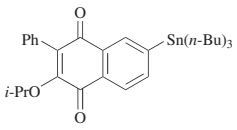
	1. *p*-Xylene, reflux, 5 h 2. Ag_2O, K_2CO_3, *p*-xylene, 7 h		312

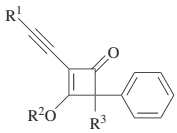
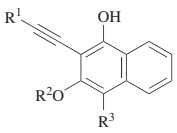
R	
Me	(27)
Et	(38)
i-Pr	(88)
Bn	(86)

$C_{16–18}$  *m*-Xylene, 140°, 20 h  251

R^1	R^2	
Me	Me	(64)
n-Bu	H	(77)

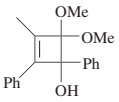
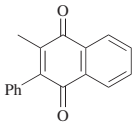
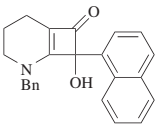
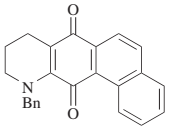
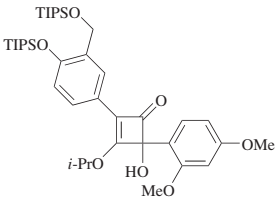
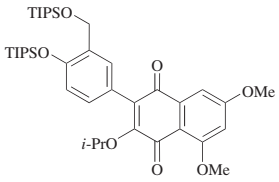
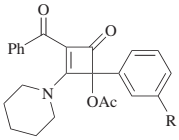
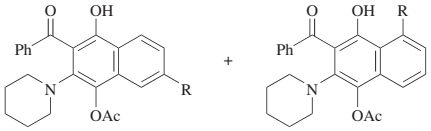
C_{16}  *m*-Xylene, 140°, 18 h  (69) 251

	1. Xylenes, reflux, 1 h 2. Air, rt, o/n	 (80)	130

$C_{16–18}$  A. Xylene, reflux, 3 h
B. Toluene, reflux, 1 h 

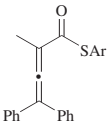
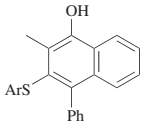
R^1	R^2	R^3	Cond		
n-Bu	Me	Cl	A	(78)	100
n-Bu	*i*-Pr	H	B	(87)	306
Ph	Me	Cl	A	(76)	100

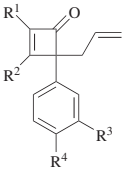
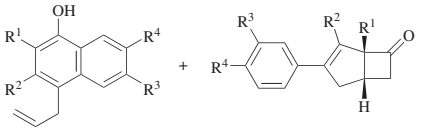
TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17}			
	1. HCl, $CHCl_3$, 0°, 0.25 h 2. Benzene, reflux, 1.75 h 3. Ag_2O, K_2CO_3, benzene, rt, 0.5 h	 (90)	135
	*o*-Xylene, air, 140°, 0.5 h	 (91)	292
	1. *p*-Xylene, reflux, 5 h 2. Ag_2O, K_2CO_3, *p*-xylene, rt, 7 h	 (53)	312
	Mesitylene, reflux		131

I **II**

R	Time (h)	I	II
MeO	72	(56)	(15)
Me_2N	11	(46)	(0)

	Xylene, reflux, 30 min		Ar		87
			Ph	(70)	
			4-MeC_6H_4	(79)	

$C_{19–23}$ 	Toluene, reflux, 3 h		111

I **II**

R^1	R^2	R^3	R^4	I/II	
n-Bu≡	*i*-PrO	H	H	2:1	(88)
n-Bu≡	*i*-PrO	H	MeO	1.5:1	(90)
n-Bu≡	*i*-PrO	MeO	MeO	3:1	(84)
Ph	MeO	H	H	1:2.6	(83)
Ph	*i*-PrO	H	H	1:2.1	(92)
4-$MeOC_6H_4$	*i*-PrO	H	MeO	1:2	(92)
Ph	Me	H	H	2:1	(96)
Ph	*i*-Bu	H	H	1.3:1	(97)

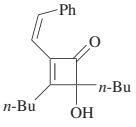
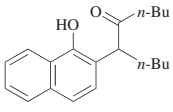
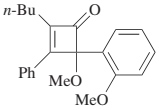
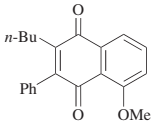
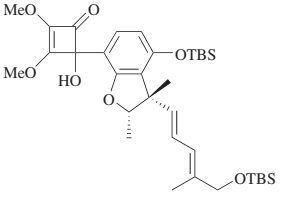
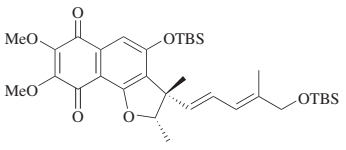
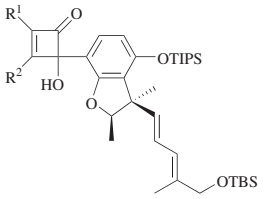
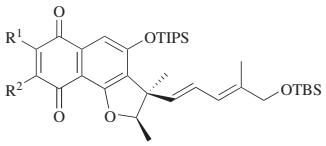
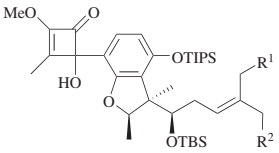
C_{20} 	Toluene, reflux, 16 min	 (67)	129
	1. *o*-Xylene, 140°, 5 h 2. CAN, MeCN, 0° to rt	 (83)	234
	1. Chlorobenzene, reflux 2. Air, rt	 (53)	187

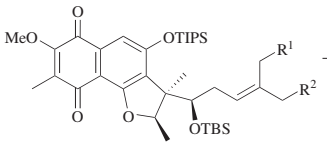
TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{20–22}$ 	1. Toluene 2. A: Air, rt, 0.5–2 h; or B: Ag_2O, K_2CO_3, rt		187, 302

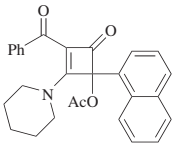
R^1	R^2	Cond	Temp (°)	Time (h)	
MeO	MeO	A	180[c]	0.5	(58)
MeO	Me	A	110	3.5	(64)
Me	MeO	A	110	2	(92)
Me	Me	B	110	2	(55)

C_{21} 

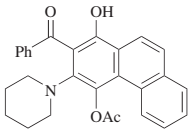
1. Toluene, 110°, 2 h
2. Air, rt



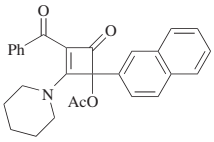
R^1	R^2		
H	TBSO	(70)	302
TBSO	H	(81)	



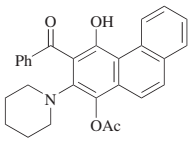
Mesitylene, reflux, 10 h



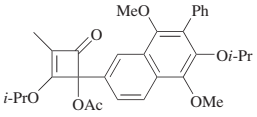
(91) 131



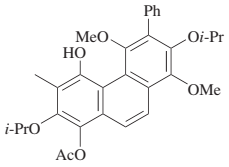
Mesitylene, reflux, 29 h



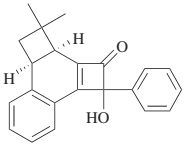
(83) 131



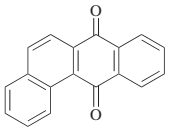
Xylene, reflux, 2.5 h



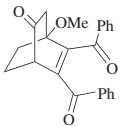
(96) 130

C_{22} 

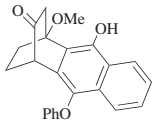
1. Benzene, reflux, 1 h
2. Ag_2O, K_2CO_3, rt, 1–2 h
3. Visible light, 2 h



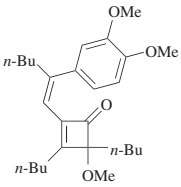
(87) 313



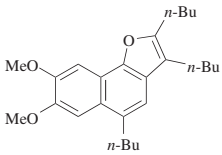
*h*ν, MeOH, 3.5 h



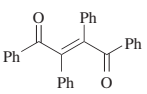
(27) 314

C_{24} 

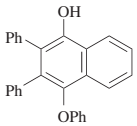
1. *p*-Xylene, reflux, 0.75 h
2. TFA, 20 min



(74) 129

C_{28} 

*h*ν, benzene, rt, 4 h



(41) 315

TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

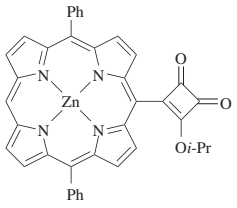
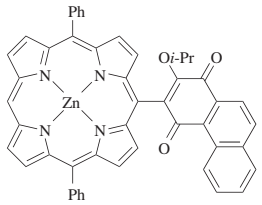
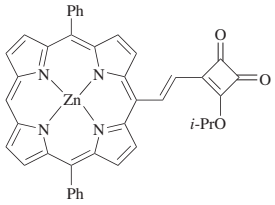
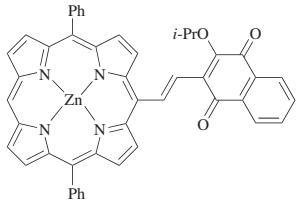
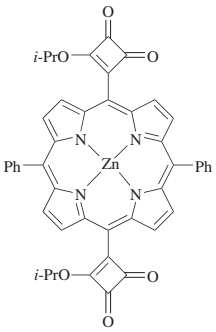
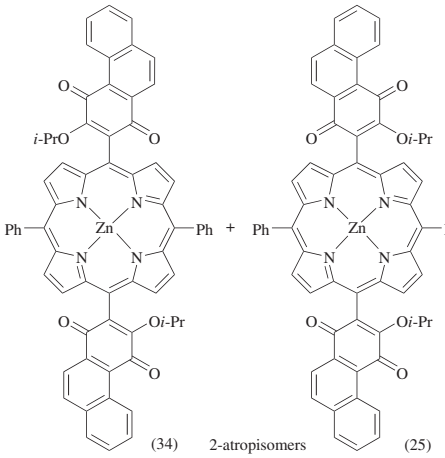
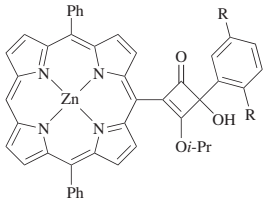
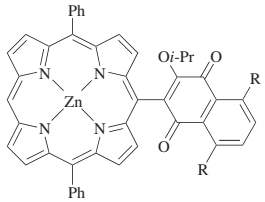
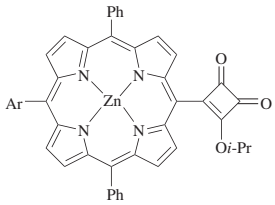
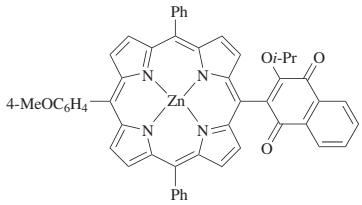
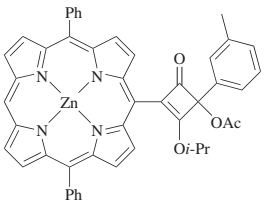
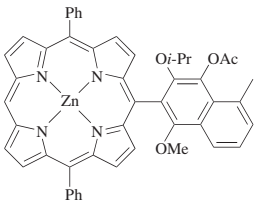
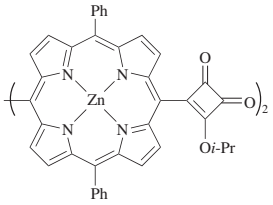
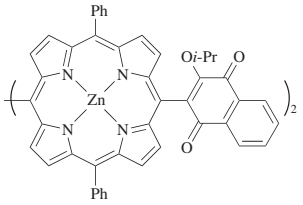
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{36} 	1. 1-$C_{10}H_7Li$, THF, –78° 2. Xylene, reflux, 0.5 h 3. Air, rt	 (78)	277
C_{38} 	1. PhLi, THF, –78° 2. Xylene, reflux, 3 h 3. Air, rt	 (46)	277
C_{40} 	1. 1-$C_{10}H_7Li$, THF, –78° 2. Xylene, reflux, 0.5 h 3. Air, rt	 (34) 2-atropisomers (25)	277
C_{42} 	1. Xylene, reflux, 20 min to 3 h 2. Air, rt, o/n	 R: H (82), MeO (57)	227
 Ar = 4-$MeOC_6H_4$	1. PhLi, THF, –78° 2. Xylene, reflux 3. Air, rt	 (57)	227

TABLE 6. ELECTROCYCLIZATIONS OF VINYLKETENES WITH AROMATIC SYSTEMS (*Continued*)

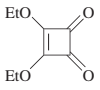
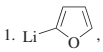
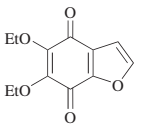
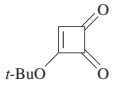
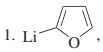
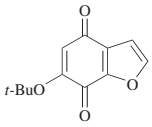
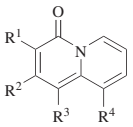
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{43} 	1. Xylene, reflux, 2 h 2. MeI, K_2CO_3, acetone, rt, o/n	 (66)	227
C_{72} 	1. PhLi, THF, –78° 2. Xylene, 150°, 1 h 3. Air, rt, o/n	 (68)	316

[a] These values were determined by ^{1}H NMR spectroscopy.

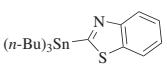
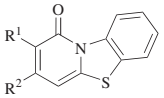
[b] This value represents the overall yield after removal of the TBS group.

[c] This reaction was carried out in a sealed tube in a microwave oven.

TABLE 7. ELECTROCYCLIZATIONS OF VINYLKETENES WITH HETEROAROMATIC SYSTEMS

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4			
	1.  , THF, –78°, 1 h 2. *p*-Xylene, reflux, 3 h 3. $FeCl_3$, Et_2O, rt	 (83–84)	137
	1.  , THF, hexane, –78°, 0.5 h 2. Toluene, reflux, 20 min 3. Ag_2O, K_2CO_3, toluene, rt, 2 h	 (53)	229
$C_{5–12}$			
	1.  , THF, –78° 2. A: Ac_2O, –78°; or B: Step 3 3. $NaHCO_3$, H_2O 4. Solvent, temp 2		138

R^1	R^2	R^3	R^4	Cond	Solvent	Temp 2 (°)	Time	
Me	*i*-PrO	AcO	H	A	dioxane	90	3 h	(50)
Et	Et	AcO	H	A	toluene	100	4 h	(41)
Ph	*i*-PrO	AcO	H	A	dioxane	90	5 h	(60)
Ph	*i*-PrO	HO	H	B	dioxane	90	2 h	(48)
Ph	*i*-PrO	AcO	MeO	A	dioxane	100	20 min	(29)
n-Bu	*n*-Bu	AcO	H	A	dioxane	90	7.5 h	(50)

$C_{5–11}$				
	 , $Pd_2(dba)_3$, (2-furyl)$_3$P, toluene, 60°, o/n; reflux, 6–8 h		138

R^1	R^2	
Me	*i*-PrO	(44)
Et	Et	(34)
Me	Ph	(58)

TABLE 7. ELECTROCYCLIZATIONS OF VINYLKETENES WITH HETEROAROMATIC SYSTEMS (*Continued*)

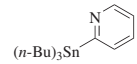
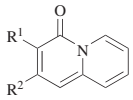
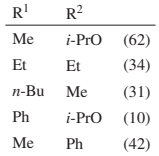
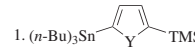
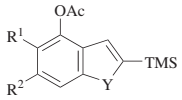
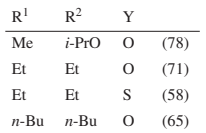
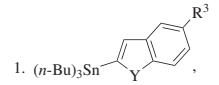
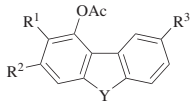
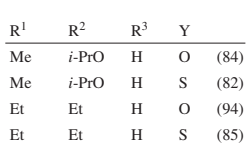
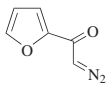
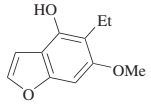
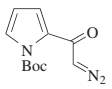
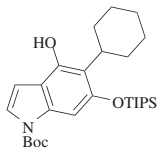
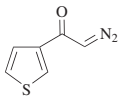
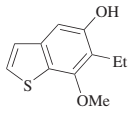
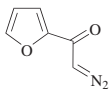
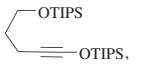
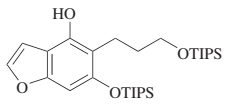
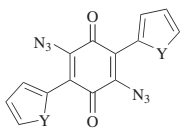
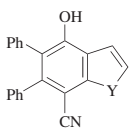
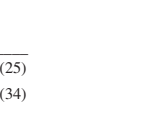
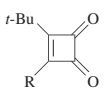
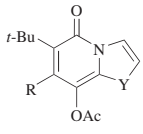
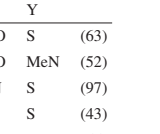
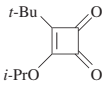
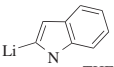
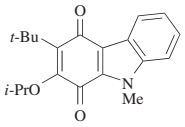
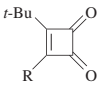
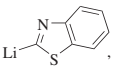
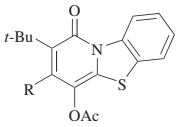
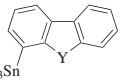
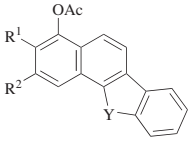
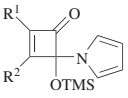
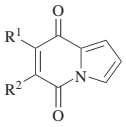
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{5–11}$ 	 $Pd_2(dba)_3$, (2-furyl)$_3$P, toluene, 60°, o/n; reflux, 3–10 h	 	138
$C_{5–12}$ 	1.  $PdCl_2(PhCN)_2$, (2-furyl)$_3$P, dioxane, 50°, 4 h; 100°, 4 h 2. Ac_2O, pyridine, 100°, 4 h	 	140
$C_{5–11}$ 	1.  $PdCl_2(PhCN)_2$, (2-furyl)$_3$P, dioxane, 50°, 12 h; 100°, 4 h 2. Ac_2O, pyridine, 100°, 4 h	 	140
C_6 	1. Et—≡—OMe, $h\nu$, $ClCH_2CH_2Cl$, rt, 46 h 2. $ClCH_2CH_2Cl$, reflux, 3.5 h	 (44)	221
	1. *c*-C_6H_{11}—≡—OTIPS, $h\nu$, $ClCH_2CH_2Cl$, rt, 4.5 h 2. $ClCH_2CH_2Cl$, reflux, 2 h	 (42)	221
	1. Et—≡—OMe, $h\nu$, $ClCH_2CH_2Cl$, rt, 48 h 2. $ClCH_2CH_2Cl$, reflux, 12 h	 (46)	221
	1.  $h\nu$, $ClCH_2CH_2Cl$, rt, 3.5 h 2. $ClCH_2CH_2Cl$, reflux, 2 h	 (60)	144
C_7 	Ph—≡—Ph (2.1 eq), CCl_4, reflux	 	143
$C_{8–9}$ 		 	232

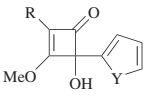
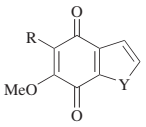
TABLE 7. ELECTROCYCLIZATIONS OF VINYLKETENES WITH HETEROAROMATIC SYSTEMS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	1.  , THF, –78° 2. Ac_2O, –78°, 20 min 3. Neat, 120°, 20 min 4. CAN, Et_2O, H_2O, rt	 (58)	232
C_{8-9}			
	1. Li  , THF, –78° 2. Ac_2O, –78° 3. Neat, 120°, 0.5 h	 R: *i*-PrO (59); Me (46)	232
C_{8-11}			
	1. $(n\text{-Bu})_3Sn$  , $PdCl_2(PhCN)_2$, (2-furyl)$_3$P, dioxane, 50°, 12 h; 100°, 4 h 2. Ac_2O, pyridine, 100°, 4 h		140

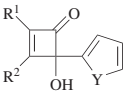
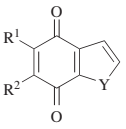
R^1	R^2	Y	
Et	Et	O	(76)
Et	Et	S	(78)
Me	Ph	O	(60)
Me	Ph	S	(62)

C_{8-16}			
	1. Toluene or *p*-xylene, reflux 2. Air or $FeCl_3$		141

R^1	R^2	
MeO	MeO	(72)
n-Bu	MeO	(49)
Ph	MeO	(75)
n-Bu—≡	MeO	(52)
Ph—≡	MeO	(72)
n-Bu	*n*-Bu	(34)

C_{8-12}			
	1. *p*-Xylene, reflux, 2 h 2. Ag_2O, K_2CO_3, benzene, 1 h		287

R	Y	
MeO	O	(93)
MeO	S	(84)
n-Bu	O	(94)

C_{8-14}			
	1. *p*-Xylene, reflux, 2 h 2. A: Ag_2O, K_2CO_3, benzene, rt, 1 h; or B: *p*-Xylene, air, rt, 6 h		133

R^1	R^2	Y	Cond	
MeO	MeO	O	A	(93)
MeO	MeO	S	A	(84)
n-Bu	MeO	O	A	(91)
MeO	*n*-Bu	O	A	(94)
Ph	MeO	MeN	B	(93)

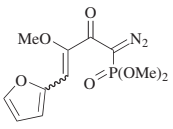
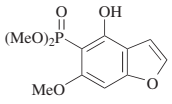
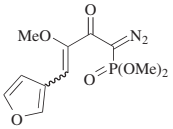
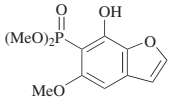
C_8			
	Toluene, reflux, 1.5 h	 (76)	300, 98
	Toluene, reflux, 1.5 h	 (82)	300

TABLE 7. ELECTROCYCLIZATIONS OF VINYLKETENES WITH HETEROAROMATIC SYSTEMS (*Continued*)

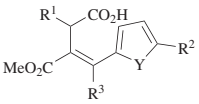
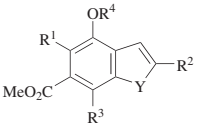
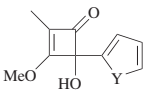
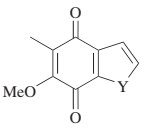
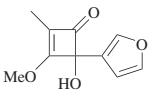
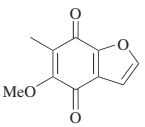
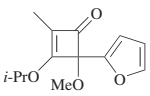
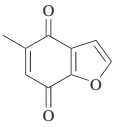
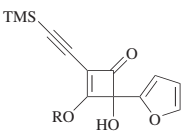
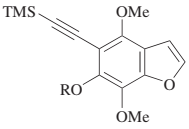
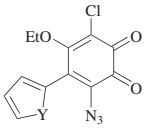
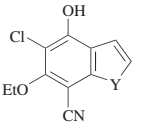
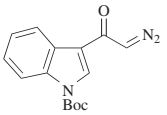
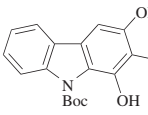
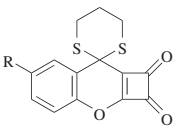
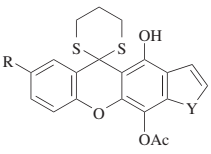
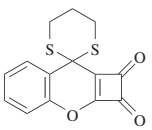
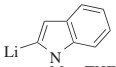
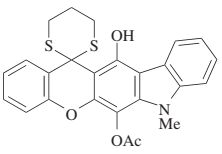
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{9–15}$ 	A: 1. Ac_2O, AcOH, toluene, reflux, 16 h 2. NaOMe, MeOH, reflux, 1 h; or B: Ac_2O, NaOAc, 30°, o/n; 60–80°, 4–6 h; or C: Ac_2O, NaOAc, 30°, o/n	 Y R^1 R^2 R^3 R^4 Cond HN H H H H A (46) HN H H H Ac B (60) MeN H H H Ac B (74) MeN Me H H Ac B (65) S H H Me Ac B (75) O H Me H Ac C (72) O Ph H H Ac B (60) MeN Ph H H Ac B (50)	142 317 317 318 319 320 318 318
C_9 	1. Xylene, 160°, 20 min to 4 h 2. $FeCl_3$	 Y O (92) TsN (60)	139
	1. Xylene, 160°, 20 min 2. $FeCl_3$	 (98)	139
	1. $LiAlH_4$, THF, –20°, 0.25 h 2. TFAA, –78° 3. *o*-Xylene, 140°, 0.5 h 4. CAN, MeCN, H_2O, rt	 (36)	234
C_{10} 	1. Toluene, reflux, 1 h 2. MeI, K_2CO_3, 18-crown-6, toluene, 60°, 12 h	 R Me (75) Et (90)	321 322
	CCl_4, reflux	 Y S (57) TsN (30)	143
	1. $R^1{-}{\equiv}{-}OR^2$, *hν*, $ClCH_2CH_2Cl$, rt, 8–19.5 h 2. Reflux, 2–5 h	 R^1 R^2 Me Me (56) c-C_6H_{11} TIPS (42)	221
C_{11} 	1. , THF, –78°, 10 min 2. Ac_2O, –78° to rt 3. THF, reflux, 1 h	 R Y H Me_2NN (57) H S (50) MeO Me_2NN (71) Cl S (41)	145
	1.  Me , THF, –78°, 1 h 2. Ac_2O, –78° to rt, o/n	 (76)	145

TABLE 7. ELECTROCYCLIZATIONS OF VINYLKETENES WITH HETEROAROMATIC SYSTEMS (*Continued*)

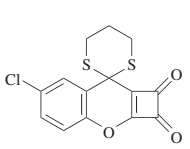
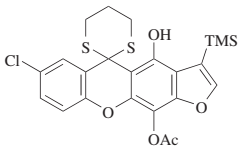
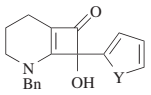
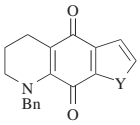
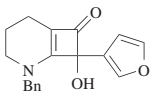
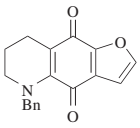
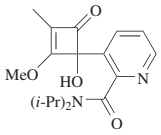
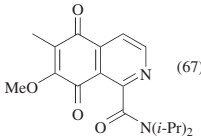
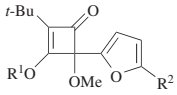
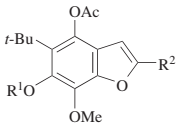
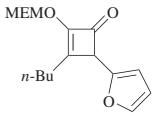
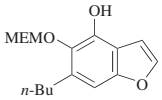
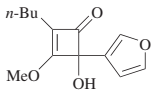
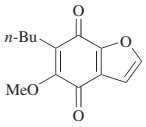
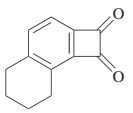
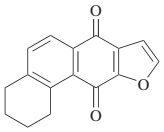
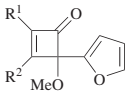
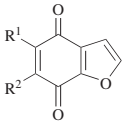
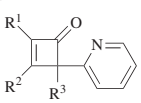
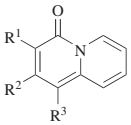
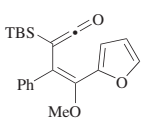
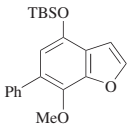
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	1. Li–(TMS-furan), THF, –78°, 10 min 2. Ac_2O, –78° to rt 3. THF, reflux, 1 h	 (55)	145
	*o*-Xylene, air, 120–130°, 0.5 h	 Y: O (76); S (84)	292
	*o*-Xylene, air, 130°, 0.5 h	 (83)	292
	1. Xylene, 160°, 20 min to 4 h 2. $FeCl_3$	 (67)	139
C_{12-13} 	Ac_2O, $(n\text{-Bu})_3N$, DMAP (cat.), xylene, reflux	 R^1 R^2 Time: *i*-Pr H 5 d (89); Me Me 18 h (81)	232
C_{12} 	*m*-Xylene, 140°, 20 h	 (82)	251
	1. *p*-Xylene, reflux, 2 h 2. Ag_2O, K_2CO_3, benzene, rt, 1 h	 (94)	133
	1. Li–(furan), THF, –78° 2. HCl, THF 3. *p*-Xylene, reflux, 24 h 4. Ag_2O, K_2CO_3, *p*-xylene, 3 h	 (91)	304
C_{13} 	1. *o*-Xylene, 140°, 0.25–1 h 2. CAN, MeCN, H_2O, rt	 R^1 R^2: Me *n*-Bu (82); *n*-Bu Me (89)	234
C_{13-17} 	Solvent	 R^1 R^2 R^3 Solvent Temp (°) Time (h): Et Et AcO toluene 100 4 (86) 138; MEMO *n*-Bu *n*-Bu *m*-xylene 140 20 (79) 251	
C_{14} 	Benzene, reflux, 2–8 h	 (89)	128

TABLE 7. ELECTROCYCLIZATIONS OF VINYLKETENES WITH HETEROAROMATIC SYSTEMS (*Continued*)

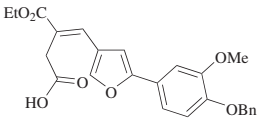
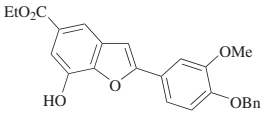
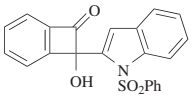
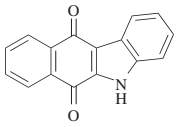
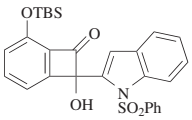
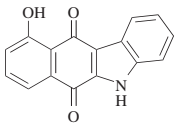
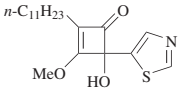
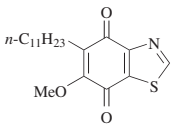
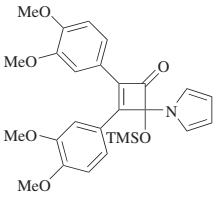
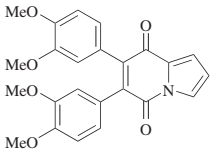
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	$ClCO_2Et$, Et_3N, THF, rt, "a few" min	 (95)	188
C_{16} 	1. *p*-Xylene, 160°, 20 min 2. CAN 3. NaOH, H_2O, 80°, 1 h	 (94)	139
	1. *p*-Xylene, 160°, 80 min 2. NaOH, H_2O, 90°, 0.5 h 3. CAN 4. TBAF	 (86)	139
C_{18} 	1. *p*-Xylene, reflux, 30 min 2. Ag_2O, $MgSO_4$, Et_2O, 6 h	 (85)	323
C_{20} 	1. *p*-Xylene, reflux, 2.5 h 2. $FeCl_3$, H_2O, MeOH, rt	 (88)	189

TABLE 8. CYCLOADDITIONS OF VINYLKETENES WITH IMINES AND DIAZENES

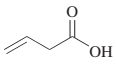
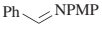
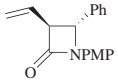
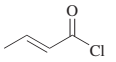
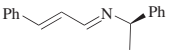
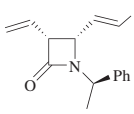
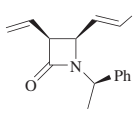
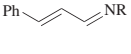
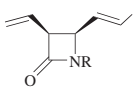
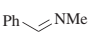
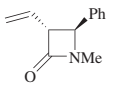
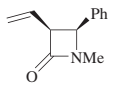
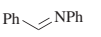
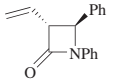
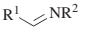
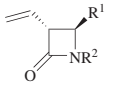
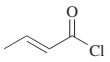
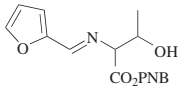
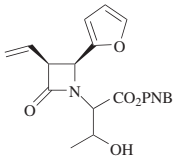
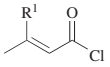
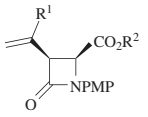
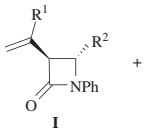
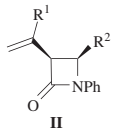
Ketene or Ketene Source	Imine or Diazene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		 $(n\text{-Pr})_3N$, CH_2Cl_2, reflux, o/n	 (70)	149
		Et_3N, CH_2Cl_2, rt, 5 h	 (34) +  (27)	153
		Et_3N, CH_2Cl_2	 R: *t*-Bu, rt, 1, (50); Bn, reflux, 5, (56)	324, 153
		4-Methylmorpholine, chlorobenzene, microwave, 108°, 5 min	 (55) +  (15)	325
		Et_3N, CH_2Cl_2, rt, o/n	 (49)	326
		Et_3N [a]	 R^1: 3-pyridinyl, R^2: PMP, (52); Ph, Ph, (65); Ph, PMP, (50); PMP, PMP, (55)	327

TABLE 8. CYCLOADDITIONS OF VINYLKETENES WITH IMINES AND DIAZENES (*Continued*)

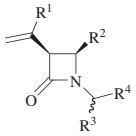
Ketene or Ketene Source	Imine or Diazene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		Et_3N[a]	 (15)	327
C_{4-5}				
	R^2O_2C=NPMP	Et_3N, CH_2Cl_2, reflux, o/n		148

R^1	R^2	
H	Me	(60)
H	Et	(62)
Me	Me	(67)
Me	Et	(68)

	R^2=NPh	Et_3N, CH_2Cl_2, 1.5 h	 + 	22

I **II**

R^1	R^2	Temp	**I**	**II**
H	Ph	20° to reflux	(40)	(—)
H	(*E*)-PhCH=CH	20°	(5)	(25)
H	(*E*)-PhCH=CH	reflux	(35)	(7)
H	2-furyl	reflux	(70)	(—)
Me	2-furyl	reflux	(70)	(—)

	R^2=N(R^3)R^4	Et_3N, CH_2Cl_2, reflux, 1.5 h		22

R^1	R^2	R^3	R^4	
H	MeO_2C	2,4-$(MeO)_2C_6H_3$	H	(40)
Me	2-furyl	$TBSOCH_2$	MeO_2C	(30)
Me	MeO_2C	2,4-$(MeO)_2C_6H_3$	H	(30)
Me	(*E*)-PhCH=CH	H	EtO_2C	(50)
Me	(*E*)-PhCH=CH	$TBSOCH_2$	MeO_2C	(70)
Me	(*E*)-PhCH=CH	H	$(EtO)_2(O)P$	(60)
Me	(*E*)-PhCH=CH	2-furyl	$(EtO)_2(O)P$	(60)

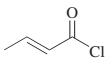
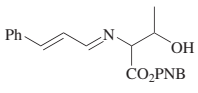
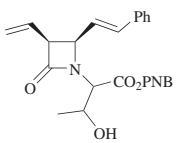
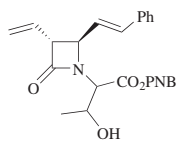
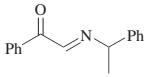
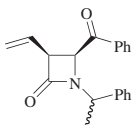
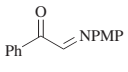
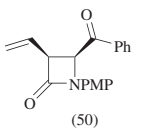
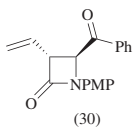
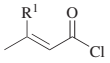
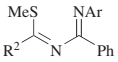
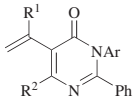
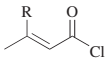
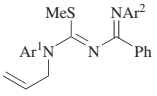
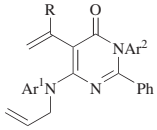
C_4				
		Et_3N, CH_2Cl_2, rt	 +  (54) (6)	327
		Et_3N, CH_2Cl_2, rt	 (55)	327
		Et_3N, CH_2Cl_2, rt	 +  (50) (30)	327

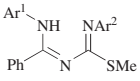
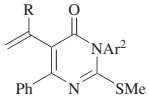
TABLE 8. CYCLOADDITIONS OF VINYLKETENES WITH IMINES AND DIAZENES (*Continued*)

Ketene or Ketene Source	Imine or Diazene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-5}				
		Et_3N, CH_2Cl_2, rt, 1.5–2 h		328

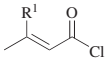
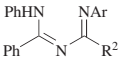
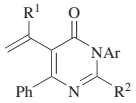
R^1	R^2	Ar	
H	Me_2N	Ph	(90)
H	1-pyrrolidinyl	Ph	(95)
H	1-piperidinyl	Ph	(88)
H	4-morpholinyl	Ph	(90)
H	1-piperidinyl	$4\text{-}MeC_6H_4$	(93)
H	4-morpholinyl	$4\text{-}MeC_6H_4$	(89)
Me	Me_2N	Ph	(94)
Me	1-pyrrolidinyl	Ph	(93)
Me	1-piperidinyl	Ph	(90)
Me	4-morpholinyl	Ph	(89)
Me	1-piperidinyl	$4\text{-}MeC_6H_4$	(93)
Me	4-morpholinyl	$4\text{-}MeC_6H_4$	(91)

		Et_3N, CH_2Cl_2, rt, 1.5–2 h		58

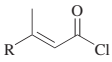
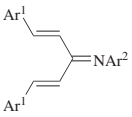
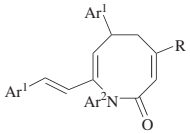
R	Ar^1	Ar^2	
H	Ph	PMP	(63)
Me	Ph	Ph	(91)
Me	Ph	PMP	(87)
Me	Ph	$4\text{-}MeC_6H_4$	(93)
Me	$4\text{-}MeC_6H_4$	PMP	(91)
Me	$4\text{-}MeC_6H_4$	$4\text{-}MeC_6H_4$	(83)

	Et_3N, CH_2Cl_2, rt, 1.5–2 h		329

R	$Ar^{2\,b}$	
H	Ph	(70)
H	$4\text{-}ClC_6H_4$	(71)
H	PMP	(75)
H	$4\text{-}MeC_6H_4$	(72)
Me	Ph	(70)
Me	$4\text{-}ClC_6H_4$	(70)
Me	PMP	(72)
Me	$4\text{-}MeC_6H_4$	(72)

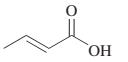
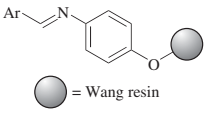
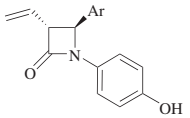
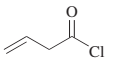
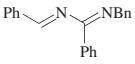
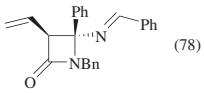
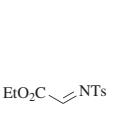
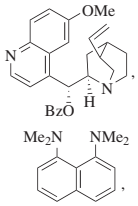
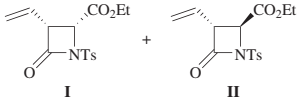
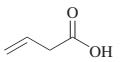
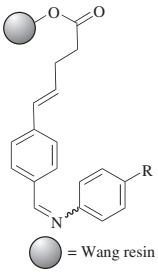
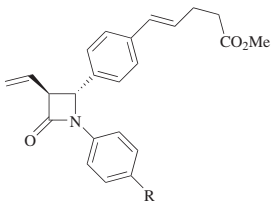
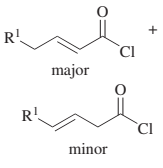
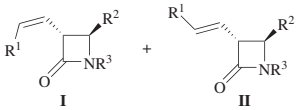
		Et_3N, CH_2Cl_2, rt, 1.5–2 h		329

R^1	Ar	R^2	
H	Ph	1-pyrrolidinyl	(76)
H	$4\text{-}MeC_6H_4$	1-piperidinyl	(73)
Me	$4\text{-}MeC_6H_4$	1-pyrrolidinyl	(71)
Me	$4\text{-}MeC_6H_4$	1-piperidinyl	(76)

		Et_3N, CH_2Cl_2, rt		152

R	Ar^1	Ar^2	
H	Ph	Ph	(76)
H	Ph	PMP	(78)
H	PMP	Ph	(83)
H	PMP	PMP	(82)
H	PMP	$4\text{-}MeC_6H_4$	(88)
H	Ph	$4\text{-}MeC_6H_4$	(80)
Me	Ph	Ph	(77)
Me	Ph	PMP	(72)
Me	PMP	Ph	(89)
Me	PMP	PMP	(85)
Me	Ph	$4\text{-}MeC_6H_4$	(86)
Me	PMP	$4\text{-}MeC_6H_4$	(81)

TABLE 8. CYCLOADDITIONS OF VINYLKETENES WITH IMINES AND DIAZENES (*Continued*)

Ketene or Ketene Source	Imine or Diazene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
	 = Wang resin	 1. Me I^-, Et_3N, $CHCl_3$, reflux, 2 h 2. TFA, CH_2Cl_2, rt, 1 h		150
Ar	R			
Ph	(—)			
PMP	(32)			
4-BrC_6H_4	(—)			
		Et_3N, toluene, 0° to rt	 (78)	330
		$In(OTf)_3$, toluene, –78° to rt, 16 h	 **I** + **II** (92), **I/II** = 10:1, er **I** 98.0:2.0	51
	 = Wang resin	 1. Me I^-, Et_3N, $CHCl_3$, reflux, 2 h 2. TFA, CH_2Cl_2, rt 3. CH_2N_2, 0°		331
R				
H	(26)			
F	(42)			
MeO	(60)			
 major minor	$R^2{=}NR^3$	Et_3N, CH_2Cl_2, 0° to reflux, 18–48 h	 **I** + **II**	151

R^1	R^2	R^3	**I + II**	**I/II**
N_3	Ph	Ph	(66)	80:20
MeO	Ph	Ph	(75)	92:8
MeO	Ph	PMP	(85)	90:10
PhO	Ph	Ph	(75)	91:9
PhO	MeO_2C	PMP	(70)	100:0
PhO	4-$MeOC_6H_4$	Ph	(73)	93:7
PhO	Ph	4-ClC_6H_4	(78)	89:11
PhO	4-$MeOC_6H_4$	PMP	(77)	92:8
PhO	Ph	PMP	(80)	90:10
PhO	Ph	4-MeC_6H_4	(83)	90:10
PhthN	Ph	Ph	(61)	85:15

TABLE 8. CYCLOADDITIONS OF VINYLKETENES WITH IMINES AND DIAZENES (*Continued*)

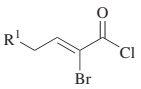
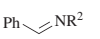
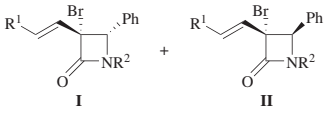
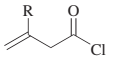
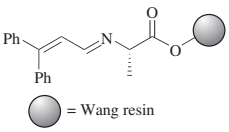
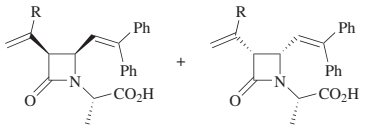
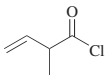
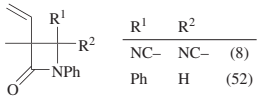
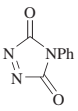
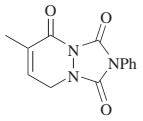
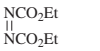
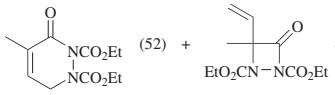
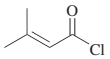
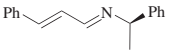
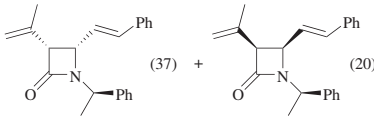
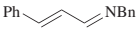
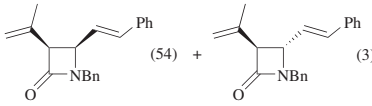
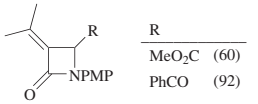
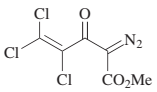
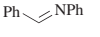
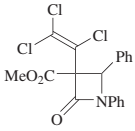
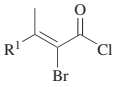
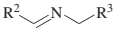
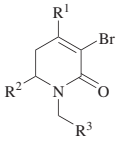
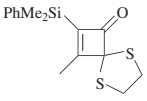
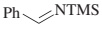
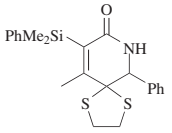
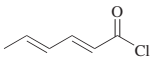
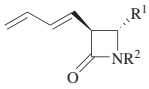
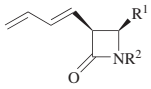
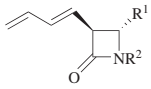
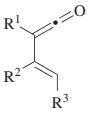
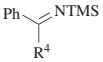
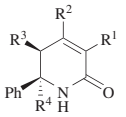
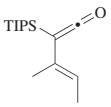
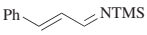
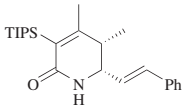
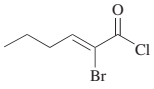
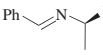
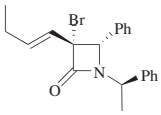
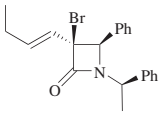
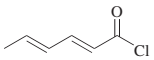
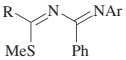
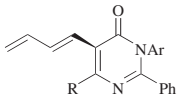
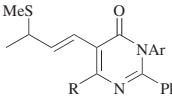
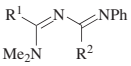
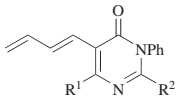
Ketene or Ketene Source	Imine or Diazene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-6} 		Et_3N, CH_2Cl_2, reflux, 4 h	 **I** + **II** R^1 R^2 **I + II** **I/II** H Bn (30) 90:10 Et Bn (60) 84:16 Et $EtO_2CCH_2CH_2$ (55) 93:7 Et CH_2=$CHCH_2$ (50) 80:20	332
C_{4-5} 	 = Wang resin	1. Et_3N, CH_2Cl_2, 0° to rt, 16 h 2. 3% TFA in CH_2Cl_2, rt, 45 min	 **I** + **II** R **I + II** **I/II**[c] H (58) 55:45 Me (91) 55:45	333
C_5 		1. Et_3N, CCl_4, 0°, 5 min 2. Add imine, –30 to 20°	 R^1 R^2 NC– NC– (8) Ph H (52)	20
		1. Et_3N, CCl_4, 0° 2. Add diazene, THF, 20°, instantaneous	 (72)	20
		1. Et_3N, CCl_4, 0° 2. Add diazene, THF, 20°, 3 d	 (52) + (23)	20
		Et_3N, CH_2Cl_2, rt, 5 h	 (37) + (20)	153
		Et_3N, CH_2Cl_2, reflux, 5 h	 (54) + (3)	153
		1. Et_3N, CH_2Cl_2, reflux, 14 h 2. DBU, benzene, reflux, 6 h	 R MeO_2C (60) PhCO (92)	334
		*hv*, benzene, rt, 52 h	 (28)	224
C_{5-7} 		Et_3N, CH_2Cl_2, 40°	 R^1 R^2 R^3 Me Ph EtO_2C (34) Me Ph CH_2=CH (96) Me Ph MeO_2CCH_2 (64) Me PMP Ph (94) Me Ph PMP (92) Me Ph Ph (92) *n*-Pr Ph Ph (94)	154
C_5 		$Zn(OTf)_2$, THF, rt, 24 h	 (35)	27

TABLE 8. CYCLOADDITIONS OF VINYLKETENES WITH IMINES AND DIAZENES (*Continued*)

Ketene or Ketene Source	Imine or Diazene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 		Et_3N, CH_2Cl_2, rt, 1.75 h		222
		Et_3N, CH_2Cl_2, rt, 1.5 h	 + 	335
C_{6-10} 		A: Neat, rt, 5 min to 2 h; or B: MeCN, reflux, 1–25 h		23
C_6 		Neat, rt, 2 h	 (78)	23
		Et_3N, CH_2Cl_2, reflux, 4 h	 +  **I + II** (55), **I/II**[c] = 3:1	332
		Et_3N, CH_2Cl_2, rt, 1 h	 + 	336
		Et_3N, CH_2Cl_2, rt, 1 h		336

I **II**

R^1	R^2	I + II	I/II
PMP	*n*-Bu	(67)	4:1
Ph	(2-furyl)CH_2	(57)	100:0
PMP	(2-furyl)CH_2	(59)	6.5:1
Ph	cyclohexyl	(63)	100:0
PMP	cyclohexyl	(69)	100:0
(*E*)-PhCH=CH	Ph	(67)	100:0
(*E*)-PhCH=CH	cyclohexyl	(71)	100:0

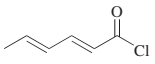
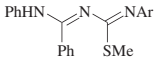
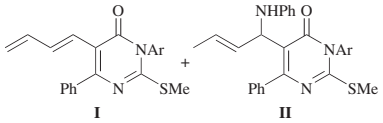
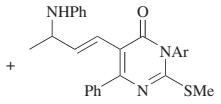
R^1	R^2	R^3	R^4	Cond	
TES	Me	Me	H	A	(76)
TIPS	Me	Me	H	B	(79–83)
TIPS	Me	Me	Ph	B	(79)
TES	Ph	H	H	B	(84)

I **II**

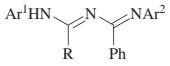
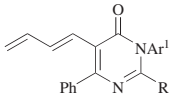
R	Ar	I	II
Me_2N	Ph	(29)	(41)
1-piperidinyl	Ph	(31)	(26)
4-morpholinyl	Ph	(30)	(33)
1-piperidinyl	4-MeC_6H_4	(36)	(28)
4-morpholinyl	4-MeC_6H_4	(39)	(32)
CH_2=$CHCH_2$(Ph)N	Ph	(42)	(21)
CH_2=$CHCH_2$(4-MeC_6H_4)N	Ph	(40)	(26)

R^1	R^2	
H	MeS	(86)
H	Ph	(63)
Me	Ph	(89)

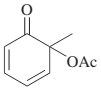
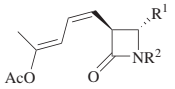
TABLE 8. CYCLOADDITIONS OF VINYLKETENES WITH IMINES AND DIAZENES (*Continued*)

Ketene or Ketene Source	Imine or Diazene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		Et_3N, CH_2Cl_2, rt, 1 h	 **I** + **II**	336
			 **III**	

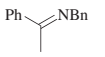
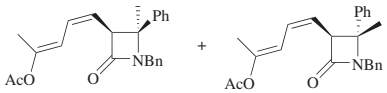
Ar	I	II	III
Ph	(33)	(21)	(30)
4-ClC_6H_4	(25)	(21)	(27)
4-MeC_6H_4	(29)	(26)	(29)

		Et_3N, CH_2Cl_2, rt, 1 h		336

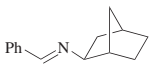
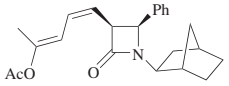
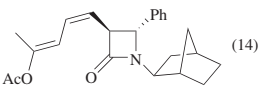
Ar^1	Ar^2	R	
Ph	Ph	1-piperidinyl	(86)
Ph	4-MeC_6H_4	1-piperidinyl	(82)
4-MeC_6H_4	4-MeC_6H_4	1-pyrrolidinyl	(80)

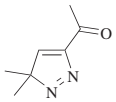
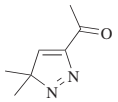
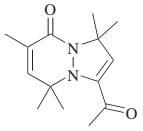
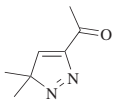
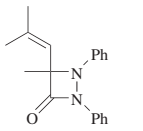
C_7				
		*hν* (>340 nm), solvent, rt, 2 h		71

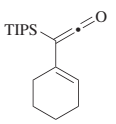
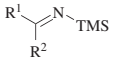
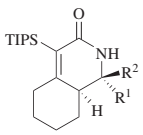
R^1	R^2	Solvent	
Ph	cyclohexyl	hexane/CH_2Cl_2 (9:1)	(98)
MeS	Bn	CH_2Cl_2/acetone (9:1)	(60)

		*hν* (>340 nm), CH_2Cl_2, rt, 5.5 h	 **I** + **II**	71

I + **II** (69), **I**/**II** = 86:13

		*hν* (>340 nm), CH_2Cl_2, rt, 2.5 h	 (16) +  (14)	71

		*hν*, Et_2O, rt	 (46)	337
	NPh ‖ NPh	*hν*, Et_2O, rt	 (—)	337

C_8				
		A: MeCN, sealed tube, 110°, 90 h; or B: MeCN, reflux, 1–25 h; or C: Neat, 5 min to 2 h		23

R^1	R^2	Cond	
t-Bu	H	A	(56)
Ph	H	B	(91)
(*E*)-PhCH=CH	H	C	(73)
Ph	Ph	B	(66)

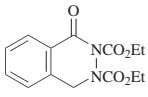
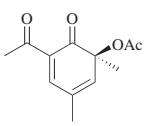
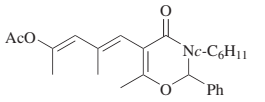
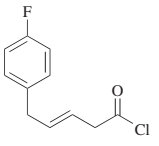
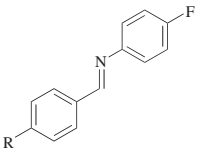
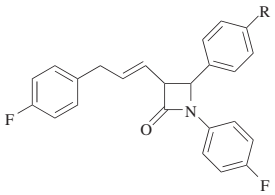
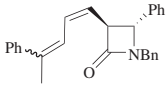
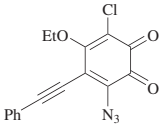
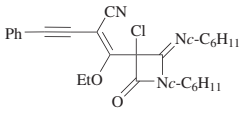
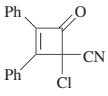
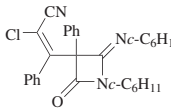
	NCO$_2$Et ‖ NCO$_2$Et	Neat, 160°	 (29)	69

TABLE 8. CYCLOADDITIONS OF VINYLKETENES WITH IMINES AND DIAZENES (*Continued*)

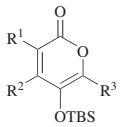
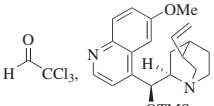
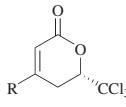
Ketene or Ketene Source	Imine or Diazene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	Ph–N=*c*-C_6H_{11}	*hν* (>340 nm), hexane/CH_2Cl_2 (9:1), –60°, 6 h	 (30)	71
C_{11} 		(*n*-Bu)$_3$N, toluene, heptane, 80°, 18 h	 R: MeO (—); BnO (—)	338
C_{13} 	Ph–N=CH–Bn	*hν* (>340 nm), CH_2Cl_2, 6 h	 (71)	71
C_{14} 	*c*-C_6H_{11}N=•=N*c*-C_6H_{11}	Cyclohexane, reflux, 2.5 h	 (44)	289, 123
C_{17} 	*c*-C_6H_{11}N=•=N*c*-C_6H_{11}	Benzene, rt, 16 h	 (76)	155

[a] No additional details were provided.

[b] Ar^1 is lost in the reaction as Ar^1NH_2. The identity of Ar^1 was given as 4-RC_6H_4 where R = H, OMe, Cl, or Me, but the correspondence between Ar^1 and Ar^2 was not given.

[c] The relative configuration between the newly formed asymmetric centers and the preexisting asymmetric center on the *N*-substituent was not defined for each product isomer. Therefore, the identity of the major product is not known.

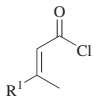
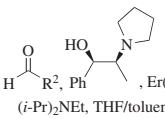
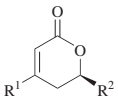
TABLE 9. CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH CARBONYL AND THIOCARBONYL GROUPS

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-10}			
	 1. Li, THF, –78°, 20 min 2. $NaHCO_3$, –78° to rt		160
	 (1 eq), $Sn(OTf)_2$, $(i\text{-Pr})_2NEt$, toluene, –15°, 5 h		157

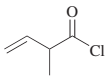
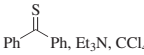
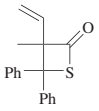
R^1	R^2	R^3	
i-PrO	*i*-PrO	2-furyl	(71)
i-PrO	*i*-PrO	$Me_2C{=}CH$	(70)
Et	Et	2-FC_6H_4	(61)
t-Bu	MeO	3-pyridinyl	(76)
n-Bu	Me_2N	1-Me-3-indolyl	(57)
Ph	*i*-PrO	Ph	(86)
Ph	*i*-PrO	1-Me-2-pyrrolyl	(71)

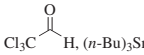
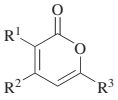
R		er
TES	(54)	98.0:2.0
$(n\text{-Pr})_3Si$	(51)	98.5:1.5
$(n\text{-Bu})_3Si$	(61)	98.5:1.5
$BnMe_2Si$	(47)	96.0:4.0
Et	(60)	77.0:23.0
i-Pr	(78)	91.0:9.0
i-Bu	(73)	85.0:15.0
t-Bu	(80)	97.5:2.5
Ph	(73)	90.5:9.5
cyclohexyl	(75)	91.5:8.5

TABLE 9. CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH CARBONYL AND THIOCARBONYL GROUPS (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-10} 	 , $Er(OTf)_3$, $(i\text{-}Pr)_2NEt$, THF/toluene, –10°, 2.5 h		158

R^1	R^2		er
Me	Ph	(24)	97.5:2.5
Et	Ph	(62)	97.5:2.5
i-Pr	Ph	(56)	97.5:2.5
i-Bu	Ph	(54)	99.0:1.0
cyclohexyl	Ph	(65)	98.0:2.0
Ph	2-furyl	(23)	97.0:3.0
Ph	2-thienyl	(40)	97.0:3.0
Ph	3-Br-2-thienyl	(46)	97.5:2.5
Ph	Ph	(64)	97.0:3.0
Ph	$2\text{-}ClC_6H_4$	(77)	94.0:6.0
Ph	$3\text{-}ClC_6H_4$	(78)	96.5:3.5
Ph	$4\text{-}ClC_6H_4$	(71)	96.0:4.0
Ph	$3\text{-}BrC_6H_4$	(77)	97.5:2.5
Ph	$4\text{-}BrC_6H_4$	(70)	96.5:3.5
Ph	$2\text{-}O_2NC_6H_4$	(91)	95.5:4.5
Ph	$4\text{-}O_2NC_6H_4$	(72)	94.0:6.0
Ph	$2\text{-}MeOC_6H_4$	(26)	97.0:3.0
Ph	$4\text{-}MeC_6H_4$	(30)	97.0:3.0
Ph	$3\text{-}CF_3C_6H_4$	(87)	96.5:3.5
Ph	(*E*)-$4\text{-}O_2NC_6H_4CH{=}CH$	(62)	96.0:4.0
Ph	2-naphthyl	(55)	97.5:2.5

C_5    (90) 20

C_{5-12}   

R^1	R^2	R^3		
Me	*i*-PrO	2-furyl	(89)	
Me	*i*-PrO	2-thienyl	(74)	159
Me	*i*-PrO	Ph	(60)	
Me	*i*-PrO	$4\text{-}MeOC_6H_4$	(62)	
Et	Et	$CH_2{=}CH$	(62)	
Et	Et	MeCH=CH	(65)	
Et	Et	3-furyl	(80)	
Et	Et	Ph	(63)	
Et	Et	$4\text{-}ClC_6H_4$	(84)	
Et	Et	$4\text{-}MeOC_6H_4$	(80)	
Me	Ph	Ph	(78)	
Me	Ph	$4\text{-}MeOC_6H_4$	(76)	
n-Bu	*n*-Bu	$4\text{-}MeOC_6H_4$	(60)	
n-Bu	*n*-Bu	3-furyl	(68)	
n-Bu	*n*-Bu	2-furyl	(72)	
n-Bu	*n*-Bu	2-EtOCH=CH	(60)	
n-Bu	*n*-Bu	1-Me-2-pyrrolidinyl	(60)	
n-Bu	*n*-Bu	Ph	(86)	
n-Bu	*n*-Bu	$4\text{-}ClC_6H_4$	(67)	

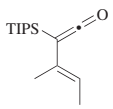
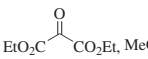
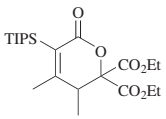
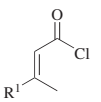
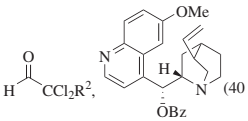
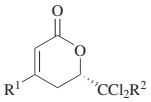
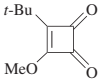
C_6    (94) 23

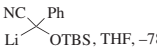
TABLE 9. CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF VINYLKETENES WITH CARBONYL AND THIOCARBONYL GROUPS (*Continued*)

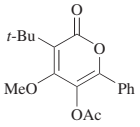
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{7-10} 	 (40 mol %), $LiClO_4$, $(i\text{-Pr})_2NEt$, toluene, –15°		156

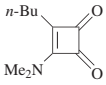
R^1	R^2		er
i-Pr	Me	(67)	87.0:13.0
i-Pr	Et	(35)	80.0:20.0
i-Pr	*n*-Pr	(29)	66.0:34.0
t-Bu	Me	(79)	85.5:14.5
Ph	Me	(57)	86.0:14.0
cyclohexyl	Me	(56)	88.0:12.0

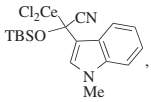
C_8

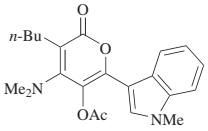


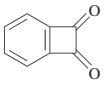
1. 
2. TBAF, Ac_2O, THF, rt, 30 min

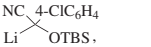
 (78) — 160

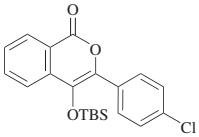


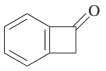
1.  , THF, –78°, 20 min
2. Ac_2O, TBAF, THF, rt, 30 min

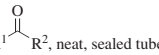
 (57) — 160

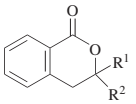


 , THF, –78°, 20 min

 (50) — 160



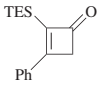
 , neat, sealed tube, 160°

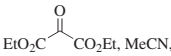


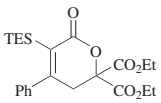
R^1	R^2	
Cl_3C	H	(92)
MeO_2C	Me	(72)
EtO_2C	EtO_2C	(91)
Ph	H	(63)

69

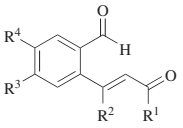
C_{10}



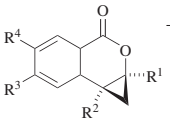
 , MeCN, reflux, 15 h

 (92) — 23

C_{10-14}

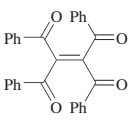


hν, benzene, rt



R^1	R^2	R^3	R^4	Time (h)		
MeO	H	H	H	2.5	(68)	
EtO	H	H	H	5	(89)	353
i-PrO	H	H	H	4	(71)	
MenthylO	H	H	H	8	(74)	
EtO	H	H	Cl	1	(75)	
EtO	H	H	MeO	5	(74)	
EtO	H	MeO	H	2	(63)	
EtO	H	Cl	H	7	(73)	
EtO	Me	H	H	1	(98)	
EtO	*n*-Bu	H	H	5	(82)	
Me	H	H	H	50	(49)	

C_{30}



hν, Et_2O, rt, 3.5 h

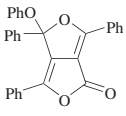
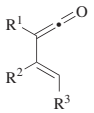
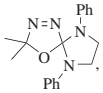
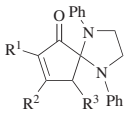
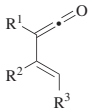
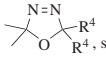
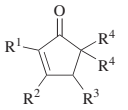
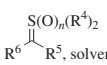
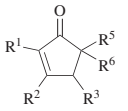
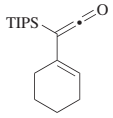
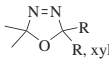
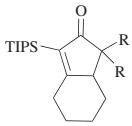
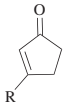
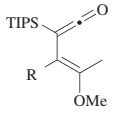
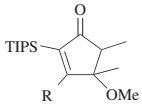
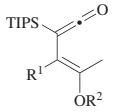
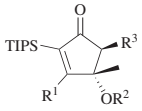
 (15) — 85

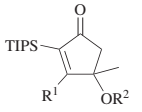
TABLE 10. CARBON-NUCLEOPHILE-INITIATED CYCLIZATION REACTIONS OF VINYLKETENES

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-10} 	 , xylene, reflux, 1–2 h		339
		R^1 R^2 R^3 TIPS Me H (76) TIPS H Me (71) TMS Ph H (55)	
C_{6-10} 	 , solvent, reflux, 1–2 h		339
		R^1 R^2 R^3 R^4 Solvent TIPS Me Me MeO xylene (80) TMS Ph H MeO xylene (63) TMS Ph H *n*-PrS benzene (88)	
	 , solvent		340

R^1	R^2	R^3	R^4	R^5	R^6	*n*	Solvent	Temp	Time (h)	
TIPS	Me	Me	Me	H	H	0	THF/DMSO	0° to rt	1	(75)
TIPS	Me	Me	Me	H	H	1	THF/DMSO	0° to rt	1.25	(43)
TIPS	Me	Me	Ph	Me	H	0	DME	–50 to –20°	1	(68)[a]
TIPS	Me	Me	Ph	Me	Me	0	THF/DMSO	–25 to –20°	3	(57)
TES	Me	Me	Me	H	H	0	THF/DMSO	0° to rt	2.25	(75)
TIPS	H	Ph	Me	H	H	0	DME	0° to rt	1	(65)

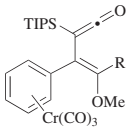
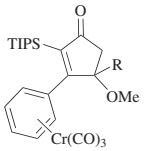
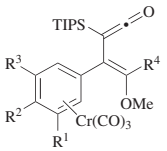
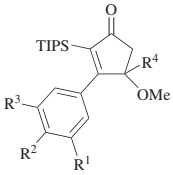
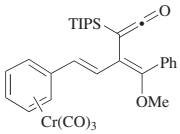
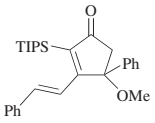
C_8 	 , xylene, reflux, 1–2 h		339
		R MeO (82) *n*-PrS (85)	
C_{8-10} 	CH_2I_2, *n*-BuLi, Et_2O, –78°, 1 h; rt, o/n		341
		R *n*-Bu (60) Ph (40)	
C_{9-11} 	$MeCHBr_2$, *n*-BuLi, Et_2O, –78°, 1 h; rt, o/n		341
		R *n*-Bu (67) $(OC)_3CrC_6H_5$ (93)	
C_{9-15} 	R^3CHX_2, *n*-BuLi, Et_2O, –78°, 1 h; rt, o/n		341

R^1	R^2	R^3	X	
n-Bu	Me	H	I	(55)
n-Bu	Me	Me	Br	(67)
1-naphthyl	Me	H	I	(61)
1-naphthyl	*i*-Pr	H	I	(40)

	CH_2I_2, *n*-BuLi, Et_2O, –78°, 1 h; rt, o/n		341

R^1	R^2	
n-Bu	Me	(55)
1-naphthyl	Me	(61)
1-naphthyl	*i*-Pr	(40)

TABLE 10. CARBON-NUCLEOPHILE-INITIATED CYCLIZATION REACTIONS OF VINYLKETENES (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11-14} 	CH_2I_2, *n*-BuLi, Et_2O, –78°, 1 h; rt, o/n	 R: Me (93); *n*-Bu (98)	341
C_{11-16} 	CH_2I_2, *n*-BuLi, Et_2O, –78°, 1 h; rt, o/n	 R^1 / R^2 / R^3 / R^4: H / MeO / H / Me (72); MeO / H / MeO / Me (85); –OCH_2O– / H / Me (64); –OCH_2O– / H / *n*-Bu (84); MeO / H / MeO / *n*-Bu (80); MeO / H / MeO / Ph (94)	341
C_{18} 	CH_2I_2, *n*-BuLi, Et_2O, –78°, 1 h; rt, o/n	 (94)	341

[a] This product was the R^3, R^5 *trans* isomer.

TABLE 11. CYCLOADDITIONS OF VINYLKETENES WITH ISOCYANIDES

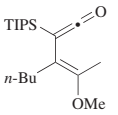
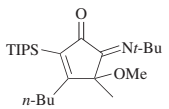
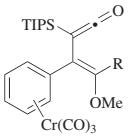
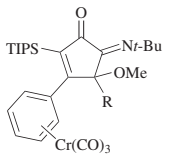
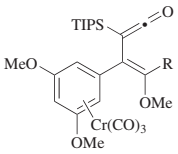
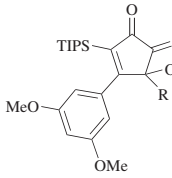
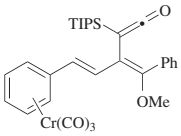
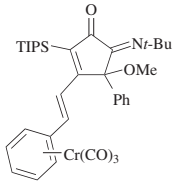
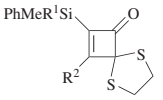
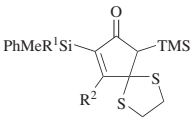
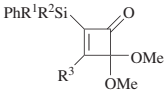
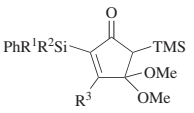
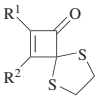
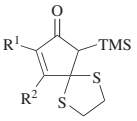
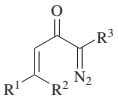
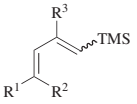
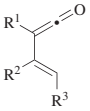
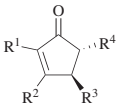
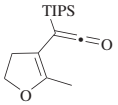
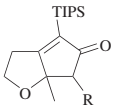
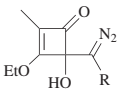
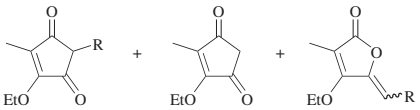
Ketene or Ketene Source	Isocyanide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	$\bar{C}\equiv\overset{+}{N}t$-Bu	THF, reflux, 4 h	 (98)	341
C_{11-14} 	$\bar{C}\equiv\overset{+}{N}t$-Bu	THF, rt, 48 h	 R: Me (95); *n*-Bu (91)	341
	$\bar{C}\equiv\overset{+}{N}t$-Bu	THF, reflux, 4 h	 R: Me (98); *n*-Bu (76)	341
C_{18} 	$\bar{C}\equiv\overset{+}{N}t$-Bu	THF, reflux, 4 h	 (73)	341

TABLE 12. DIAZOALKANE-INITIATED CYCLIZATION REACTIONS OF VINYLKETENES

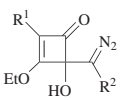
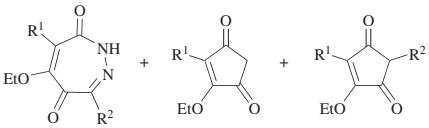
Ketene or Ketene Source	Diazoalkane	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-10} 		Toluene, 95°, 12 h		27
			R^1 R^2 Me MeO (74) Ph MeO (trace) Me Me (74) Me Ph (50)	
		Toluene, 95°, 12 h		27
			R^1 R^2 R^3 Me Me MeO (51) Me Ph MeO (54) Ph Me Me (trace) Me Me Ph (77)	
		Toluene, 95°	 R^1 = MeO, Me, Ph, R_3Si R^2 = MeO, Me (84–96)[a]	342
C_{5-10} 		1. $Rh_2(OAc)_4$, benzene, heat 2. Add $TMSCHN_2$, rt		343
			R^1 R^2 R^3 Me H $(MeO)_2(O)P$ (69) Ph H $(MeO)_2(O)P$ (74) Ph H PhO_2S (71) Ph MeO $(MeO)_2(O)P$ (62)	
C_{6-10} 		See table.		340

R^1	R^2	R^3	R^4	Solvent	Temp	Time (h)	
TIPS	Me	Me	H	CH_2Cl_2	–120° to rt	3	(96)
TIPS	Me	Me	TMS	CH_2Cl_2/hexane	rt	21–32	(84–92)
TES	Me	Me	TMS	CH_2Cl_2/hexane	rt	21–32	(95)
TIPS	H	Ph	TMS	CH_2Cl_2	rt	21–32	(81)

Ketene or Ketene Source	Diazoalkane	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 		Et_2O, 0° to rt, 18 h		344
			R TMS (73) Ph (76)	
C_{7-13} 	—	Promoter, CH_2Cl_2		345

I **II** **III**

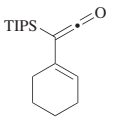
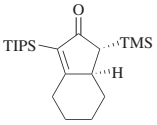
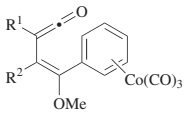
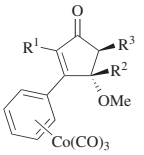
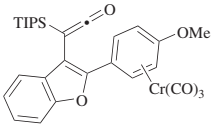
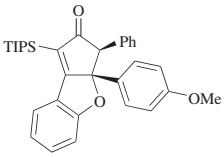
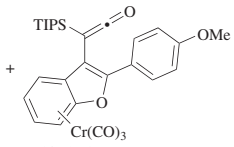
R	Promoter	Temp	Time (h)	I	II	III	(*E*)/(*Z*) III
t-BuO_2C	$TiCl_4$	0°	0.5	(—)	(18)	(—)	—
t-BuO_2C	TFA	0°	0.5	(—)	(50)	(23)	58:42
t-BuO_2C	TMSOTf	rt	0.5	(—)	(42)	(36)	73:27
t-BuO_2C	$Rh_2(OAc)_4$	0°	0.5	(—)	(77)	(6)	0:100
t-BuO_2C	*h*ν	rt	19	(—)	(45)	(14)	75:25
EtO_2C	TFA	0°	0.5	(—)	(—)	(51)	50:50
EtO_2C	TMSOTf	rt	0.5	(—)	(—)	(58)	75:25
EtO_2C	$Rh_2(OAc)_4$	0°	0.5	(69)	(17)	(—)	—
PhCO	TFA	0°	0.5	(83)	(—)	(—)	—
PhCO	TMSOTf	rt	0.5	(50)	(—)	(47)	64:36
PhCO	$Rh_2(OAc)_4$	0°	0.5	(70)	(—)	(—)	—

	—	*p*-Xylene, reflux, 2 h		345

I **II** **III**

R^1	R^2	I	II	III
Me	EtO_2C	(46)	(—)	(—)
Me	*t*-BuO_2C	(56)	(—)	(—)
n-Bu	*t*-BuO_2C	(44)	(16)	(—)
Ph	*t*-BuO_2C	(—)	(46)	(—)
Me	PhCO	(24)	(—)	(24)

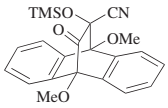
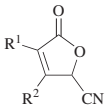
TABLE 12. DIAZOALKANE-INITIATED CYCLIZATION REACTIONS OF VINYLKETENES (*Continued*)

Ketene or Ketene Source	Diazoalkane	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 		CH_2Cl_2, hexane, rt, 21–32 h	 (83)	340
C_{11-16} 		Et_2O, rt, 12 h		346
C_{16} 		1. Et_2O, 0° to rt, 18 h 2. CAN, MeOH, 0° to rt, 0.5 h	 (81)	344
 unpurified mixture				

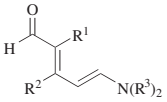
R^1	R^2	R^3	
TIPS	Me	H	(84)
TIPS	Me	TMS	(93)
TIPS	Me	Ph	(80)
TIPS	*n*-Bu	H	(83)
TIPS	*n*-Bu	TMS	(79)
TIPS	*n*-Bu	Ph	(83)
TIPS	Ph	H	(72)
TIPS	Ph	TMS	(62)
TIPS	Ph	Ph	(73)
TBS	Ph	H	(70)
TBS	Ph	TMS	(86)
TBS	Ph	Ph	(76)
TIPS	4-$MeOC_6H_4$	Ph	(77)

[a] No additional information was provided in the publication.

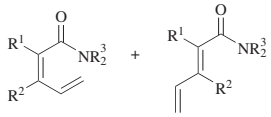
TABLE 13. HETEROATOM-INITIATED CYCLIZATION REACTIONS OF VINYLKETENES

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	$R^1{\equiv}R^2$, 1,2-$Cl_2C_6H_4$, sealed tube, 220°, 48–72 h		177

R^1	R^2	
Me	Ph	(74)
Ph	Ph	(67)
Bn	Bn	(73)

$C_{5–11}$ 

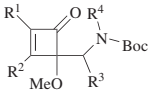
1,2-$Cl_2C_6H_4$, microwave, 200–220°



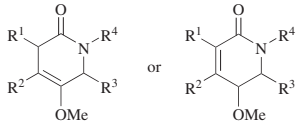
I **II** (—)

R^1	R^2	R^3_2N	**I**	**I/II**
H	H	Me_2N	(39)	>20:1
H	H	PhMeN	(79)	>20:1
H	H	Bn_2N	(61)	7:1
Me	H	Me_2N	(87)	10:1
H	Me	Me_2N	(62)	>20:1
Me	H	4-morpholinyl	(75)	>20:1
Ph	H	Me_2N	(76)	>20:1
H	Ph	Me_2N	(78)	>20:1

28

$C_{6–17}$ 

1. TFA, CH_2Cl_2, rt, 2 h
2. Neat, 155–160°, 2–3 h



I **II**

R^1	R^2	R^3	R^4	**I**	**II**
Me	*i*-PrO	H	Me	(75)	(—)
t-Bu	*i*-PrO	H	Me	(87)	(—)
Et	Et	H	Me	(71)	(—)
Et	Et	EtO_2C	Me	(32)	(—)
Ph	*i*-PrO	H	Me	(86)	(—)
Ph	Me_2N	H	Me	(—)	(89)
Ph	*i*-PrO	EtO_2C	Me	(73)	(—)
Ph	Me_2N	Ph	Bn	(—)	(83)

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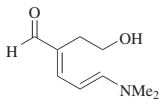
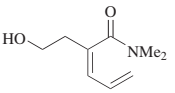
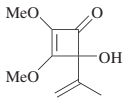
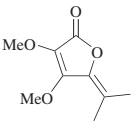
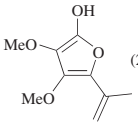
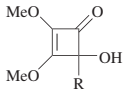
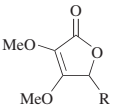
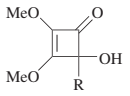
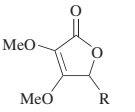
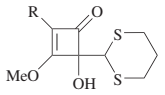
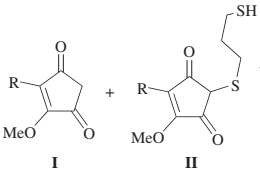
TABLE 13. HETEROATOM-INITIATED CYCLIZATION REACTIONS OF VINYLKETENES (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	1,2-$Cl_2C_6H_4$, 200°	 (54)	82
	*hν*, THF, 0°, 2.5 h	 (33) +  (22)	348
$C_{8–10}$ 	*hν*, THF, 0°		348

R	Time (h)	
t-Bu	5.5	(39)
2-furyl	4	(60)
2-thienyl	1.5	(37)
Ph	4	(27)
2-$MeOC_6H_4$	2.5	(51)

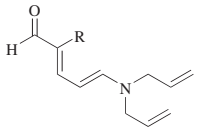
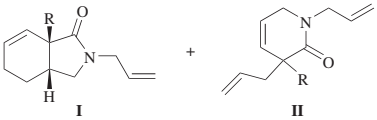
$C_{8–14}$ 	*hν* (9 W lamp, 280–370 nm), MeCN, continuous flow, rt, 1.5 h		49

R	
n-Bu	(95)
t-Bu	(96)
3-pyridinyl	(94)
Ph	(99)
2-$MeOC_6H_4$	(97)
4-$TMSC_6H_4$	(93)
Ph—≡	(95)
4-*t*-BuC_6H_4	(92)

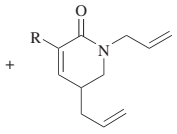
 *p*-Xylene, reflux 

I **II**

R	Time (h)	I	II	Refs.
MeO	60	(77)	(—)	349
MeO	2	(—)	(48)	
n-Bu	2	(—)	(79)	
Ph	3	(60)	(—)	

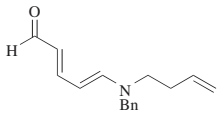
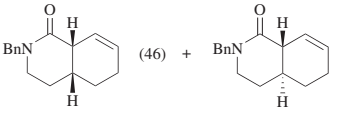
$C_{8–9}$  1,2-$Cl_2C_6H_4$, microwave, 200°  84

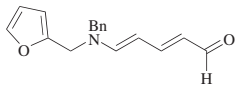
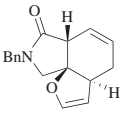
I **II**

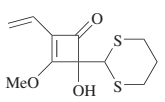
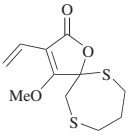


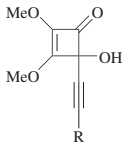
III

R	Time (h)	I	II	III
H	4	(48)	(3)	(0)
Me	8	(60)	(0)	(15)

C_9  1,2-$Cl_2C_6H_4$, microwave, 200°, 1 h  84

C_{10}  1,2-$Cl_2C_6H_4$, microwave, 200°, 4 h  (76) 84

 *p*-Xylene, reflux, 3 h  (90) 349

$C_{10–13}$ 

R	Time (h)	
n-Bu	2.5	(50)
Ph	4	(28)
Bn	2	(52)

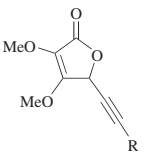
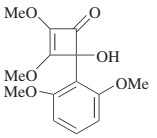
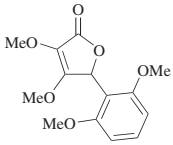
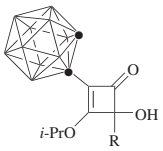
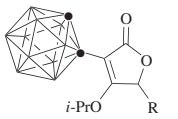
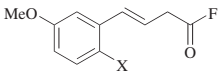
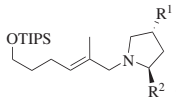
hν, THF, 0°  348, 26

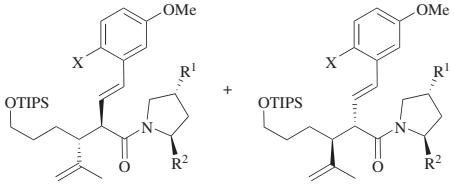
TABLE 13. HETEROATOM-INITIATED CYCLIZATION REACTIONS OF VINYLKETENES (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	1. *p*-Xylene, reflux, 14 h 2. Silica gel, CH_2Cl_2, rt, 2 h	 (70)	133
C_{10-12} 	*p*-Xylene, reflux, 1 h	 (—)[a]	359

R
2-furyl
2-thienyl
Ph
2-$MeOC_6H_4$

C_{10} 

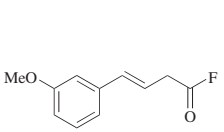
 (0.67 eq), Me_3Al (2.0 eq), Na_2CO_3, CH_2Cl_2, toluene, 6 h

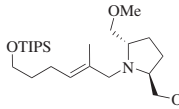


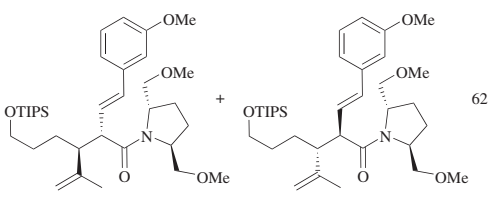
I **II**

X	R^1	R^2	Temp (°)	**I + II**[b]	**I/II**
H	H	$TBSOCH_2$	0	(63)[c]	>2:1
H	H	MeO_2C	0	(97)	1:1
H	MeO	$MeOCH_2$	0	(86)	3:1
H	MeO	$MeOCH_2$	–20	(80)	3.8:1
H	MeO	*t*-$BuOCH_2$	0	(85)	2.9:1
H	MeO	*t*-$BuOCH_2$	–20	(86)	3.7:1
H	*t*-BuO	$MeOCH_2$	0	(99)	5.3:1
H	*t*-BuO	$MeOCH_2$	–20	(92)	5.6:1
H	*t*-BuO	$MeOCH_2$	–50	(68)[d]	6.0:1
H	*t*-BuO	*t*-$BuOCH_2$	0	(96)	3.9:1
H	*t*-BuO	*t*-$BuOCH_2$	–20	(96)	4.0:1
H	*t*-BuO	$PhOCH_2$	0	(88)	4.8:1
H	*t*-BuO	$PhOCH_2$	–20	(92)	7.5:1
H	TIPSO	MeO_2C	0	(100)	4.5:1
Br	MOMO	$MeOCH_2$	0	(100)	3.2:1
Br	MOMO	$MOMOCH_2$	0	(95)	2.8:1
Br	MOMO	$TIPSOCH_2$	0	(45)	1.5:1

62



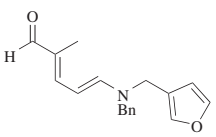
 (0.67 eq), Me_3Al (2.0 eq), Na_2CO_3, CH_2Cl_2, toluene, 6 h



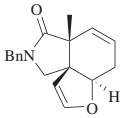
I **II**

Temp (°)	**I + II**	**I/II**
0	(67)	7.7:1
–20	(71)	11.2:1

62

C_{11} 

1,2-$Cl_2C_6H_4$, microwave, 200°, 4 h

 (76)

84

TABLE 13. HETEROATOM-INITIATED CYCLIZATION REACTIONS OF VINYLKETENES (*Continued*)

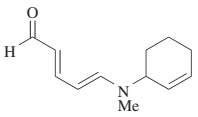
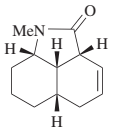
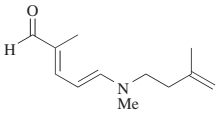
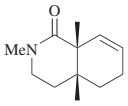
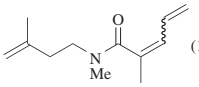
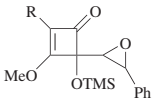
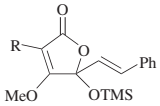
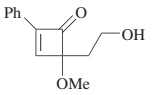
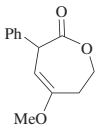
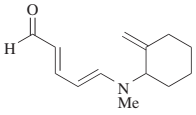
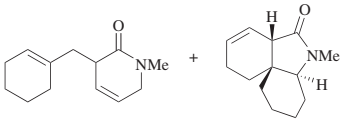
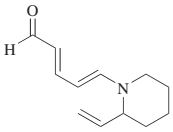
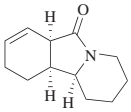
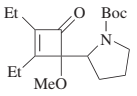
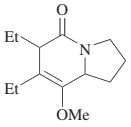
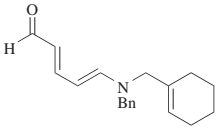
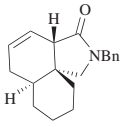
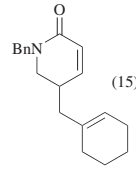
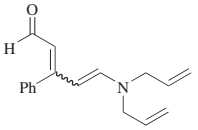
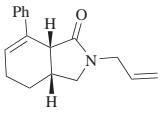
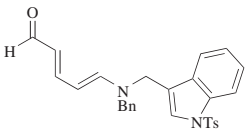
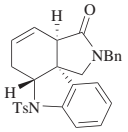
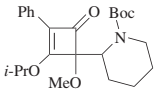
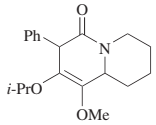
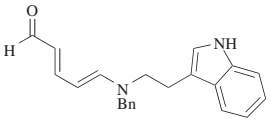
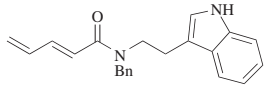
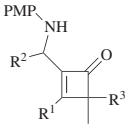
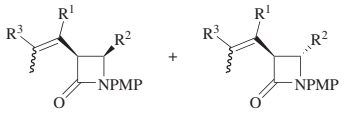
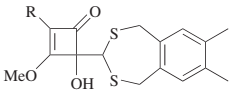
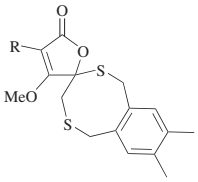
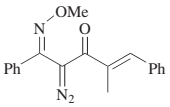
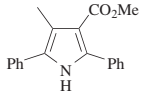
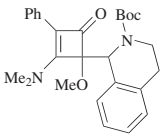
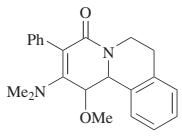
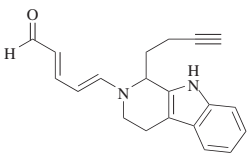
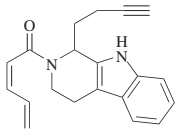
Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
	1,2-$Cl_2C_6H_4$, microwave, 200°, 2 h	 (65)	84
	1,2-$Cl_2C_6H_4$, microwave, 230°, 17 h	 (47) +  (14) mixture of isomers	84
C_{12-18}			
	*p*-Xylene, reflux, 5 h		349
		R | (MeO 90) | (Ph 87)	
C_{12}			
	Benzene, reflux, 7 h	 (60)	350
	1,2-$Cl_2C_6H_4$, microwave, 200°, 2 h		84
		I **II**	
		I + **II** (61), **I/II** = 2:1	
	1,2-$Cl_2C_6H_4$, microwave, 200°, 4 h	 + stereoisomer + stereoisomer **II** **III**	84
		I **I** + **II** + **III** (82), **I/II/III** = 4:2:1	
	1. TFA, CH_2Cl_2, rt, 2 h 2. Neat, 155–160°, 2.5 h	 (80)	347
	1,2-$Cl_2C_6H_4$, microwave, 200°, 4 h	 (52) +  (15)	84
C_{14}			
	1,2-$Cl_2C_6H_4$, microwave, 200°, 1 h	 (73)	84
	1,2-$Cl_2C_6H_4$, microwave, 200°, 4 h	 (30)	84

TABLE 13. HETEROATOM-INITIATED CYCLIZATION REACTIONS OF VINYLKETENES (*Continued*)

Ketene or Ketene Source	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	1. TFA, CH_2Cl_2, rt, 2 h 2. Neat, 155–160°, 2.5 h	 (68)	347
	1,2-$Cl_2C_6H_4$, microwave, >150°	 (—)	351
$C_{17–23}$			
	Octane, 110°	 **I** + **II**	352

R^1	R^2	R^3	Time (h)	**I + II**	**I/II**
Ph	2-furyl	Me	48	(76)	74:26
Ph	2-thienyl	Me	48	(89)	79:21
Ph	Ph	EtS	48	(65)	80:20
Ph	Ph	Me	24	(61)	80:20
Ph	1-naphthyl	Me	40	(69)	75:25
1-naphthyl	Ph	Me	48	(51)	79:21

$C_{17–21}$				
	*p*-Xylene, reflux, 3 h		R CH_2=CH (91) Ph (71)	349

C_{19}				
	$Rh_2(OAc)_4$, toluene, 110°	 (90)		353
	1. TFA, CH_2Cl_2, rt, 2 h 2. Neat, 155–160°, 2.5 h	 (40)		347
C_{20}				
	1,2-$Cl_2C_6H_4$, microwave, 160°	 (—)		28

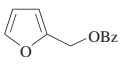
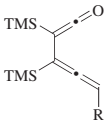
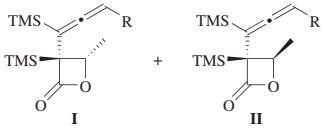
[a] The yield is described as "fair to good".

[b] This represents the total yield of products and includes small amounts (1 to <10% of the total) of the two isomeric 2,3-*syn* diastereoisomers.

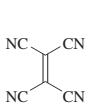
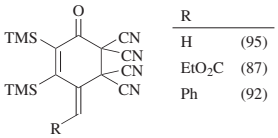
[c] This represents the yield of pure diastereoisomer **I**.

[d] The reaction was incomplete. This yield is based on recovered starting material.

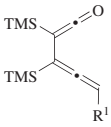
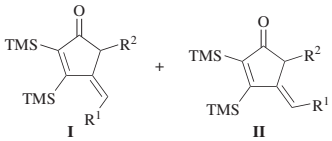
TABLE 14. CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF ALLENYLKETENES

Ketene or Ketene Source	Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	—	FVP, 600–700°, collect at –196°; then $CHCl_3$, –10°	 (40)	164
$C_{5–11}$ 		BF_3•Et_2O, CH_2Cl_2, rt, 1 h	 **I** + **II**	169

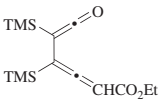
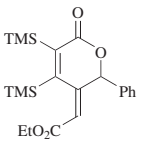
R	I + II	I/II
H	(88)	11:1
EtO_2C	(94)	9:1
Ph	(89)	9:1

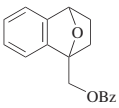
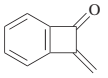
		CH_2Cl_2, rt, 8 h		169

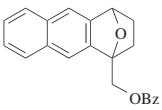
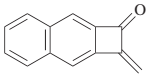
R	
H	(95)
EtO_2C	(87)
Ph	(92)

		Et_2O, rt, 12–24 h	 **I** + **II**	169

R^1	R^2	I	II
H	TMS	(83)	(–)
EtO_2C	H	(42)	(32)
Ph	H	(34)	(32)

C_6   BF_3•Et_2O, CH_2Cl_2, rt, 1 h  (43) 169

C_{11}  — FVP, 600°  (17) 167

C_{15}  — FVP, 550°  (48) 166

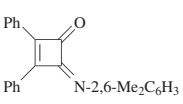
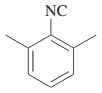
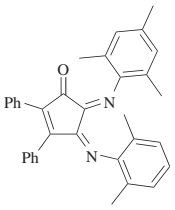
C_{16}   *h*ν, benzene, 15°  (80) 170

TABLE 15. CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF ALKYNYLKETENES

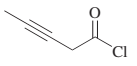
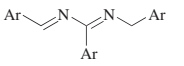
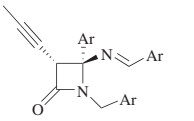
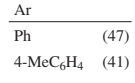
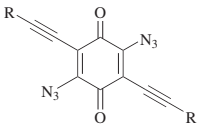
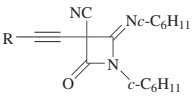
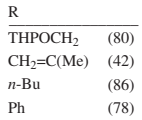
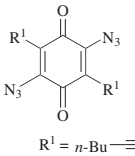
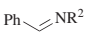
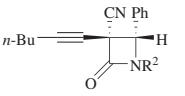
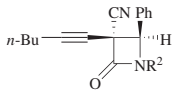
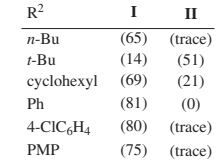
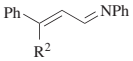
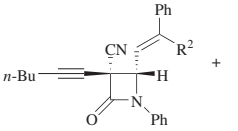
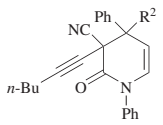
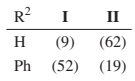
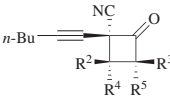
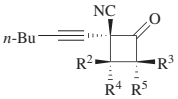
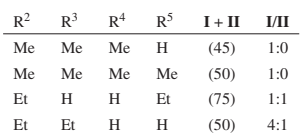
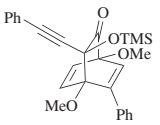
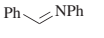
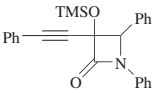
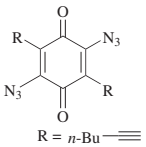
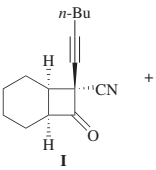
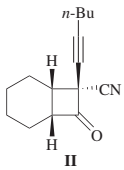
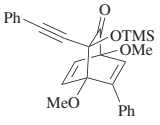
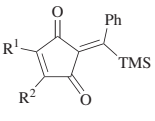
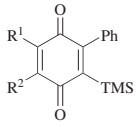
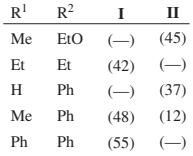
Ketene or Ketene Source	Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 		$(n\text{-Bu})_3N$, toluene, rt	 	181
C_{6-13} 	$c\text{-}C_6H_{11}N{=}\bullet{=}Nc\text{-}C_6H_{11}$	CCl_4, reflux, 1.5 h	 	178
C_9  $R^1 = n\text{-Bu}{-}{\equiv}$		Benzene, reflux, 3 h	 +  **I** **II** 	180
		Benzene, reflux, 3 h	 +  **I** **II** 	180
		Benzene, reflux, 4 h	 +  **I** **II** 	178
C_{10} 		Xylenes, reflux, 8 h	 (72)	124
C_9  $R = n\text{-Bu}{-}{\equiv}$		Benzene, reflux, 4 h	 +  **I** **II** **I + II** (44), **I/II** = 4:1	178
C_{10} 	$R^1{-}{\equiv}{-}R^2$	Xylenes, reflux, 8 h	 +  **I** **II** 	182

TABLE 15. CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF ALKYNYLKETENES (*Continued*)

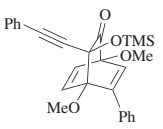
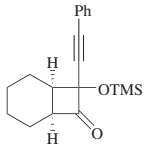
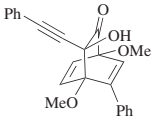
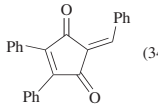
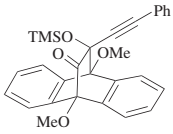
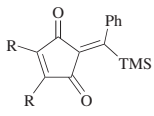
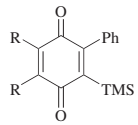
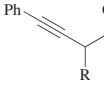
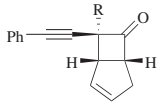
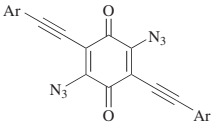
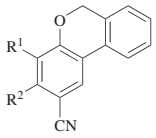
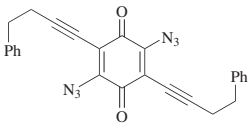
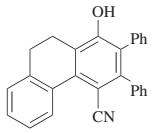
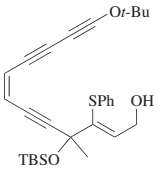
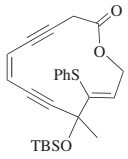
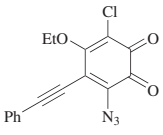
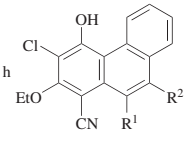
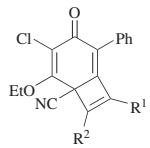
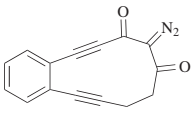
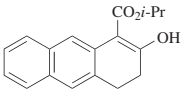
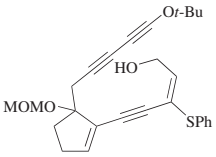
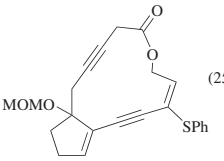
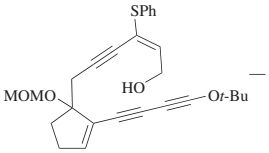
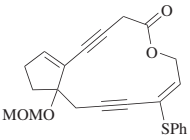
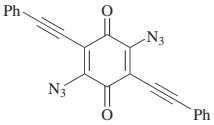
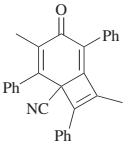
Ketene or Ketene Source	Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 		*p*-Xylene, reflux, 8 h	 (50)	124
	Ph—≡—Ph	Xylenes, reflux, 8 h	 (34)	182
	R—≡—R	*p*-Xylene, sealed tube, 220°, 48 h	 **I** +  **II**	177
			R **I** **II** *n*-Bu (54) (12) Ph (70) (—)	
C_{11-14} 		Et_3N, pentane, 0° to rt, 4 h		175
			R (74) Me (45) Et (88) *i*-Pr (77) *t*-Bu	
C_{12}  Ar = 2-MeC_6H_4		R^1—≡—R^2, CCl_4, reflux		78
			R^1 R^2 Time (h) Me EtO 3 (58) Et Et 2 (29) H Ph 2 (19) Ph Ph 3 (68)	
C_{13} 		Ph—≡—Ph, CCl_4, reflux, 1.5 h	 (40)	78
	—	Et_3N, benzene, reflux	 (60)	354
		R^1—≡—R^2, CCl_4, reflux, 4 h	 **I** +  **II**	78
			R^1 R^2 **I** **II** Me EtO (39) (—) H *n*-Bu (10) (—) Et Et (—) (46) H Ph (60) (3) Me Ph (5) (58) Ph Ph (—) (35)	

TABLE 15. CYCLOADDITIONS AND ELECTROCYCLIZATIONS OF ALKYNYLKETENES (*Continued*)

Ketene or Ketene Source	Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}				
	—	*hν*, 1,4-cyclohexadiene, *i*-PrOH, 10°, 17 h	 (31)	183, 184
	—	Et_3N, benzene, reflux	 (25)	354
	—	Et_3N, benzene, reflux	 (45)	354
C_{22}				
		, benzene, reflux, 4 h	 (40)	78

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CHAPTER 3

CARBOZINCATION REACTIONS OF CARBON–CARBON MULTIPLE BONDS

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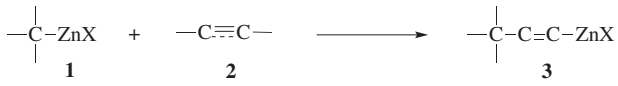
INTRODUCTION

Since the first carbometalation reaction was discovered in the pioneering studies of Ziegler and Bähr[1], an ever-increasing number of additions of organometallic reagents to carbon–carbon multiple bonds has been reported.[2–9] Carbozincations involve the addition of the carbon–zinc bond of an organozinc reagent **1** across a carbon–carbon multiple bond **2**, leading to a new organozinc species **3**, in which the newly formed carbon–metal bond can be used for further transformations (Scheme 1). To be synthetically useful, the newly formed organozinc species **3** must have reactivity different from that of zinc species **1** to avoid the polymerization of the carbometalated product. Therefore, the carbometalating ability of the organozinc reagent **1** must be higher than that of product **3**, except for intramolecular carbometalation reactions, in which entropy factors favor mono-addition even if starting organozinc derivatives and the products have similar reactivities. Addition of organozinc reagents to alkenes and alkynes activated by electron-withdrawing groups is not covered in this chapter as they are best considered conjugate additions. As the addition of organozinc reagents across carbon–carbon multiple bonds depends critically on the structure of the substrates and of the organozinc species, this chapter is divided into two sections, namely the carbozincation of alkynes and alkenes, and

each of these sections is organized so that the following representative classes of reagents may be distinguished: alkylzinc reagents that exhibit low intrinsic reactivity, followed by allylic and allenic/propargylic organozinc reagents, and finally zinc enolates and aza-enolates that display unique behavior in carbozincations. One of the most distinguishing features of organozinc reagents is their ability to undergo several transmetalation reactions with transition-metal complexes leading to further functionalization.[10−13] Transition metal promoted or catalyzed additions to alkenes and alkynes are also included in this chapter as they still conform to the general definition of carbozincations (Scheme 1), even though the active species itself is not an organozinc reagent.[8,10,14]



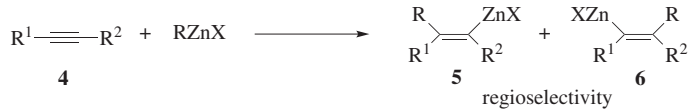
Scheme 1

Di-*tert*-butyl- and diallylzinc species are able to add to alkenes and alkynes, whereas other types of organozinc derivatives are usually inert toward non-functionalized multiple carbon–carbon bonds.[7] In marked contrast, allylic zinc halides add readily to alkenyl and alkynyl organometallic derivatives under mild conditions to give sp^3 and sp^2 1,1-diorganometallic species, respectively.[15,16] Interestingly, zinc malonates add to various alkynes in fair yields.[17]

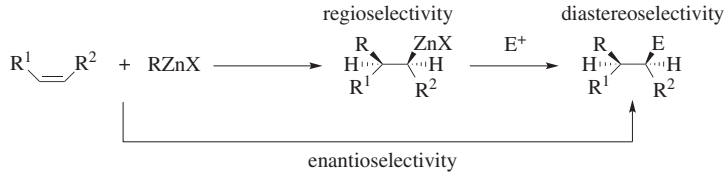
This chapter treats only relevant examples that are specifically used for the preparation of organozinc derivatives undergoing further carbozincation reactions. The literature has been covered to April 2013.

MECHANISM AND STEREOCHEMISTRY

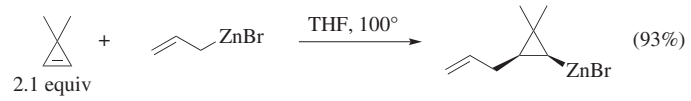
The addition of an organozinc species to an alkyne is usually a *syn* process, leading to a unique stereoisomer. However, if the carbozincation is performed on an unsymmetrical alkyne such as **4**, two constitutional isomers **5** and **6** may be obtained (Scheme 2). The ratio of products **5** and **6** depends on the nature of the organometallic species, the organic substrate, and the reaction conditions used. If the carbozincation is performed on a 1,2-disubstituted alkene, two constitutional isomers may also be obtained, and after reaction with an electrophile, two sp^3 stereogenic centers are created (Scheme 3). For a process of this type to become a powerful reaction in organic synthesis, it is necessary to control the regio- and diastereoselectivities of such carbozincations. Diastereoselective reactions require the control of the configurational stability of sp^3 organometallic derivatives and their reactions toward electrophiles. Moreover, if an efficient method were available to render such an asymmetric process, it would acquire significant utility as a method for the creation of vicinal carbon stereogenic centers (Scheme 3).[9] However, the *syn* or the *anti* character of the addition of organozinc derivatives to alkenes has not yet been rigorously established. Only in the case of cyclopropenes, which lead after carbozincation to configurationally stable cyclopropylzinc derivatives, is a *syn* addition always observed (Scheme 4).[18]



Scheme 2



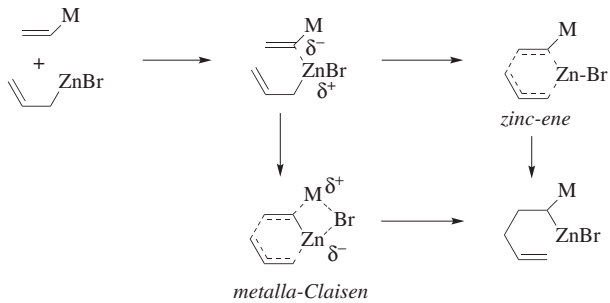
Scheme 3



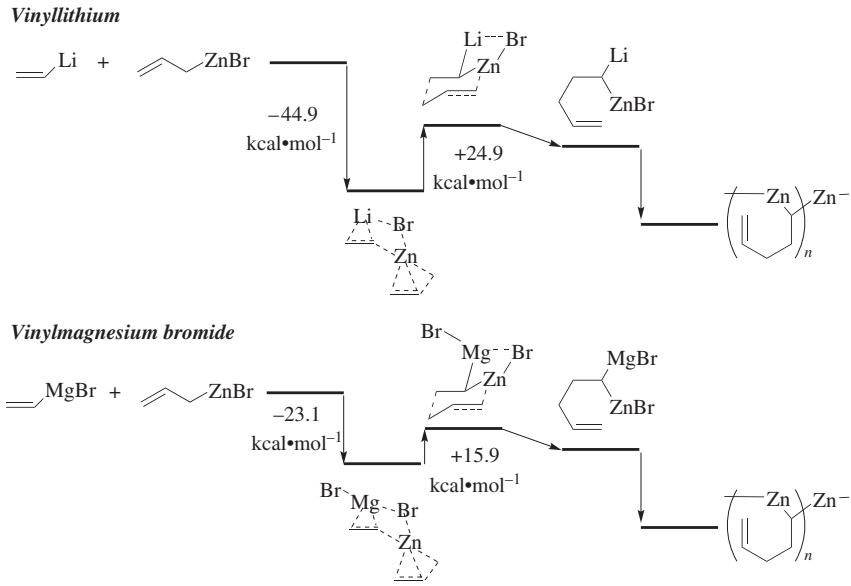
Scheme 4

Allylzinc bromide adds to a large variety of alkenyl and alkynyl metal species to give sp^3 and sp^2 bismetalated species, respectively (Scheme 5).[15,16] Whereas the calculated potential energy surface for the addition of allylzinc bromide to ethylene reveals that the formation of the initial complex is endothermic with no favorable pre-organization of the reactants, allylzinc bromide and vinyllithium (or vinylmagnesium bromide) form a rather strong complex, bringing the reactants in close contact through the square-planar arrangement of the Li–C–Zn–Br or Mg–C–Zn–Br atoms.[19] This initial pre-complexation is strongly exothermic. Owing to an initial rapid transmetalation, vinyllithium (or vinylmagnesium bromide) and allylzinc bromide, or the reverse combination of vinylzinc bromide and allyllithium (or allylmagnesium bromide) lead to the same complex in what constitutes the key step of the reaction, as the metalated carbon of the vinylmetal is already attached to zinc.[19–21] The calculated activation barriers for allylzincation of vinyllithium and vinylmagnesium bromide are 24.9 kcal•mol^{-1} and 15.9 kcal•mol^{-1}, respectively, although the latter is inferior because of a less exothermic initial pre-complexation (Scheme 6).[19] Whereas the formation of the initial heterodimetallic species appears to be endothermic, the overall driving force of the reaction derives from the formation of linear or cyclic 1,1-dizinc-oligomers, presumably trimers or tetramers, which display considerable stabilization due to the formation of stable carbon–zinc bonds.[20,21] Although a [3,3]-sigmatropic rearrangement of an allyl alkenylzinc species, initially generated by rapid transmetalation, is a chemically unlikely and energetically unfavorable process as it would generate a zinc alkylidene carbene, theoretical calculations indicate that placing a molecule of $MgCl_2$ close to the metalated carbon in a vinyl allylzinc species results in a dramatic drop of the activation energy.[20,21] This outcome

arises because of the stabilization of the developing negative charge on this carbon by the magnesium atom. The addition proceeds through a late, six-centered, chair-like transition state (fused to a four-centered μ-halo bridge) and is conveniently described as a magnesium-assisted metalla-Claisen rearrangement.[15] Some similarities can be drawn to a metallo-ene reaction between an allylic organozinc reagent and an alkenylmetal. In fact, as the carbon–metal bond of the vinylmetal becomes more ionic, the rate of the reaction increases.[21] With a carbon–magnesium bond, transmetalation to an allyl alkenylzinc species occurs and a magnesium-assisted metallo-Claisen rearrangement may then operate. These two initially different processes lead to the same regioselectivity and may be in fact indistinguishable at the transition state (Scheme 5).



Scheme 5

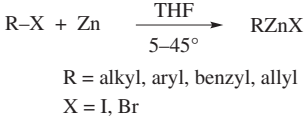


Scheme 6

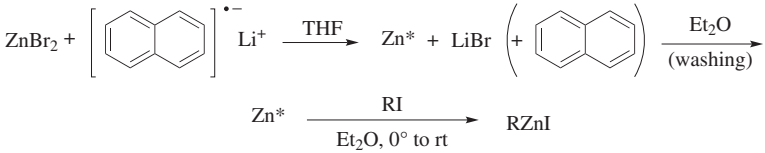
SCOPE AND LIMITATIONS

Preparation of Organozinc Precursors

A large variety of methods are known for the preparation of organozinc compounds.[13,22] The insertion of zinc metal into organic halides is the most general method for the preparation of organozinc halides. The reaction is sensitive to the reaction conditions (solvent, concentration, temperature), to the nature of the organic halide, and to the method of zinc activation. Whereas several solvent systems can be used, performing the reaction in THF as originally described is usually the most convenient method (Scheme 7).[23] However, polarity of the medium plays an important role in carbozincation reactions and the more polar the solvent, the less efficient the addition of the organozinc derivatives across the unsaturated carbon–carbon multiple bonds. Therefore, insertion of zinc into carbon–iodine bonds requires solvents such as diethyl ether that are less polar than THF. For this purpose, a particularly reactive zinc powder is prepared by reducing zinc bromide with lithium napthalenide in THF (Scheme 8).[24] The highly reactive zinc produced by this reaction is washed several times with anhydrous ether to remove the lithium bromide and naphthalene and allows the easy oxidative insertion of alkyl iodides in ether.[25]



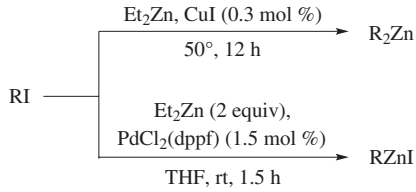
Scheme 7



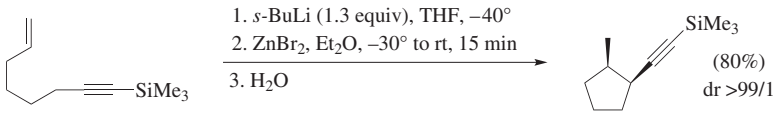
Scheme 8

Diorganozincs are also an important class of reagents because they are usually more reactive than organozinc halides.[10] An iodine–zinc exchange reaction is the most practical way for preparing them from an alkyl iodide and dialkylzinc, followed by removal of the volatile alkyl iodide. Without any catalyst, the reaction requires a large excess of Et_2Zn (3–5 equivalents) and long reaction times.[26] On the other hand, the addition of a catalytic amount of a copper(I) salt, such as CuI or CuCN, speeds up the reaction considerably.[27] This method provides general access to functionalized dialkylzincs and has been used in various carbocyclization reactions (Scheme 9).[28] The use of palladium or nickel catalysts is also extremely efficient but produces an organozinc iodide instead of a dialkylzinc, with evolution of ethane and ethylene (Scheme 9).[29] When the Pd-catalyzed exchange protocol is applied to γ-alkenyliodides, the cyclized organozinc reagents are obtained directly and may be

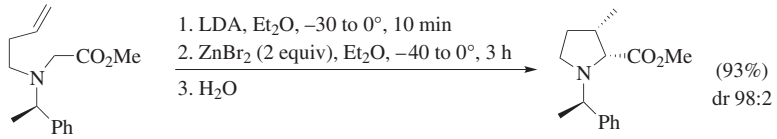
further functionalized.[30] The transmetalation reaction of alkyllithiums or alkylmagnesium halides with zinc salts to provide organozinc species is also a powerful method for the preparation of the carbozincation precursors.[22] These methods are used extensively for the preparation of propargyl/allenylzinc species[31] as well as for the preparation of zinc enolates generated from the corresponding lithium enolates.[32] In the two examples shown in Scheme 10[3] and Scheme 11,[4] the carbozincation reaction occurs smoothly. More recent developments show that propargyl/allenylzinc bromides can be prepared by a new zinc-promoted Brook rearrangement followed by the ene-allene carbozincation reaction (Scheme 12).[33]



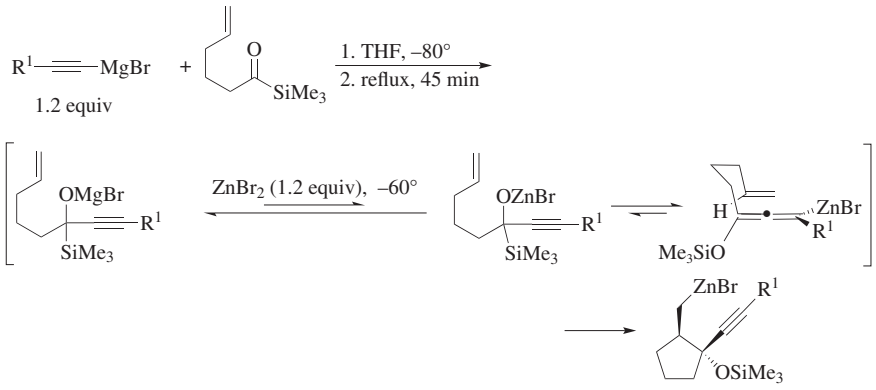
Scheme 9



Scheme 10

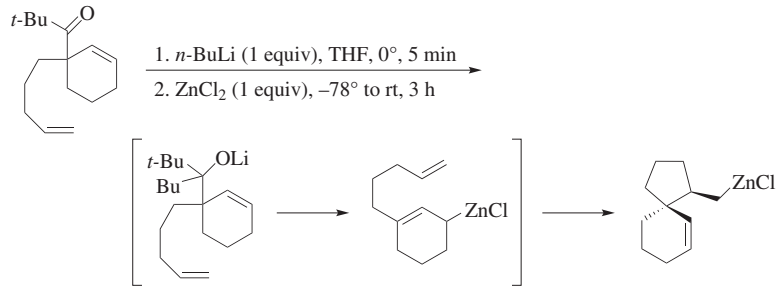


Scheme 11

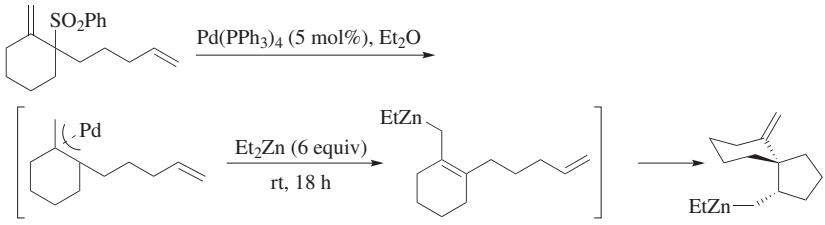


Scheme 12

Substituted allylic zinc reagents are usually difficult to prepare by direct zinc metal insertion because of extensive formation of Wurtz-coupling-homocoupling products. This problem can be solved by two different approaches. The first one entails the fragmentation of zinc homoallylic alcoholates with concomitant formation of allylzinc derivatives, which undergo intramolecular ene-reactions as shown in Scheme 13.[13,34] The second one consists of the use of a π-allylpalladium complex as a nucleophile via an alkyl–allyl exchange reaction with alkylzinc (Scheme 14).[35–39]



Scheme 13



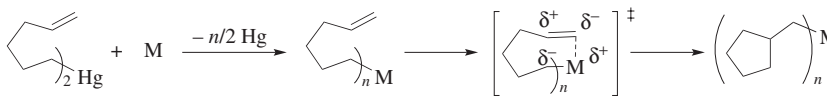
Scheme 14

Chemoselectivity

Although the carbon–zinc bond in Et_2Zn has a dissociation energy of only 34.5 kcal/mol,[40] it has a highly covalent character (~85%) because of the similar electronegativities of zinc and carbon,[41] which is comparable to the carbon–tin bond. The carbon–zinc bond is therefore inert to moderately polar electrophiles such as aldehydes, ketones, esters, or nitriles,[10] but not to carbon–carbon multiple bonds. On the other hand, the presence of empty low-lying orbitals at the zinc center allows transmetalations with a number of transition-metal complexes.[10,42]

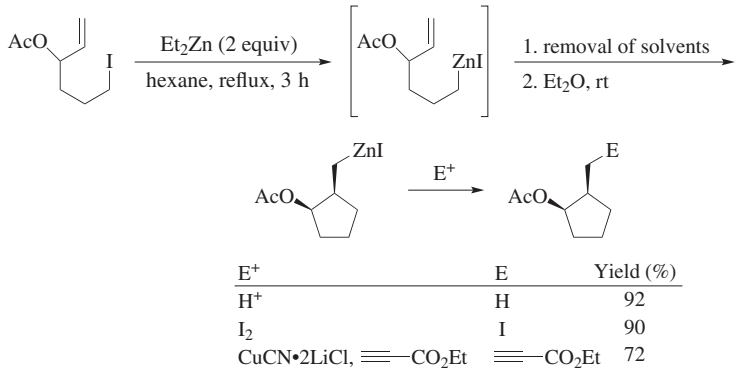
Cyclization reactions of 5-hexenylzincs proceed with relative ease compared to the analogous intermolecular carbozincations and constitute an interesting entry into five- and six-membered ring systems. Reductive metal-exchange reactions applied to bis(5-hexenyl)mercury are used to prepare various 5-hexenylmetals and their propensity to cyclize to the corresponding methylenecyclopentanes has been evaluated (Scheme 15).[43] The observed order of reactivity, Al > Mg > Li > Zn ≫ Ga,

In ≫ Hg (no cyclization), seems to be affected by the polarity of the carbon–metal bond as well as the availability of a vacant orbital on the metal (Scheme 15).[44] Thus, the zinc–mercury exchange (M = Zn) at 120° for 24 hours quantitatively leads to a 90:10 mixture of open-chain and cyclized organozinc species. After a further 24 hours, di(cyclopentylmethyl)zinc is found to be the major component (90%). By comparison, the rates of Hg/Mg exchange and cyclization (M = Mg) are similar. Di(4-pentenyl)zinc is prepared in the same manner but fails to cyclize to the corresponding four-membered ring organozinc species. However, examination of the ^{1}H NMR chemical shifts of this compound or its complex with 2,2′-bipyridine suggests an intramolecular interaction between the double bond and zinc, resulting in a lower energy conformer.[45,46] Gas-phase electron diffraction studies also support this result.[47] This weak dipole-dipole interaction arises from the inherent polarity of the carbon–zinc bond and the partial negative charge on the terminal alkenyl carbons. Whereas a metal–alkene interaction is not required to interpret the NMR spectral data of di(5-hexenyl)zinc, probably because the chain is not appropriate to accommodate this ground state interaction, it may play a crucial role in the reactive complex leading to the intramolecular carbozincation process. Conversely, the chain is not sufficiently long in the case of di(4-pentenyl)zinc to achieve the requisite conformation for addition to the double bond, but it is favorable for zinc–alkene interaction.[48] A related zinc–alkyne interaction is suggested on the basis of the ^{13}C NMR and Raman spectra of di(4-hexynyl)zinc.[49] Interestingly, addition of coordinating additives such as pyridine prevents the formation of the latter interaction, whereas weaker Lewis bases such as diethyl ether do not. It is worth mentioning that the rates of cyclization of di(5-hexenyl)metals were initially evaluated for the organometallic species but in fact, it was observed that additives could exert a marked influence. Whereas the cyclization of 5-hexenyllithium (M = Li) requires several days in benzene at room temperature, it is complete within less than one hour in ether,[50] probably due to the stabilization of the polar transition state via the solvation of the metal. However, for more covalent organometallic species having a carbon–metal bond of lower intrinsic polarity (M = Al, Zn), a too strongly Lewis basic solvent would be detrimental to the success of the intramolecular carbometalation as it would compete with the double bond for coordination of the metal. Therefore, ether is usually the solvent of choice, but a few examples can be found where THF is also used.



Scheme 15

Finally, one of the unique advantages of carbozincation as compared to reactions involving organolithium or organomagnesium reagents lies in the tolerance of organozinc reagents toward a large variety of functional groups. Organozinc species react preferentially with covalent carbon–carbon double or triple bonds in the presence of polar electrophiles, as shown in Scheme 16.[25,51]

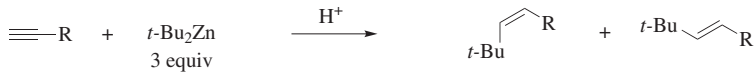


E^+	E	Yield (%)
H^+	H	92
I_2	I	90
CuCN•2LiCl, ≡—CO_2Et	≡—CO_2Et	72

Scheme 16

Carbozincation of Alkynes

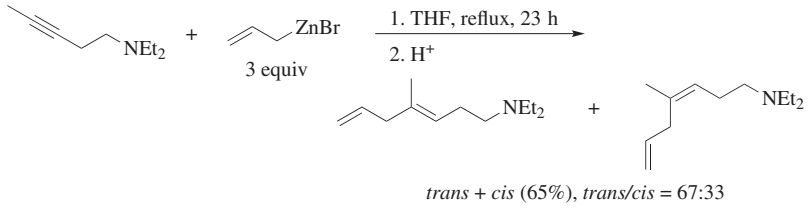
Uncatalyzed Carbozincation Reactions. Only di(*tert*-butyl)zinc and allylzinc species are able to add to alkynes. Di(*tert*-butyl)zinc reacts with a large variety of terminal alkynes, including those bearing functional groups such as alcohols, ethers, acetals, and amines in refluxing THF (Scheme 17),[50] but it does not add to disubstituted alkynes. Although the bulky *tert*-butyl group is always introduced at the less substituted carbon atom, the reaction is not stereoselective and affords mixtures of geometrical isomers in variable ratios, depending on the starting materials. When the addition is performed on conjugated (*E*)- or (*Z*)-enynes in refluxing THF, the reaction is regio- but not stereoselective, most probably due to further isomerization of the carbometalated adduct.[52,53] Phenylacetylene displays a higher reactivity and the addition of *t*-Bu_2Zn in refluxing ether leads to the (*Z*)-alkene through a formally *anti* addition process.[54]



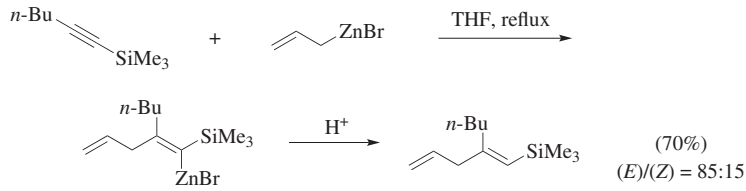
Scheme 17

Terminal alkynes are usually deprotonated by allylic organozinc reagents and the resulting metalated alkynes undergo further addition reactions.[16] Such reactions are described in the next section on carbozincation of metalated alkynes. Allylic organozinc species do not usually react with unactivated disubstituted alkynes.[55] A few exceptions to this general rule are known, particularly when heteroatoms are appropriately located on the carbon skeleton. For instance, allylzinc bromide adds to homopropargylic tertiary amines to provide two geometrical isomers in a 67:33 ratio (Scheme 18).[56] On the other hand, allylzinc bromide reacts regio- and stereoselectively with a variety of 1-(trimethylsilyl)-1-alkynes, with the zinc atom

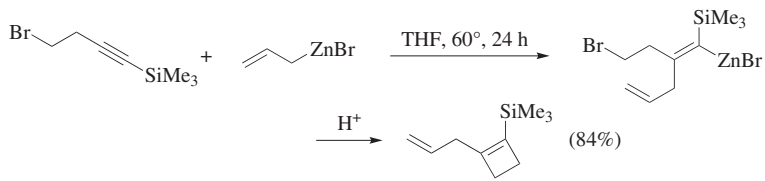
being placed at the carbon bearing the silicon. The stereostructure of the products is determined by the structure of the alkynylsilanes and the reaction conditions (Scheme 19).[57] The authors suggest that the reaction proceeds through a cyclic transition state that leads to the formation of *cis* products. Prolonged reaction times and elevated temperatures, which are required for less reactive substrates, lead to isomerization of the initially formed intermediate and result in a mixture of stereoisomers. The newly formed organozinc species can be functionalized for further synthetic transformations. For example, when the allylzincation is performed on 4-bromo-1-(trimethylsilyl)-1-butyne, 2-allyl-1-(trimethylsilyl)cyclobutene is obtained by a formal *syn* addition followed by an isomerization and further nucleophilic substitution (Scheme 20).[58,59]



Scheme 18



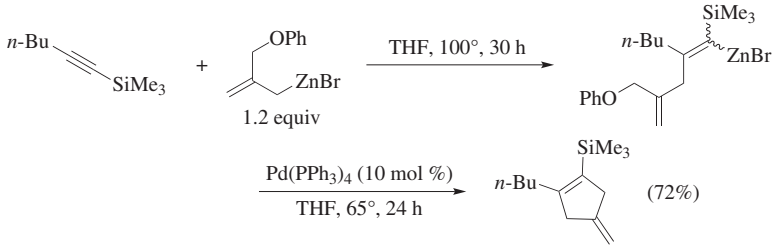
Scheme 19



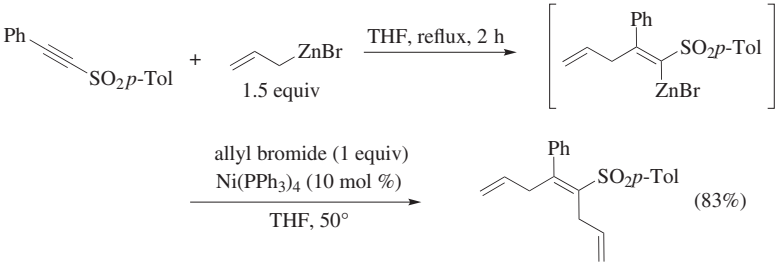
Scheme 20

Alternatively, when 2-phenoxymethyl- and 2-benzyloxymethylallylzinc bromides add to various alkynylsilanes, the initially obtained carbometalated products can be converted easily into 4-methylenecyclopentenes (Scheme 21).[60] This tandem carbozincation-Pd(0)-catalyzed cyclization constitutes an interesting entry to

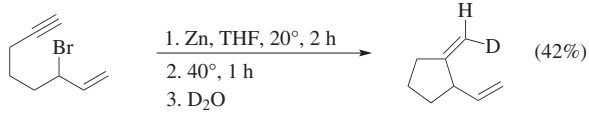
methylenecycloalkanes of various ring sizes.[60] Polysubstituted alkenes containing a 1,4-diene structural unit can be regio- and stereoselectively constructed by the allylzincation of acetylenic sulfones (Scheme 22).[61] The addition is *syn* and the zinc atom is exclusively placed next to the sulfonyl moiety. When the carbozincation reaction occurs in an intramolecular fashion, the Type I zinc-ene cyclization leads to the corresponding 2-(vinyl)methylenecyclopentane (Scheme 23)[62]. Deuterolysis confirms the formation of an alkenylzinc species arising from an intramolecular *syn* carbozincation. Despite the presence of the terminal alkyne, no alkyne deprotonation occurs.[62]



Scheme 21



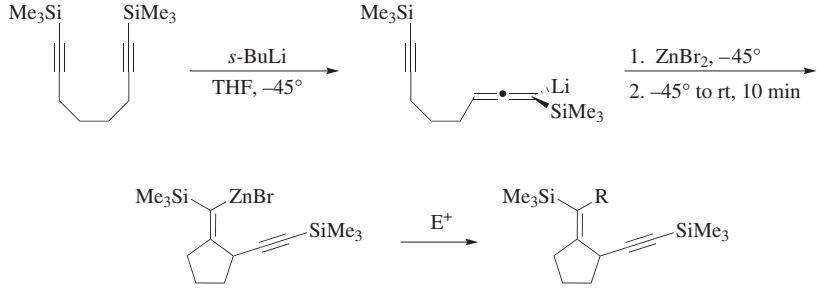
Scheme 22



Scheme 23

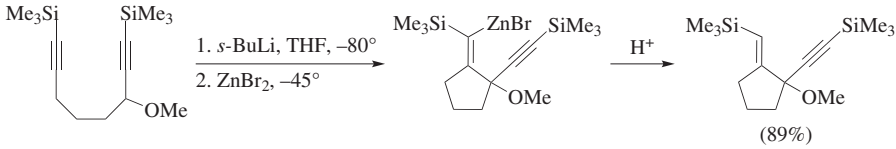
Analogous to the above-mentioned allylic organometallic species undergoing zinc-ene cyclization, intramolecular carbozincation involving allenylzinc species has been investigated.[63] Such reactions are called zinc-yne-allene carbocyclization reactions. Metalation of 1,8-bis(trimethylsilyl)octa-1,7-diyne with *s*-BuLi in THF

leads to a propargyl-allenyllithium that is transmetalated to the corresponding allenylzinc species (Scheme 24). Upon warming to room temperature, a smooth cyclization takes place leading to the alkenylzinc species. The latter species results from a *syn* addition across the silylated alkyne and it appears to be configurationally stable under the reaction conditions. Subsequent electrophilic trapping with a proton, iodine, or allyl bromide in the presence of CuCN or an alkenyl iodide in the presence of a catalytic amount of $Pd(PPh_3)_4$ affords the corresponding functionalized five-membered ring products (Scheme 24).[63] This method has been extended to the intramolecular carbozincation of ω-acetylenic-metalated propargylic ethers to afford substituted tetrahydrofuran derivatives.[64] ω-Acetylenic-metalated propargylic ethers are also used for the preparation of functionalized exomethylene cyclopentanes (Scheme 25).[63] Metalation of the diyne with *s*-BuLi at −80° takes place selectively at the propargylic ether position. After addition of $ZnBr_2$, the resulting allenylzinc cyclizes to the alkynylsilane moiety to afford the corresponding five-membered ring product as a single stereoisomer after protonation. By contrast, if the propargylic ether possesses larger substituents such as thexyldimethylsilyl (TDMS), then kinetic deprotonation with *s*-BuLi in THF at − 40° preferentially occurs at the less congested propargylic position. After transmetalation with $ZnBr_2$, the two allenylzinc species are generated and both cyclize to the alkynylsilane moiety to afford an 86:14 mixture of the two five-membered rings as single diastereomers in 79% isolated yields after protonation (Scheme 26).[63]

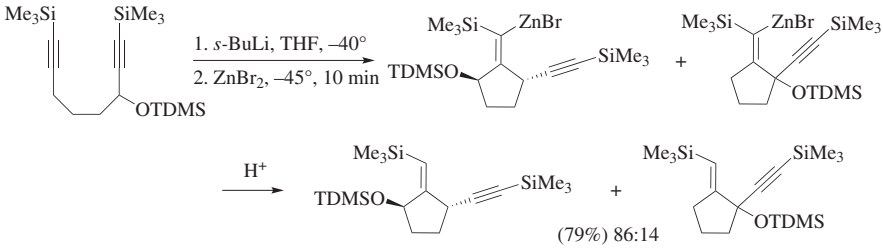


E^+	R	Yield (%)
H_3O^+	H	85
I_2	I	78
allyl bromide, CuCN	allyl	67

Scheme 24

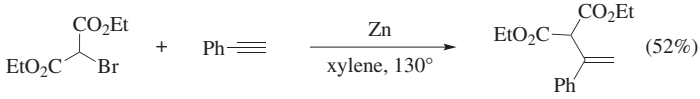


Scheme 25

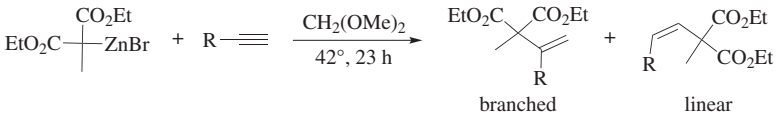


Scheme 26

Preformed zinc enolates add to a wide variety of alkynes.[65] Nucleophilic addition of the zinc enolate derived from diethyl bromomalonate to phenylacetylene in refluxing xylene is one of the first reports of the addition of stabilized zinc enolates across alkynes (Scheme 27).[66] The reaction is usually regioselective and affords the branched isomer.[17] However, when the steric hindrance becomes more important at the propargylic position, as in the case of propargylic ethers or substituted amines, the formation of an increased amount of the linear constitutional isomer is observed (Scheme 28).[67] The (*Z*)-configuration of the latter suggests an *anti* addition mechanism. No addition is detected when the alkyne is disubstituted.



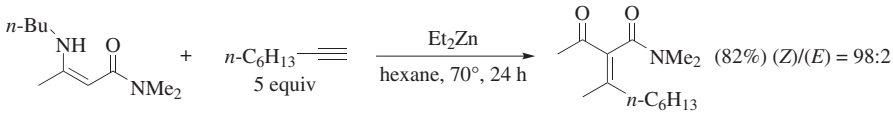
Scheme 27



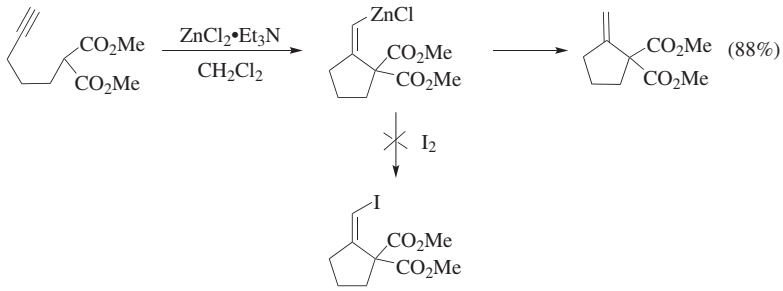
R	Branched/Linear	Combined Yield (%)
$EtO(CH_2)_2$	100:0	56
Et_2NCH_2	48:52	50

Scheme 28

Zinc enolates from β-aminocrotonamides undergo a smooth addition to terminal alkynes upon being heated in hexane and afford the corresponding tetrasubstituted (2-alkylidene)acetoacetamides with high (*Z*)-stereoselectivity (Scheme 29).[68] An intramolecular version of this reaction involves treatment of a pent-4-ynyl-substituted malonate with $ZnCl_2$ and Et_3N in CH_2Cl_2.[69] However, the carbozincated product could not be trapped by electrophiles, suggesting that the sp^2 organozinc species obtained after carbocyclization is rapidly protonated in situ by $Et_3N{\bullet}HCl$ (Scheme 30).[69]

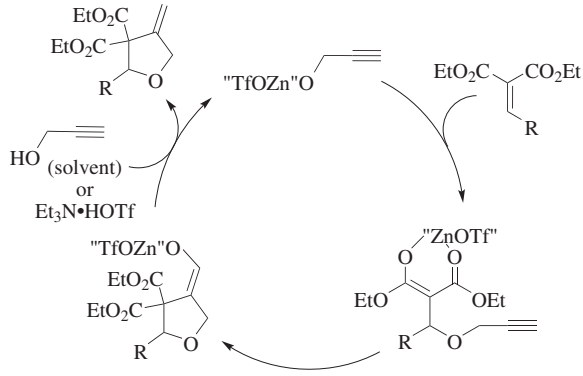


Scheme 29



Scheme 30

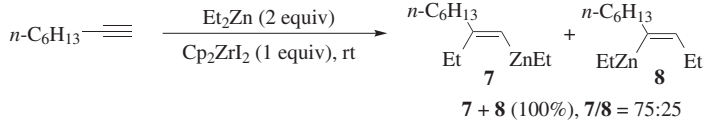
The tandem, zinc-catalyzed, 1,4-addition-carbocyclization of propargylic alcohols and 2-alkylidene-1,3-dicarbonyl compounds constitutes a straightforward preparation of 3-methylenetetrahydrofurans.[70] The use of $Zn(OTf)_2$ is critical for the reaction to proceed; when a different source of zinc such as $ZnCl_2$, $ZnBr_2$, ZnI_2, or even Et_2Zn is used, the reaction proceeds only in low yields. The authors postulate a mechanism involving the initial formation of the zinc alkoxide and its conjugate addition to the Michael acceptor. The resulting zinc enolate intermediate further promotes the intramolecular carbozincation of the triple bond and generates an alkenylzinc intermediate, which is then protonated in situ by the triethylammonium salt (Scheme 31).[70]



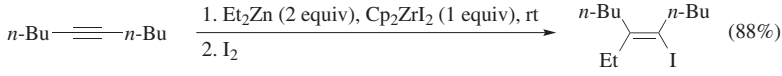
Scheme 31

Catalyzed Carbozincation Reactions. Addition of Et_2Zn or EtZnCl to 1-octyne in the presence of Cp_2ZrI_2 produces a 75:25 mixture of constitutionally isomeric

alkenylzincs **7** and **8** with the ethyl group preferentially delivered to the more substituted carbon. The reaction is *syn* stereoselective (Scheme 32).[71] Zirconocene diiodide is found to be much more efficient than Cp_2ZrBr_2 or Cp_2ZrCl_2 for such transformations. Internal alkynes can also undergo the ethylzincation to afford the corresponding tetrasubstituted alkenyl iodide as a single geometrical isomer after treatment with iodine (Scheme 33).[71]

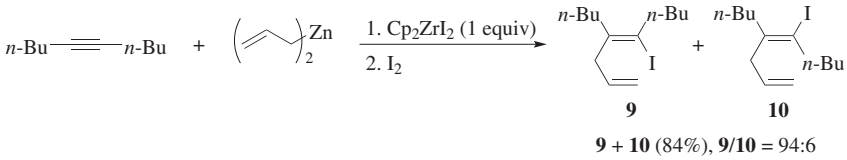


Scheme 32



Scheme 33

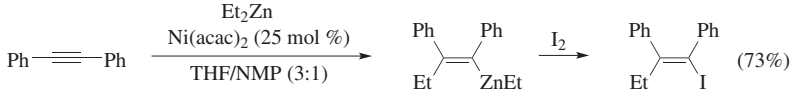
Zirconocene diiodide also promotes the addition of diallylzinc to disubstituted unactivated alkynes. In the case of 5-decyne, the two stereoisomers **9** and **10** are obtained in a 94:6 ratio after treatment with iodine, derived respectively from *syn* and *anti* addition (Scheme 34).[72] The zirconium-promoted crotylzincation of 5-decyne occurs without allylic transposition, presumably via a four-centered transition state.[72]



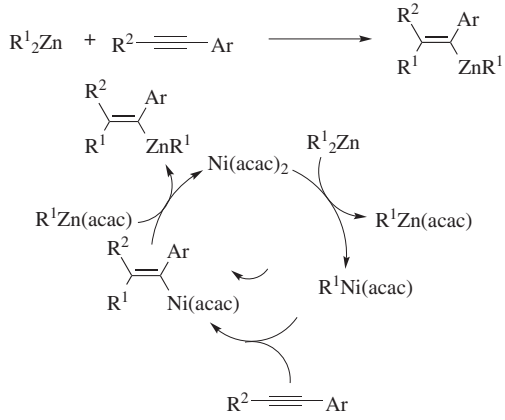
Scheme 34

The carbozincation of disubstituted arylacetylenes by diorganozincs can also be catalyzed by $Ni(acac)_2$ in THF/NMP. Under these conditions, reaction between Et_2Zn and diphenylacetylene leads, via a *syn* addition, to the corresponding tetrasubstituted alkenes after reaction with electrophiles (Scheme 35).[73] With unsymmetrically substituted acetylenes, such as alkyl arylacetylenes, the regioselectivity is excellent only when the alkyl group is either methyl or ethyl.[73,74] Similarly, diphenylzinc reacts selectively with arylacetylenes to form only one constitutional isomer after addition of iodine.[74] Trimethylsilylphenylacetylene reacts with dialkylzincs in the presence of a nickel catalyst to provide the reverse constitutional isomer, namely the α-silylalkenylzinc derivative.[74] The suggested mechanism involves a transmetalation of the dialkylzinc with $Ni(acac)_2$ to generate an organonickel species. Carbonickelation of the alkyne then leads to the corresponding alkenylnickel complex followed

by a further transmetalation of RZn(acac) with the $Ni(acac)_2$ species to form the carbozincated product (Scheme 36).[74]

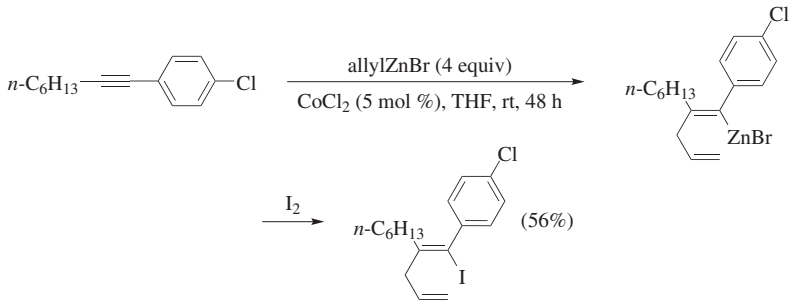


Scheme 35



Scheme 36

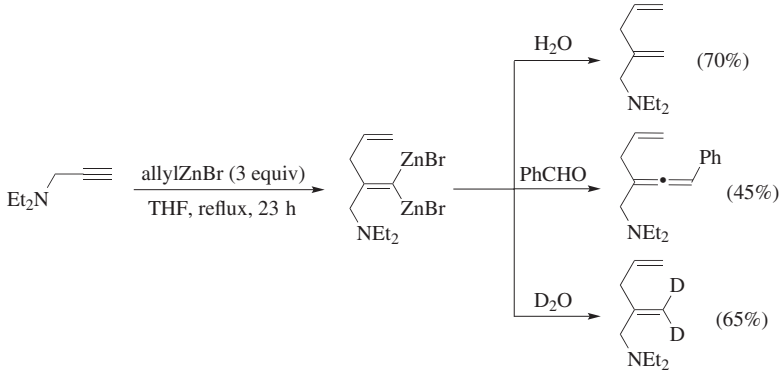
Cobalt (II) chloride can also be used as an efficient catalyst for the allylzincation of 1-arylalkynes.[75] A clean *syn* addition occurs to afford the corresponding α-arylzinc species which can be functionalized (Scheme 37).[75]



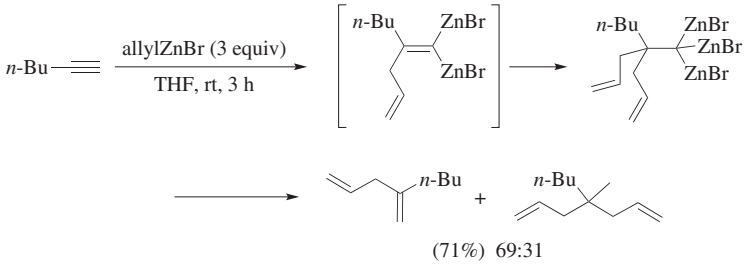
Scheme 37

Carbozincation of Metalated Alkynes. Addition of allylzinc bromide to terminal propargylic amines gives first the metalated propargyl amine and then leads to the formation of 1,1-dimetallic species in good yields (Scheme 38).[56] Reaction of the alkenyl 1,1-dimetallic species with deuterium oxide or benzaldehyde gives

the corresponding *gem*-dideuterated allylic or homoallenic amine, respectively (Scheme 38).[56] This carbozincation reaction is not restricted to propargylic amines as a large variety of metalated alkynes undergo the addition reactions.[76–78] However, bis addition occurs and the 1,1,1-trimetallo species is obtained with unhindered alkynes (Scheme 39).[79,80]



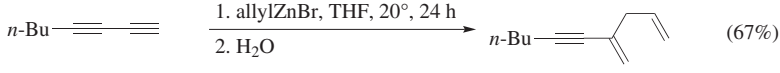
Scheme 38



Scheme 39

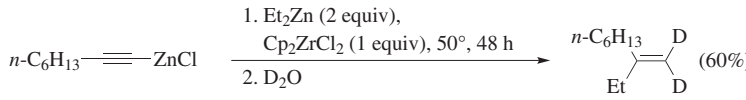
Conjugated enynes (Scheme 40),[81,82] as well as monosubstituted conjugated diynes (Scheme 41),[83] react chemoselectively with allylzinc bromide at the terminal alkyne.

Scheme 40



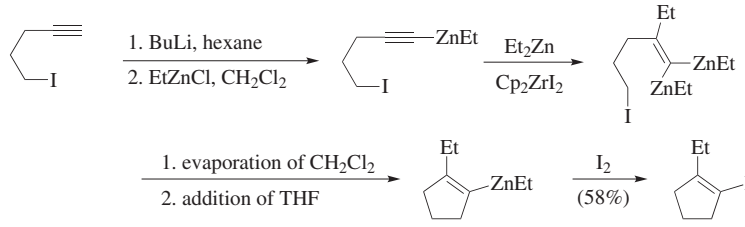
Scheme 41

Zirconium–promoted carbozincations of alkynylzinc derivatives lead to the formation of the corresponding sp^2-diorganometallic species as evidenced by deuteration (Scheme 42).[71]



Scheme 42

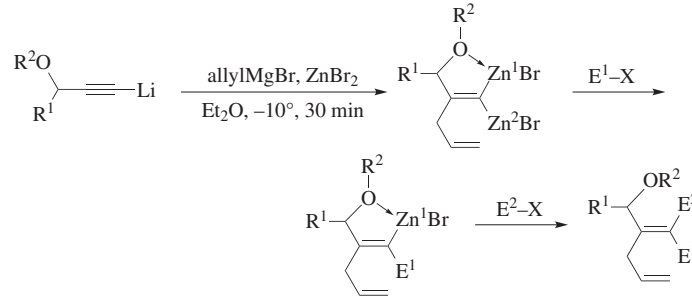
The formation of bismetalated species can be followed by σ-type cyclization reactions. For instance, when allylzinc bromide is added to an ethylzinc alkynylide, the alkenyl 1,1-dimetallic species undergoes a cyclization reaction to produce the substituted cyclopentenylzinc derivative.[84] Similarly, 5-iodo-1-pentyne is converted into the alkynyl ethyl zinc reagent and the subsequent zirconium-promoted ethylzincation affords the *gem*-diorganozinc. Replacement of the initial nonpolar solvent with a more Lewis basic solvent such as THF induces the σ-type cyclization process, leading to the cyclopentenylzinc derivative as demonstrated by the formation of cyclopentenyl iodide after treatment with iodine (Scheme 43).[84]



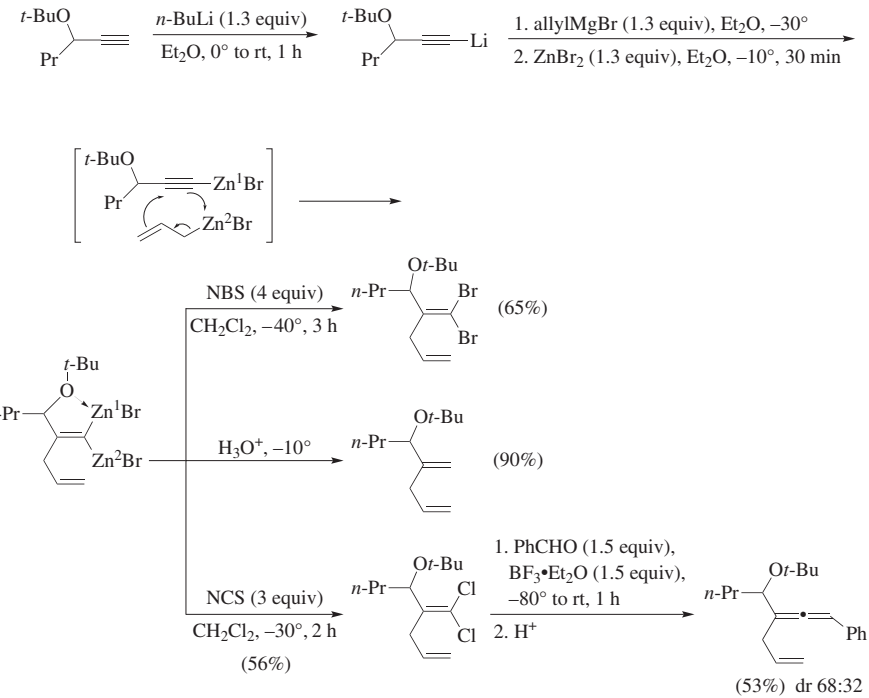
Scheme 43

Diastereoselectivity. The observation that allylmetalation of alkynylmetals leads to vinylic organo-1,1-bismetallic species forms the basis of a new strategy for the stereoselective formation of carbon–carbon double bonds. This strategy requires a secondary propargylic substrate to avoid the double addition and a Lewis basic functional group such as an ether to differentiate the reactivity of the two metals toward electrophiles (Scheme 44).[85] The coordination of the oxygen atom to Zn^1X decreases its reactivity toward the first electrophile, and thus the nonchelated Zn^2X reacts preferentially with this electrophile. The allylmetalation step is performed under mild conditions in a nonbasic solvent such as ether, and the presence of the 1,1-dianionic species is proved by reaction with two equivalents of an electrophile (Scheme 45).[85,86] For the stereoselective reaction of the bismetallic species with different electrophiles, mild halogenating agents such as phenylsulfonyl halides are used, which are known to react selectively with sp^2-bismetallic species.[87] Thus, addition of phenylsulfonyl chloride to the bismetalated species leads to the corresponding chlorovinylzinc reagent. The protonation (or deuteration) of the latter gives the unsaturated vinyl chloride in good isolated yield as a single isomer.[86] This

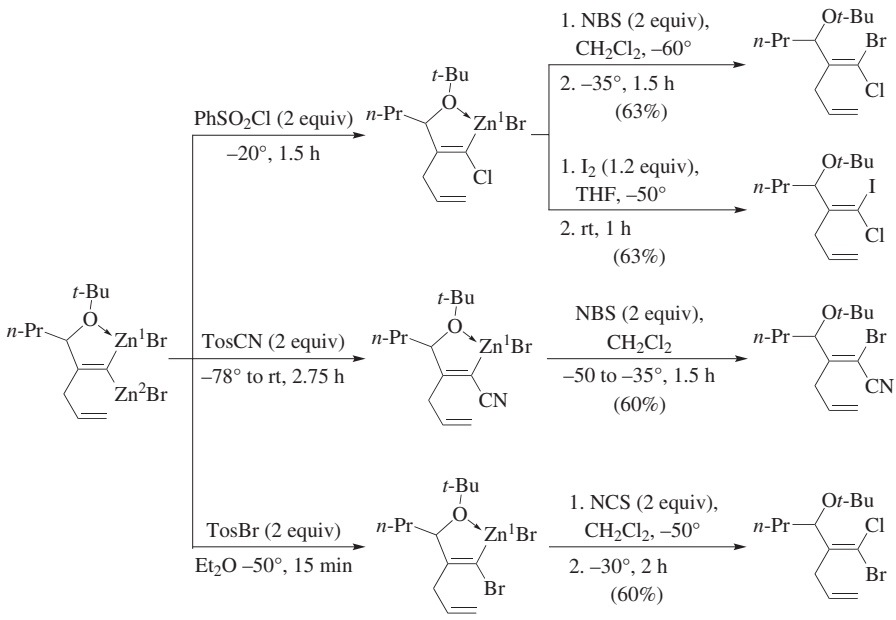
result reflects the coordination of the Zn^1X unit by the *tert*-butoxy group. Moreover, even an excess of $PhSO_2Cl$ (4 equivalents) does not lead to the vinylic *gem*-dichloro derivative, suggesting that the resulting vinylic zinc has a lower reactivity than the bismetallic species. Other sulfonyl derivatives also produce only one stereoisomer (Scheme 46).[87] Interestingly, the addition of *p*-toluenesulfonyl cyanide[88] leads to a unique metalated α,β-ethylenic nitrile (Scheme 46). The coordination is absolutely necessary to discriminate the reactivity of the two metals toward the first electrophile. The remaining Zn^1X can also react with a stronger halogenating agent to give the dihalogenated vinylic compound as a single isomer. This reaction is of value for the synthesis of either geometrical isomer starting from the same propargylic ether.[86]



Scheme 44

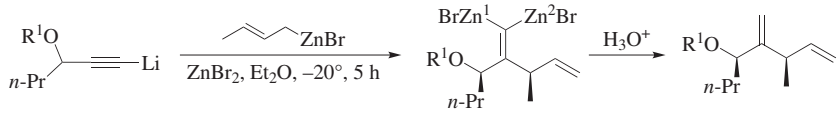


Scheme 45



Scheme 46

The diastereoselectivity of this process has been studied by the addition of crotylzinc bromide, generated in situ by the addition of crotylmagnesium bromide and zinc bromide, across the triple bond of two secondary metalated propargylic ethers (Scheme 47).[89] Although a moderate diastereoselectivity is observed for the crotylmetalation when R^1 = *t*-Bu, the replacement of the *tert*-butyl ether with the methoxyethoxymethyl ether (OMEM) raises the diastereoselectivity to 92:8. Using this strategy, two stereogenic centers and a bismetalated exomethylene moiety are created with a very good diastereomeric ratio.

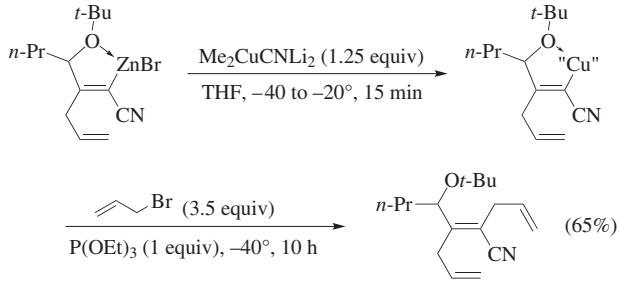


R^1	Yield (%)	dr
t-Bu	75	70:30
MEM	60	92:8

Scheme 47

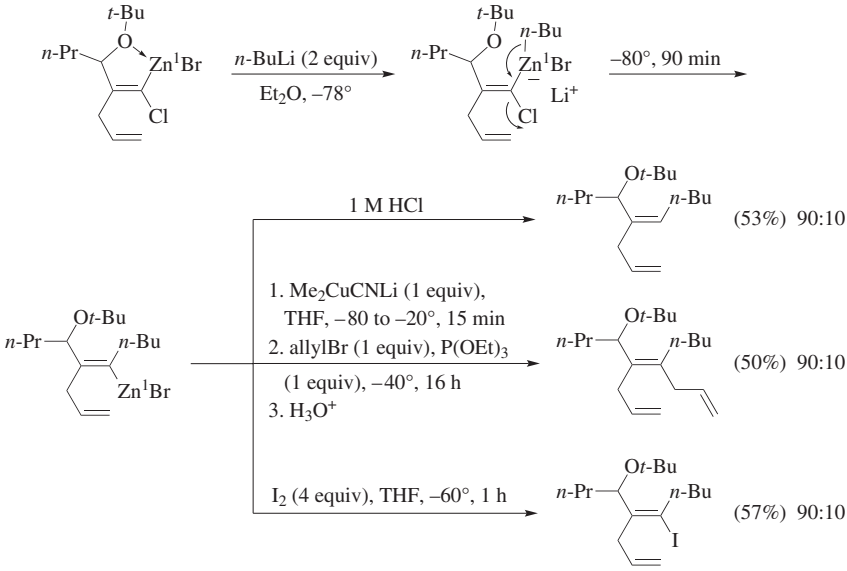
With an α-metalated alkenylnitrile, the reactivity of the remaining metal Zn^1X can be increased by transmetalation to form an organocuprate that reacts with allyl bromide to afford the skipped triene as a single isomer in good overall yield (Scheme 48).[86] To increase the stereodifferentiation of the bismetallic species

toward transmetalation, a secondary propargylic alcohol rather than an ether may be employed.[86]



Scheme 48

Alkylidene chlorocarbenoids can act as ordinary nucleophiles as shown in Scheme 46, but they can also act as electrophiles toward organometallic nucleophiles. For example, the dropwise addition of two equivalents of *n*-BuLi to an α-chlorocarbenoid at −78° leads to the formation of the zincate species, which undergoes a smooth intramolecular nucleophilic substitution reaction to afford the alkenyl organozinc derivative. The latter reacts with a variety of electrophiles as shown in Scheme 49.[86]

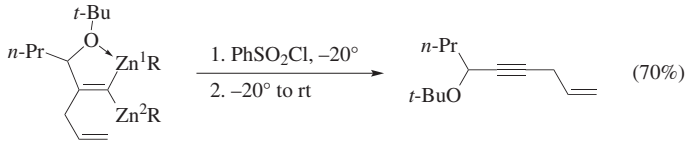


Scheme 49

A third possible reaction pathway of chlorocarbenoids, namely the Fritsch–Buttenberg–Wiechell (FBW) rearrangement, has also been exploited (Scheme 50).[90] However, when R^1 and R^2 are alkyl groups, the yield of alkynes is less than

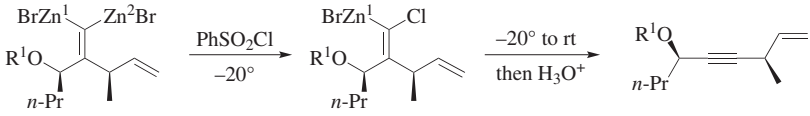
10% because of competitive C–H insertion reactions to form cyclopentenes.[91] An example of a zincated species undergoing the FBW rearrangement is shown in Scheme 51.[89] The alkylidene carbenoid, generated from the 1,1-dizincoalkene, rearranges cleanly to the disubstituted alkyne in 70% yield just by warming the reaction mixture to room temperature.[89] This FBW rearrangement of a zincated species is in contrast to the result with the lithium, sodium, and potassium species. Thus, when the same reaction is performed with the lithium carbenoid, a complex array of products is obtained in which the alkyne accounts for less than 10% of the mixture.

Scheme 50



Scheme 51

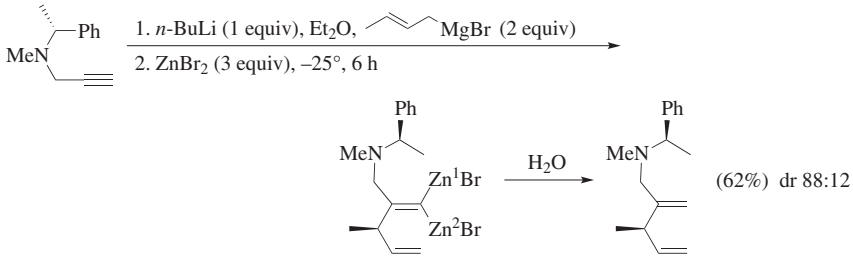
The fate of a stereogenic sp^3 carbon center as a migrating group in FBW reactions is of interest. The bismetalated species is first treated with $PhSO_2Cl$ as previously described, and then the resulting carbenoid is warmed to room temperature whereupon a clean rearrangement takes place (Scheme 52).[89] Moreover, by chemical correlation, it was demonstrated that such FBW rearrangement occurs with a complete retention of configuration at the migrating center.



R^1	Yield (%)	dr
t-Bu	71	70:30
MEM	52	92:8

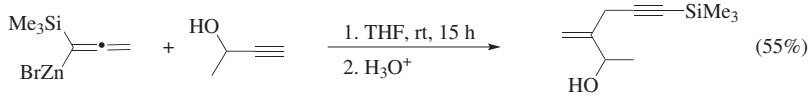
Scheme 52

The behavior of propargylic amines has also been investigated, as the use of chiral amines would potentially enable control of the absolute configuration of the newly formed stereocenter. Crotylzincation of the enantiomerically enriched amine proceeds diastereoselectively to afford the corresponding allylic amine as an 88:12 mixture of diastereomers (Scheme 53).[92]



Scheme 53

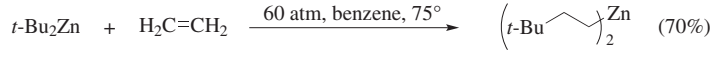
Allenylzinc bromide, prepared from propargyl bromide and metallic zinc in THF, adds to alkynylzinc bromide to provide the alkenyl 1,1–dimetallic species.[93] Despite the allenyl–propargyl metallotropic equilibrium only adducts possessing the propargyl moiety are formed with no trace of any isomeric allenic product. In general, monoaddition is observed when an alkynylzinc bromide is added to the allenylzinc bromide. In contrast, a double addition can be the major pathway when alkynylmagnesium bromide is used as the electrophilic partner.[94] Zincated trimethylsilylpropargyl bromide undergoes a regioselective monoaddition to a large variety of alkynes, including propargylic alcohols and ethers. The corresponding 1,4–enynes are obtained in moderate yields (Scheme 54).[95]



Scheme 54

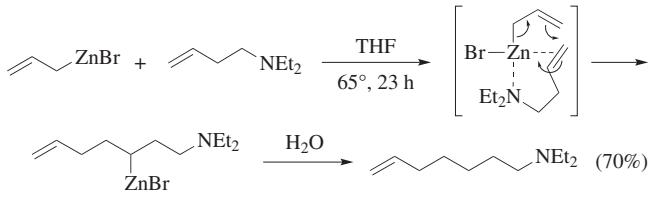
Carbozincation of Alkenes

Uncatalyzed Carbozincation Reactions. Uncatalyzed additions of alkylzincs or arylzincs to alkenes do not generally occur except for the more reactive di(*tert*-butyl)zinc.[96] Carbozincation of ethylene requires the use of pressure and high temperature to afford the primary dialkylzinc derivative (Scheme 55).[96] Reaction also occurs with less reactive monosubstituted alkenes and the addition of the *t*-Bu group is favored on the less substituted carbon of the alkene. 1,3-Butadiene can also be used as the electrophilic partner for the addition of *t*-Bu_2Zn, but the allylic diorganozinc species generated may further react with the butadiene.[96] The monoadduct can be isolated under carefully controlled experimental conditions. Similarly, monoaddition of *t*-Bu_2Zn to styrene can be achieved at a precise temperature to give the benzylic diorganozinc species. At higher temperatures, oligomerization occurs.[96]

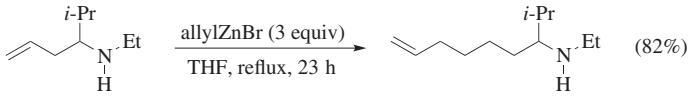


Scheme 55

As discussed previously, allylic organozinc reagents are far more reactive towards unsaturated systems than alkylzincs. For instance, allylzinc bromide adds to a homoallylic amine in refluxing THF (Scheme 56).[97] When a lower or higher homolog of the unsaturated amine is used, the allylzincation does not proceed.[98] This result led the authors to suggest an intramolecular assistance of the addition by nitrogen coordination to the zinc.[98] In support of this mechanistic interpretation, the yield drops considerably when the double bond of the homoallylic amine is 1,2-disubstituted and no reaction is observed when it is 1,1-disubstituted.[56] Moreover, the reaction is also dependent on the steric hindrance around the nitrogen atom and its coordinating ability. The best yields are obtained with secondary homoallylic amines, which are rapidly deprotonated by allylzinc bromide (Scheme 57).[56]

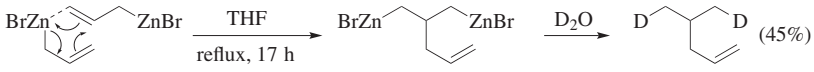


Scheme 56



Scheme 57

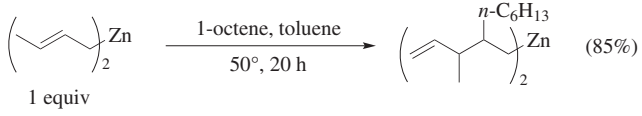
Addition of allylzinc bromide to allyl or homoallyl alcohols proceeds far less efficiently.[56] Carbozincation can also occur in the absence of external alkenes. Thus, when a solution of allylzinc bromide is heated to reflux, an allylzincation reaction of one molecule across another is observed (Scheme 58).[99]



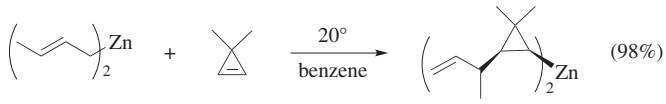
Scheme 58

Diallyl-, dicrotyl-, dimethallyl-, and diprenylzinc derivatives react with ethylene under pressure in toluene and the resulting dialkylzincs are obtained in uniformly high yields.[100] With dicrotylzinc or diprenylzinc, complete allylic transposition is observed in the addition reaction.[101] Monosubstituted alkenes also undergo crotylzincation to afford the primary dialkylzinc (Scheme 59).[101] The relative reactivity order of the alkenes towards allylzincation is 1-alkenes < styrene < 1,3-butadiene < ethylene. 1,1- or 1,2-Disubstituted alkenes are unreactive unless they are structurally

strained.[100] Thus, dimethylcyclopropene affords the corresponding dicyclopropylzinc reagent resulting from a *syn* addition (Scheme 60).[100]

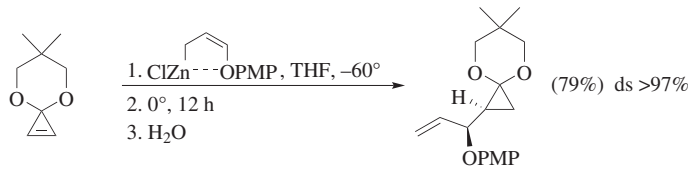


Scheme 59

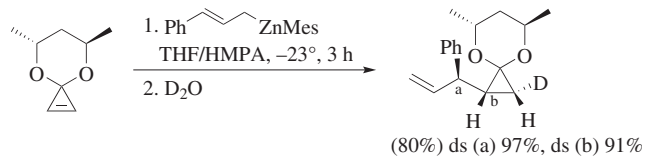


Scheme 60

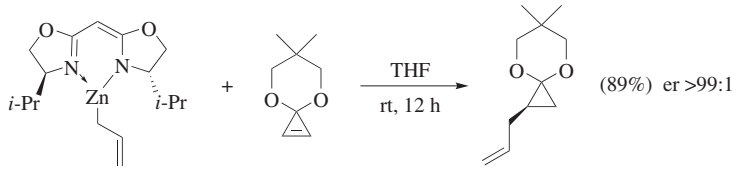
3-Alkoxyallylzinc reagents react with cyclopropenone ketals to provide the γ-adducts as major products[102–104] with excellent diastereoselectivities (Scheme 61),[103] as does the cinnamylzincation of a chiral cyclopropenone ketal (Scheme 62).[104] Similarly, a chiral ligand attached to the allylzinc leads to a highly enantiomerically enriched product (Scheme 63).[105]



Scheme 61

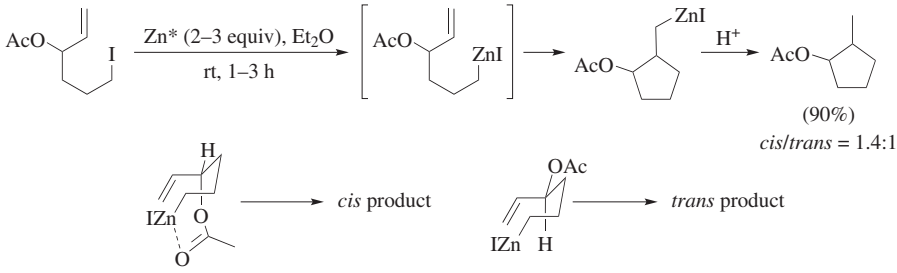


Scheme 62

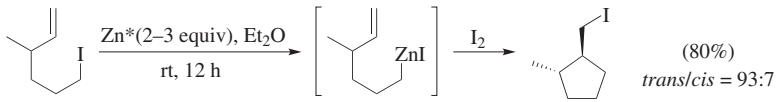


Scheme 63

Cyclization reactions usually proceed with relative ease as compared to the analogous intermolecular carbozincations.[2,7,11,13] The greatest advantage of organozincs as compared to organolithium reagents lies in their tolerance toward a variety of functional groups. For instance, the reaction of a functionalized iodide with a two- or three-fold excess of activated zinc in ether at room temperature leads to clean and rapid insertion of activated metal into the carbon–iodine bond followed by a cyclization reaction across the unactivated double bond (Scheme 64).[25] However, the diastereomeric ratio is disappointing (*cis/trans,* 1.4:1). This result can be explained on the basis of a chair-like transition state. The lack of stereocontrol has been attributed to a mixture of steric and chelation interactions: the acetoxy group must occupy an unfavorable axial position to coordinate the zinc atom.[51] Cyclization of the methyl-substituted substrate proceeds with much higher *trans* selectivity and the yields and selectivities are the same irrespective of whether the metal is zinc or lithium (Scheme 65).[25,51] This result clearly indicates that the stereocontrol is attributable to the lack of steric interactions when the methyl group occupies a pseudoequatorial position in the chair-like transition state.



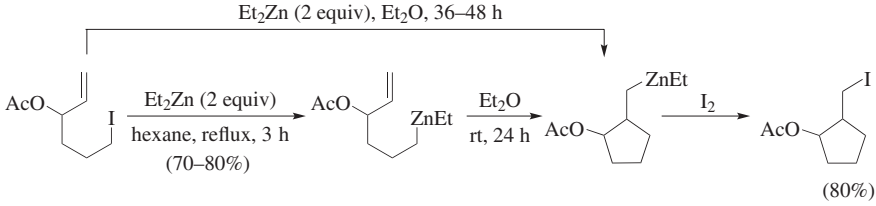
Scheme 64



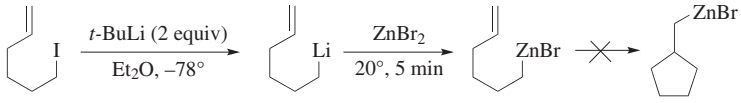
Scheme 65

To gain additional insights into the carbocyclization of dialkylzinc species as opposed to that of alkylzinc iodides, a functionalized alkyl iodide was refluxed with two equivalents of Et_2Zn in hexane for 3 hours to yield the linear organozinc reagent in 70–80% yield, with the balance of material being the starting iodide (10–15%) (Scheme 66).[51] Removal of the hexane and addition of anhydrous ether results in complete cyclization after 12–24 hours, a longer reaction time than required with the organozinc iodide. The diastereomeric ratio is still low (*cis/trans,* 1.2:1). The same iodine/ethylzinc exchange reaction can be performed directly in 36–48 hours in ether using two equivalents of Et_2Zn.[25,51] Noteworthy is the fact that ether is the solvent of choice for organozinc cyclization because only 15% cyclization occurrs in refluxing hexane after 3 hours. Although the direct iodine/zinc exchange allows cyclization of

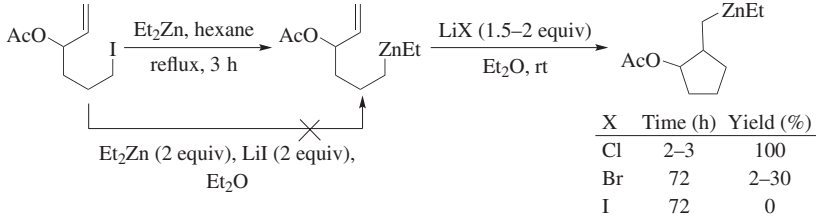
functionalized compounds, the iodine/lithium exchange followed by transmetalation to zinc has also been investigated.[51] This study also reveals the importance of lithium halide in the solution. Thus, as shown in Scheme 67,[51] a cyclization similar to that of Scheme 66 no longer operates, even though it is performed in ether. The only difference lies in the presence of LiI (formed in the first step) and LiBr (formed in the transmetalation step). If the same precursor is stirred with two equivalents of Et_2Zn in the presence of two equivalents of LiI in anhydrous ether, no exchange or cyclization occurs and the starting iodide is recovered quantitatively. The linear organozinc reagent is also generated in refluxing hexane and reacts further with various lithium halides (1.5 to 2 equivalents). No cyclization product is observed with lithium iodide, and only 20–30% with lithium bromide even after 72 hours at room temperature, but the cyclization reaches completion after the usual reaction time of 2–3 hours with lithium chloride. These results clearly demonstrate the negative influence of lithium iodide and bromide on the reactivity of the linear intermediate (Scheme 68).[51] These two lithium halides may modify the character of the zinc atom, probably via a zincate species,[106] and prevent the efficient coordination of the zinc atom to the double bond that is required for carbocyclization. Therefore, in Rieke's method, it is essential to wash the active zinc thoroughly since the lithium naphthalenide reduction of zinc bromide also generates lithium bromide (Scheme 8). The insertion of Rieke zinc in the presence of LiBr leads to the linear organozinc iodide but not to the cyclic product.



Scheme 66



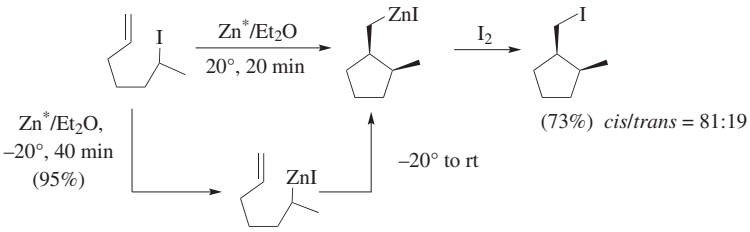
Scheme 67



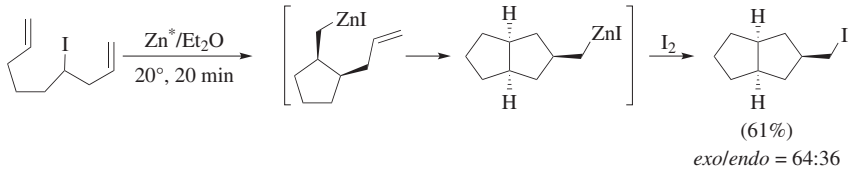
X	Time (h)	Yield (%)
Cl	2–3	100
Br	72	2–30
I	72	0

Scheme 68

The carbocyclization of secondary organozinc iodides has also been investigated.[51,107] Treatment of 6-iodo-1-heptene with Rieke zinc in ether leads quantitatively to the cyclized organozinc iodide in less than 20 minutes, as shown by iodinolysis of the species present (Scheme 69).[107] At low temperature, rapid oxidative insertion of activated zinc metal into the carbon–iodine bond affords the acyclic zinc derivative in 95% yield with 5% of the cyclized product. These reactions are of synthetic value for the preparation of each of the two diastereomers, starting from either primary (Scheme 65) or secondary alkyl iodides.[107] An extension of this method to the preparation of bicyclic products is exemplified in Scheme 70.[51]



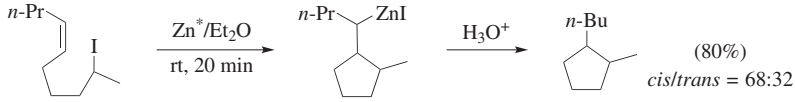
Scheme 69



Scheme 70

In all of these reactions, the observed *cis* stereoselectivity is attributed to steric interactions that favor a geometry in which the R substituent preferentially occupies an outside equatorial position in the chair-like transition state. The highly covalent nature of the carbon–zinc bond as well as the favorable intramolecular association of the zinc atom with the double bond may explain the *cis* stereoselectivity observed here via a product-like transition state.[107]

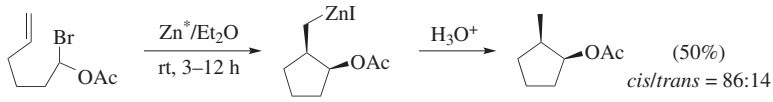
Intramolecular addition of a secondary organozinc derivative to a (*Z*)-1,2-disubstituted alkene proceeds at room temperature (Scheme 71).[51,107]



Scheme 71

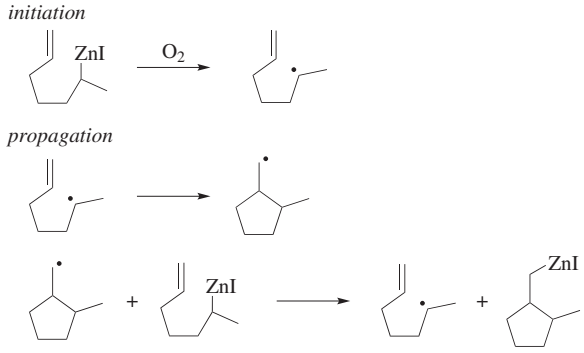
An α-bromoalkyl acetate undergoes cyclization by treatment with activated zinc in ether (Scheme 72)[51]to provide the cyclic product in moderate yields (the balance

being the uncyclized material), but with much higher diastereoselectivity (*cis/trans,* 86:14) than that obtained (58:42) via the strategy depicted in Scheme 64.



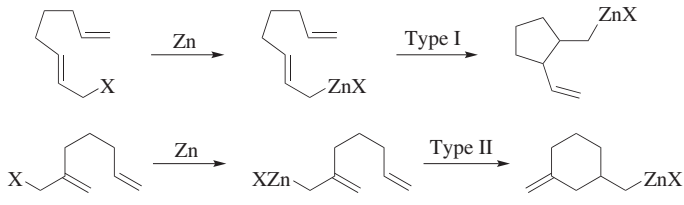
Scheme 72

On the basis of later reports,[108] a radical mechanism proceeding from the organozincs themselves is conceivable for those intramolecular carbozincations that were previously believed to occur by an ionic or polar mechanism.[2,109] Therefore, oxidation of alkylzinc to a radical species initiates a chain reaction whose propagation steps lead to radical cyclization and group transfer of ZnI as depicted in Scheme 73.[110]



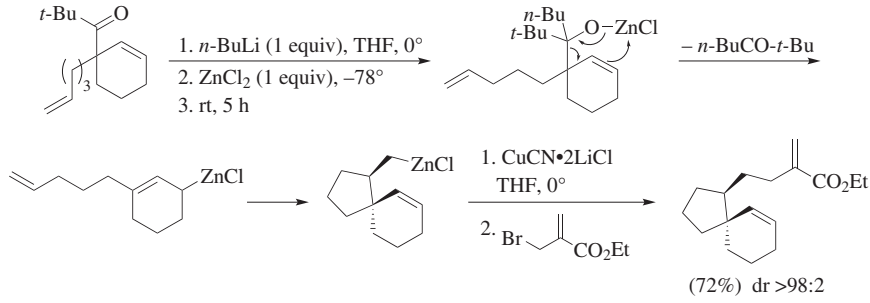
Scheme 73

Zinc-Ene Reactions. Two types of intramolecular zinc-ene reactions are known depending on which carbon of the allylic organometallic ene-component is linked to the alkene (enophile) (Scheme 74).[8] Type I cyclizations are generally restricted to the formation of five–membered rings, whereas formation of six–membered rings occurs more readily in Type II cyclizations. The palladium-catalyzed zinc-ene reaction has been extensively investigated and is discussed in the next section.



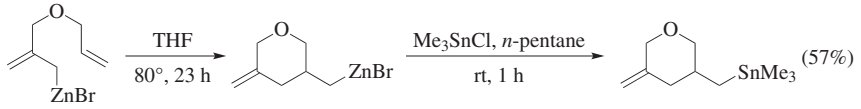
Scheme 74

An alternative approach uses the fragmentation of a sterically hindered tertiary homoallylic zinc alkoxide into *tert*-butyl *n*-butyl ketone and the corresponding allylzinc species, which undergoes a diastereoselective Type I zinc-ene cyclization to give a spirobicyclic organozinc derivative (Scheme 75).[34]



Scheme 75

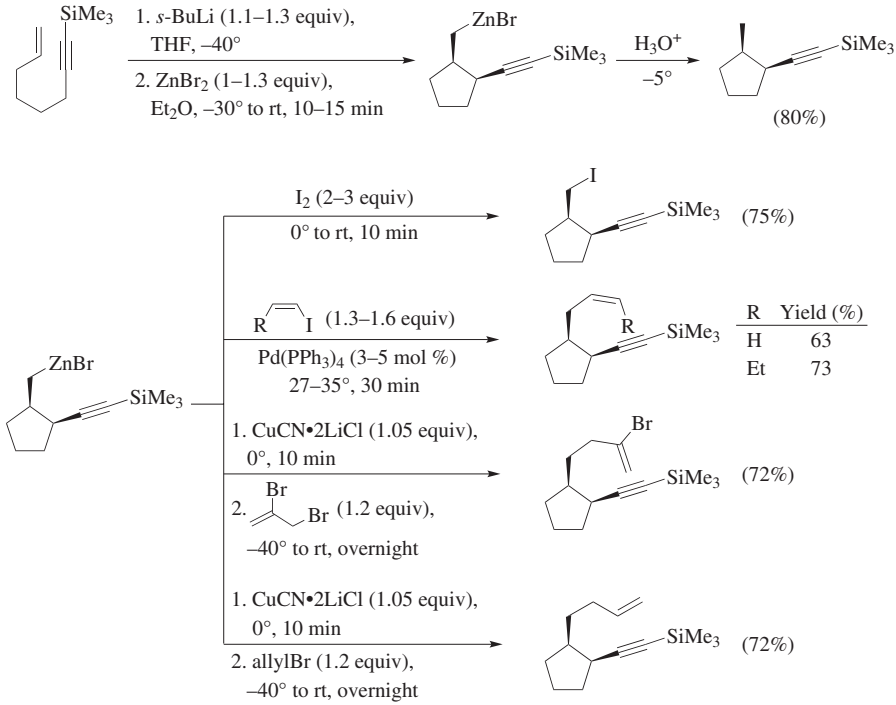
The first report of a Type II zinc-ene reaction involved substrates containing a heteroatom in the tether. The superiority of zinc for carbocyclization as compared to magnesium is clearly demonstrated in these examples. Thus, the carbomagnesiation reaction analogous to that shown in Scheme 76 fails even at 100–130° in THF.[111] Type II cyclizations are known involving α,α and α,β-disubstituted double bonds, although the resulting organozinc species could not be trapped efficiently. Even a seven-membered oxygen heterocycle can be generated by the Type II zinc-ene reaction.[12]



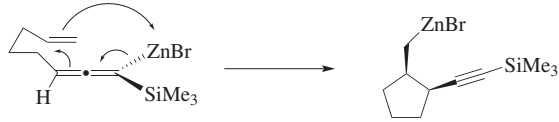
Scheme 76

Although an ene-allene reaction was postulated thirty years ago[112] to interpret the formation of cyclic products from the pyrolysis of 2,3,8-nonatriene and 1,2,7-octatriene, investigation of the corresponding metallo-ene-allene reaction is more recent. Metalation of 8-(trimethylsilyl)-1-octen-7-yne with *s*-BuLi either in THF at −45° (or in ether at 10°), warming to 20° for 1–2 hours, and subsequent protonation results in a mixture of the starting enyne and its allenic isomer in a ratio of 60:40. Addition of one equivalent of a magnesium salt to the lithium derivative also does not promote the cyclization. However, addition of 1–1.3 equivalents of $ZnBr_2$ at −30° not only alters the propargyl/allenyl ratio of the hydrocarbons (98:2) as determined by protonation of the organometallic species at low temperature, but also results in an efficient cyclization reaction after stirring for a few minutes at room temperature (Scheme 77).[113] Acidic quenching of the reaction mixture affords the cyclic product in 80% yield as a single diastereomer. The formation of a discrete

organometallic species is confirmed by iodinolysis, by a coupling reaction with vinyl iodides in the presence of a catalytic amount of $Pd(PPh_3)_4$, and by reaction with an allylic halide after transmetalation of the organozinc bromide into an organocopper reagent.[113] Heating the solution of the cyclized organozinc bromide in toluene at 120° does not produce the thermodynamically more stable *trans* derivative, indicating the nonreversibility of this cyclization. The *cis* stereoselectivity is explained by a metallo-ene-allene reaction in which the allenyl metal moiety plays the role of the ene and fixes the *cis* relationship of the two substituents (Scheme 78).[113] By comparison, the known metallo-ene reaction of allylic organomagnesium reagents requires heating to 60° for 24 hours.[8]

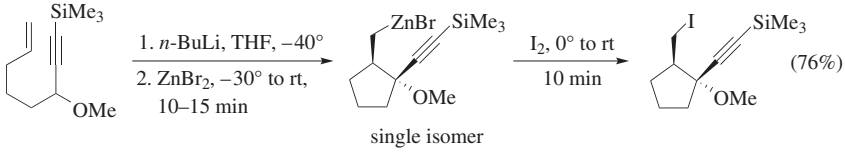


Scheme 77

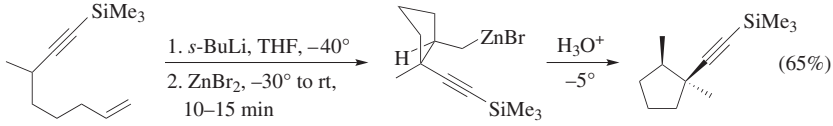


Scheme 78

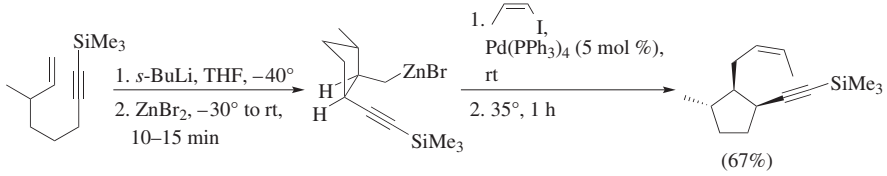
More elaborate systems can be prepared easily by simple metalation–transmetalation sequences as exemplified in Schemes 79–82.[113]



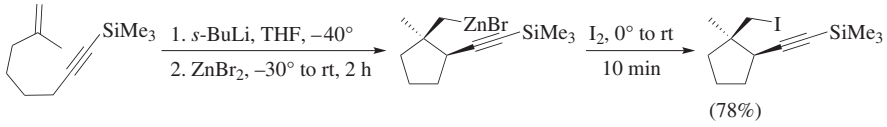
Scheme 79



Scheme 80



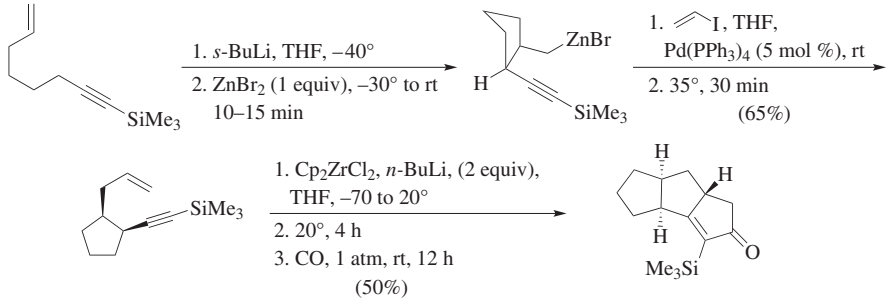
Scheme 81



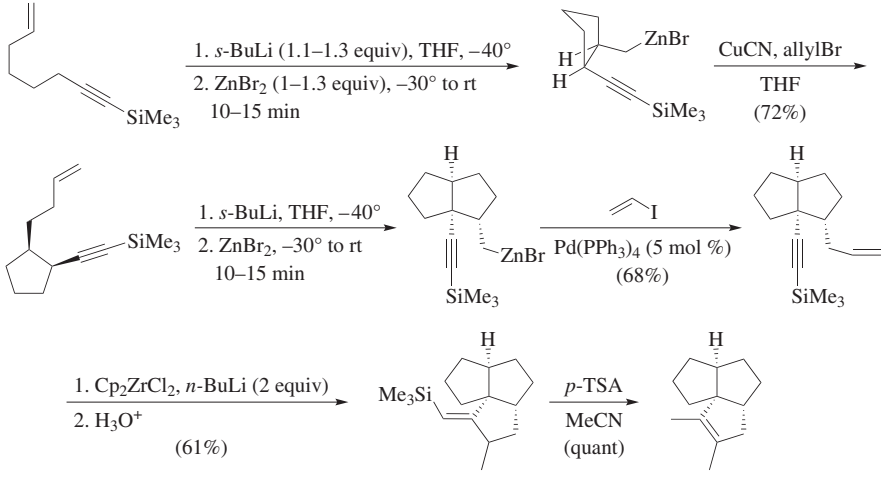
Scheme 82

This method can be applied to the diastereoselective synthesis of either linear or angular tricyclopentanoids starting from the same precursor. Thus, metalation of 8-(trimethylsilyl)-1-octen-7-yne with *s*-BuLi in THF at −45° followed by the addition of one equivalent of zinc bromide affords the corresponding allenyl zinc bromide intermediate.[114] After warming the solution to room temperature, the allenylzinc species reacts in less than 5 minutes to produce the cyclic organozinc bromide, which is further functionalized by a coupling reaction[42] with 1-iodoethene in the presence of a catalytic amount of $Pd(PPh_3)_4$. The enyne is isolated as a single isomer. Treatment with Cp_2ZrCl_2 and two equivalents of *n*-BuLi,[115] followed by a carbonylation reaction of the zirconacyclopentane derivative, produces the tricyclic ketone as a single diastereomer in good overall yield (Scheme 83).[113,116] By treating the product of the zinc-ene-allene carbocyclization with allyl bromide after transmetalation into an organocopper reagent, a new enyne is obtained in good yield and as a single isomer (Scheme 84).[116] By submitting this product to the zinc-ene-allene reaction (metalation–transmetalation–cyclization), the corresponding bicycloorganozinc bromide is obtained. Treatment of the latter with vinyl iodide

in the presence of a catalytic amount of $Pd(PPh_3)_4$ followed by reaction with the Negishi reagent and an acidic hydrolysis leads to the tricyclic derivative, which can be directly subjected to the desilylation procedure. Under these conditions, the exomethylene double bond migrates to form the thermodynamically more stable alkene, the structure of which is found in natural triquinanes.[116]



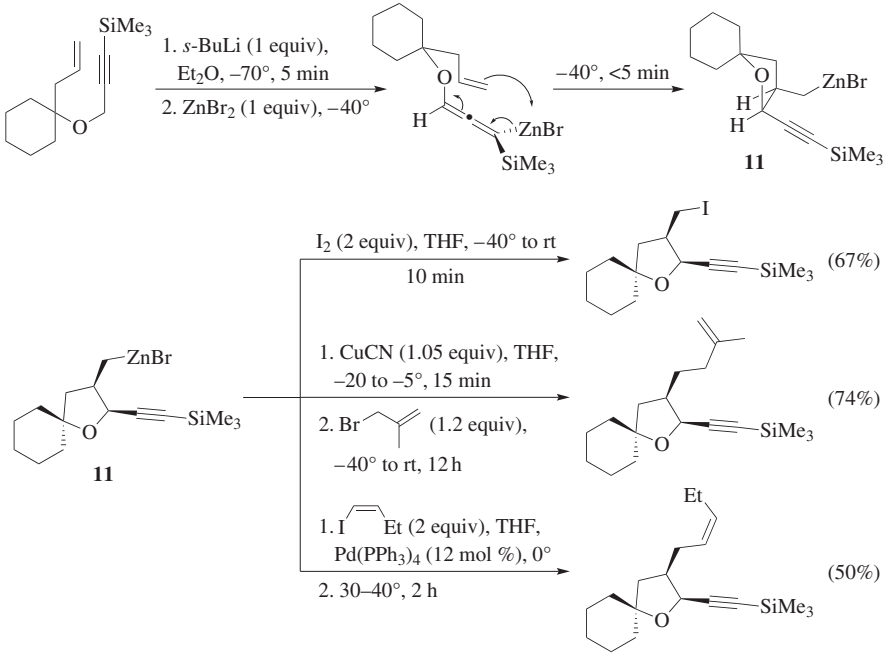
Scheme 83



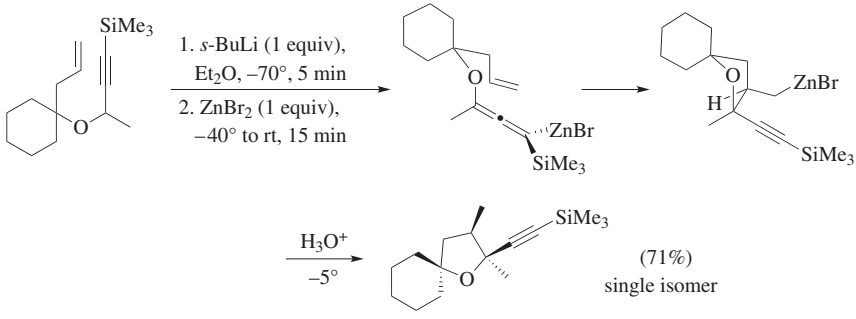
Scheme 84

The zinc-ene-allene reaction has also been applied to the synthesis of heterocycles. Metalation of the propargylic ether in Scheme 85 [64,117] with *s*-BuLi in ether at −70°, and transmetalation with one equivalent of $ZnBr_2$ leads to the allenylzinc bromide, which undergoes a highly diastereoselective cyclization reaction in less than 5 minutes at −40° to give the bicyclic organozinc bromide **11**.[64,113,117] The cyclic organozinc bromide can be functionalized and in all cases, the substituted oxaspirodecane products are isolated as single isomers. This very mild and diastereoselective cyclization allows the intramolecular carbometalation of diverse propargylic ethers in which

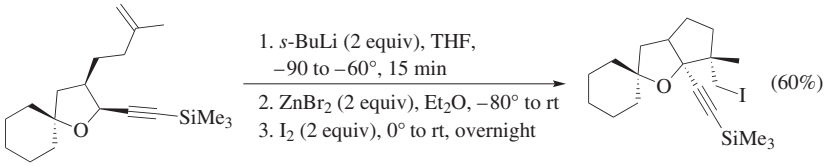
new stereogenic centers are created. An additional substituent may be also positioned at the propargylic position. The initial metalation–transmetalation–cyclization sequence followed by protonation leads to the formation of a single oxaspirodecane product with two quaternary and one tertiary stereogenic centers on the tetrahydrofuran ring in 71% overall yield (Scheme 86).[64,117] Finally, submitting the bicyclic oxaspirodecane derivative to the cyclization conditions leads to the corresponding tricyclic product as a single isomer in 60% yield with the creation of vicinal tetrasubstituted and quaternary centers (Scheme 87).[64,117]



Scheme 85

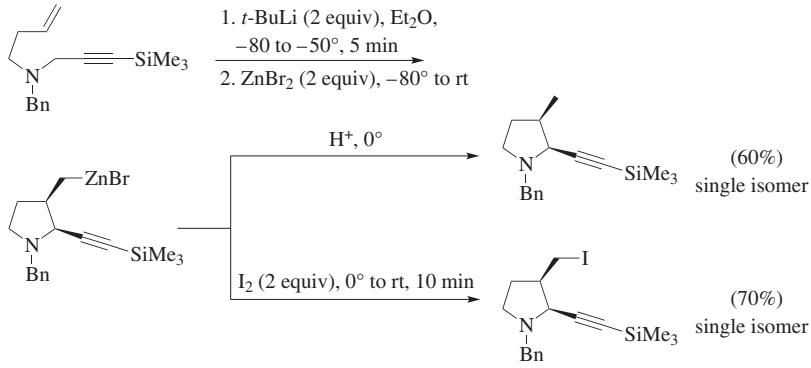


Scheme 86



Scheme 87

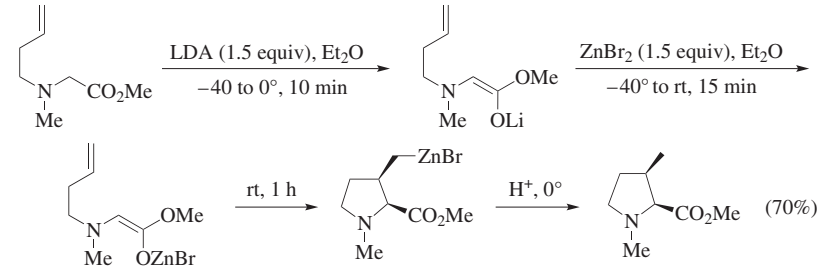
An extension of this strategy to the preparation of pyrrolidines is shown in Scheme 88.[64,118]



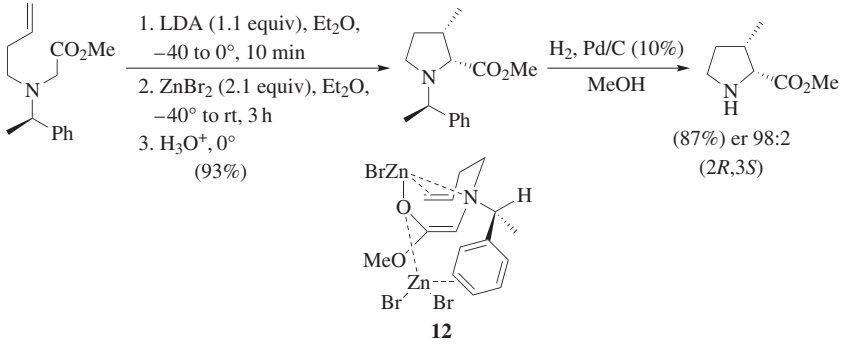
Scheme 88

Additions of Zinc Enolates and Aza-Enolates. The first intramolecular carbometalation reaction of a zinc enolate on an unfunctionalized or non-strained double bond was reported in 1997.[118,119] *N*-Methyl-*N*-(but-3-enyl)glycinate methyl ester is cleanly metalated by treatment with 1.5 equivalents of LDA in ether at −40°, and no cyclization of the lithium (or magnesium) enolate is observed after stirring at room temperature for two hours. However, addition of 1.5 equivalents of zinc bromide provides the zinc enolate, which undergoes a cyclization within one hour at room temperature (Scheme 89).[118,120] Acidification of the reaction mixture affords the cyclic product in 70% isolated yield as a single diastereomer. The formation of a new functionalized organometallic species is confirmed by reaction with different electrophiles. As the (*Z*)-configuration of the zinc enolate is imposed by intramolecular Zn–N chelation,[32] the *cis* relative configuration of the cyclic product is attributed to a chair-like transition state, in which the (*Z*)-enolate is in a plane parallel to that of the alkenyl double bond. Using this simple strategy, several tri- and tetra-substituted pyrrolidines are easily prepared, and the diastereoselectivity of the carbocyclization has been studied in detail.[120] Subjecting (*R*)-*N*-1-(phenylethyl)-*N*-(but-3-enyl)glutamate methyl ester to this reaction sequence generates the chiral, cyclic organozinc bromide diastereoselectively, and the chiral β-methylproline derivative is obtained as a single *cis* diastereomer with a 98:2 diastereomeric ratio and in 93% yield after protonation (Scheme 90).[118,120]

After hydrogenolysis, the secondary amine is obtained in 98:2 er. Interestingly, the enantiomeric purity drops to 75:25 er when the reaction is performed with only one equivalent of zinc bromide. Moreover, if the aromatic ring of the chiral auxiliary is replaced by a cyclohexyl group, no diastereoselection is observed. In view of these results, the authors postulate a π-chelation between the aromatic ring and the amino-zinc enolate as in the transition state structure **12**. The excess zinc bromide, which is necessary for high diastereoselection, may act as a tether between the aromatic ring and the zinc enolate as shown in Scheme 90. Several non-natural chiral amino acids used as probes in structure-activity relationship studies of biologically active peptides, including 3-prolinomethionines,[121] 3-prolinoglutamic acid,[122] and 3-alkyl-substituted prolines[123] are easily prepared by this method.



Scheme 89

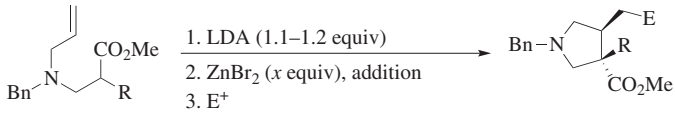


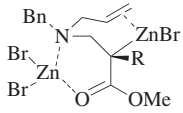
Scheme 90

The amino-zinc enolate carbocyclization has also been applied in solid-phase organic synthesis, allowing the preparation of libraries of 3-substituted proline derivatives.[124]

Executing this metalation–transmetalation–cyclization with a homologous β-(*N*-allyl)amino ester, employing dropwise addition of the lithium enolate to an ethereal zinc bromide solution, leads to a smooth carbocyclization reaction to give the corresponding substituted carbomethoxypyrrolidine in good yields after protonation or reaction with different electrophiles (Scheme 91).[125] Interestingly, the stereoselectivity of the carbocyclization is now different from that of cyclization

of the α-(*N*-homoallyl)amino ester enolate previously described in Scheme 88. A reasonable explanation involves a carbon-bound zinc enolate, with the R group adopting a pseudo-equatorial position and the carbomethoxy group adopting a pseudo-axial position as a result of their relative size and possibly additional chelation of an external zinc species between the oxygen and the nitrogen atoms, as depicted in structure **13** (Scheme 91).



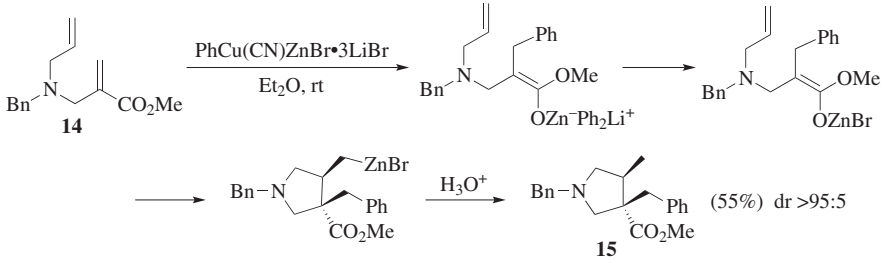


13

R	Addition	*x*	E	Yield (%)	dr
H	inverse	5	H	51	87:13
Me	regular	1.2	H	75	>99:1
Me	regualr	1.2	I	68	>99:1
Me	regular	1.2	4-TolS	67	>99:1

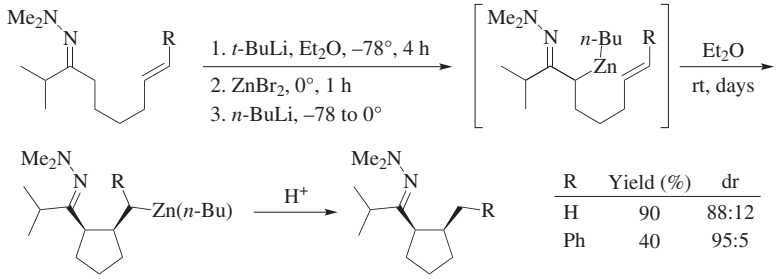
Scheme 91

An alternative and elegant method for the preparation of substituted pyrrolidines consists of a domino 1,4-addition/carbocyclization/functionalization reaction of various Michael acceptors, with a mixed copper–zinc reagent or a triorganozincate–zinc bromide combination.[126] For example, the reaction of PhCu(CN)ZnBr•LiBr, prepared from PhLi and a mixture of $ZnBr_2$ and CuCN in ether, with the α,β-unsaturated ester **14** affords the carbomethoxypyrrolidine **15** in 55% yield as a single diastereomer after protonation (Scheme 92).[126] The carbometalated product can be functionalized with various electrophiles.[126]



Scheme 92

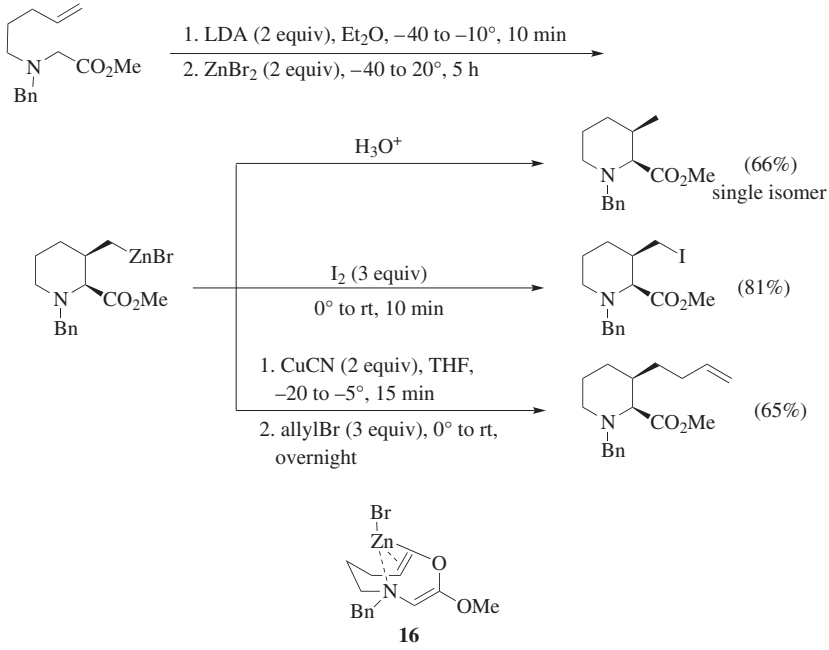
N,N-Dimethylhydrazones of alkenyl ketones also undergo carbocyclization when deprotonated and transmetalated to provide the butylzinc aza enolate (Scheme 93).[127] However, the diastereoselectivity of this carbocyclization is only fair (*cis/trans*, 88:12). Both 5-exo and 6-exo products can be accessed using this method. However, the 6-exo-trig cyclization of a zincated ketone hydrazone onto a disubstituted double bond is much slower and leads to the cyclic derivative in 40% yield with a diastereoselectivity of 95:5 (Scheme 93).[127]



R	Yield (%)	dr
H	90	88:12
Ph	40	95:5

Scheme 93

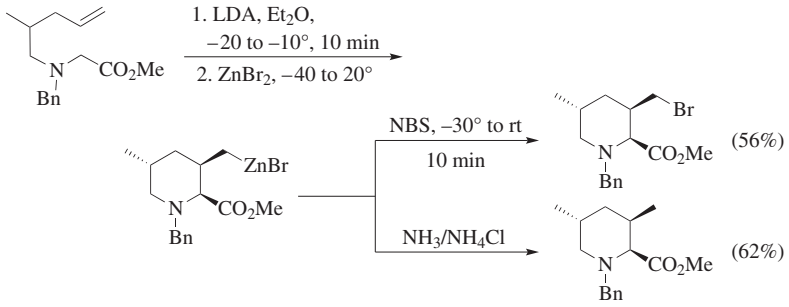
6-Exo-trig cyclization is usually much slower than the analogous 5-exo-trig cyclization and therefore fewer examples of this transformation are known. However, the cyclization reaction of a zinc enolate has been successfully applied to the formation of six-membered rings in a new route to substituted piperidine derivatives (Scheme 94).[128] After lithiation in ether and transmetalation with zinc bromide, the corresponding (Z)-α-aminozinc enolate cyclizes at room temperature to afford the metalated piperidines. Protonation, iodinolysis, or allylation of the reaction mixture after a subsequent transmetalation step affords the functionalized piperidines in 66, 81, and 65% yields, respectively. In all cases, only the *cis* isomers are detected. The stereoselectivity is explained by a boat-like transition structure **16** in which coordination of the double bond with zinc forces the alkene to be up and positions the two hydrogens attached to the alkenes *cis* to each other as shown in Scheme 94.[128]



16

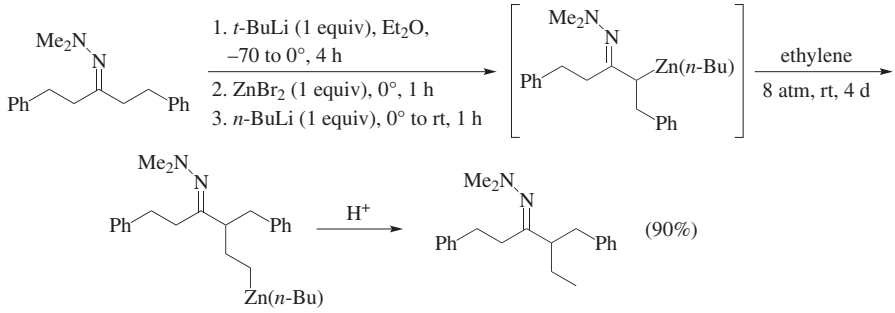
Scheme 94

The stereochemical influence of substituents in the starting linear substrates in the carbocyclization reaction has been studied in detail, and it has been found that the stereochemical outcome is principally due to the presence of a substituent in the homoallylic position (Scheme 95).[128]



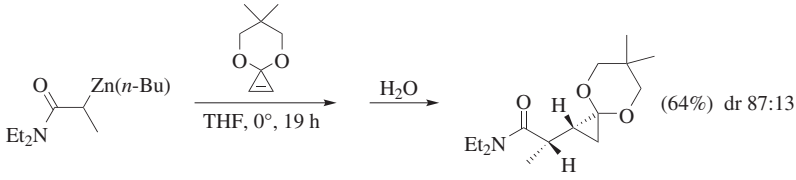
Scheme 95

Not unexpectedly for intermolecular carbometalation reactions, isolated alkenes are rather unreactive electrophiles toward enolates, and good yields are obtained only with slightly activated[129] or strained[130] alkenes. The addition of a zincated hydrazone to ethylene is performed under pressure for four days at room temperature, leading to the carbometalated product in good yield (Scheme 96).[131] Aliphatic alkenes such as 1-octene, as well as aromatic alkenes (styrene, 4-methoxystyrene and 2-trifluoromethylstyrene) also participate, albeit slowly and in lower yields.[131] On the other hand, vinylsilanes[132] and vinylstannanes[129] react readily with zincated hydrazones to give the carbometalated products. Cyclohexanone SAMP [(*S*)-1-amino-2-methoxymethylpyrrolidine] hydrazone also reacts with an excess of ethylene to form the allylated product in moderate yield and with a diastereomer ratio of 82:18.[131]



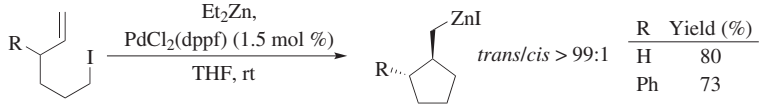
Scheme 96

Zinc enolates and zincated hydrazones react with cyclopropenone ketals in a highly diastereoselective manner to give β-cyclopropylcarbonyl derivatives (Scheme 97).[130] This carbometalation reaction takes place in a *cis* manner with a high level of 1,2-diastereoselectivity for the newly formed C–C bond.

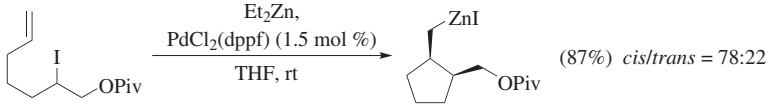


Scheme 97

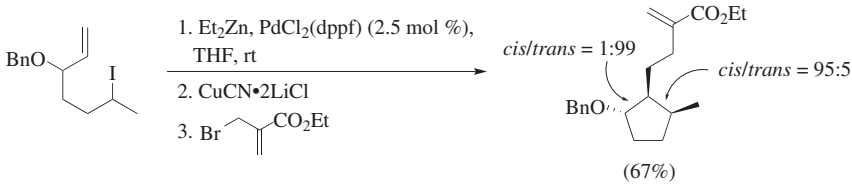
Catalyzed Carbozincation Reactions. *Palladium- and Nickel-Catalyzed Intramolecular Carbozincation.* Alkylzinc iodides are produced from alkyl iodides and Et_2Zn by a palladium- (or copper) catalyzed exchange reaction (Scheme 9).[29] Executing the palladium-catalyzed reaction with unsaturated alkyl iodides affords the cyclized products directly with excellent *trans* diasteroselectivity, irrespective of the nature of the substituent (R = H or Ph) at the allylic position (Scheme 98).[29] Secondary alkyl iodides are even more reactive and undergo smooth palladium-catalyzed carbozincation, which, however, produces predominantly the *cis* isomer (Scheme 99).[134] Involvement of an open-chain organozinc species is thus unlikely and indeed mechanistic studies support a radical cyclization.[135] Nevertheless, if the secondary alkyl iodide bears an additional substituent at the allylic position, a highly diastereoselective carbocyclization occurs (Scheme 100).[134]



Scheme 98

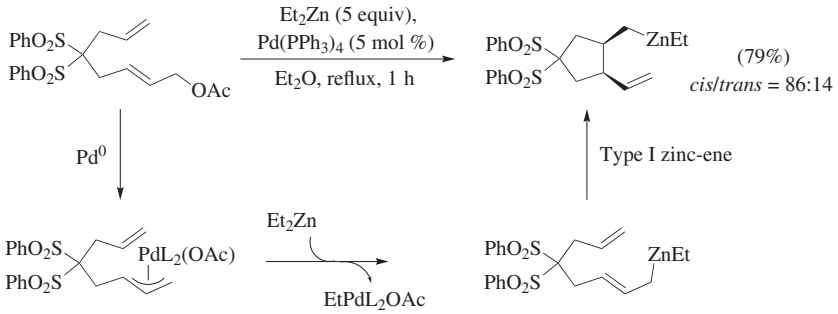


Scheme 99

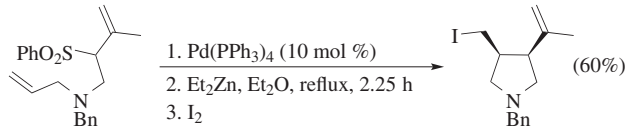


Scheme 100

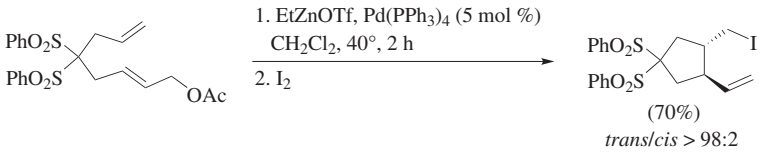
The palladium-catalyzed zinc-ene reaction involves treatment of an allylic acetate with an excess of Et_2Zn in the presence of $Pd(PPh_3)_4$ in refluxing ether. The reaction favors the formation of *cis*-1,2-disubstituted cyclopentanes as the major diastereomers with diastereoselectivities ranging from 83:17 to 98:2, depending on the substrate (Scheme 101).[136] Pyrrolidines can also be easily prepared using the zinc-ene reaction of the allyl sulfone derived from the 1,2-addition of an amine to 2-phenylsulfonyl-1,3-butadiene (Scheme 102).[39] Surprisingly, a reversal of diastereoselectivity is observed when EtZnOTf is used as the zinc precursor in the zinc-ene reaction of an allyl acetate (Scheme 103).[137]



Scheme 101



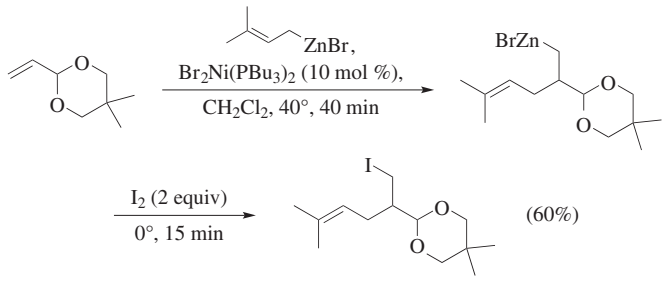
Scheme 102



Scheme 103

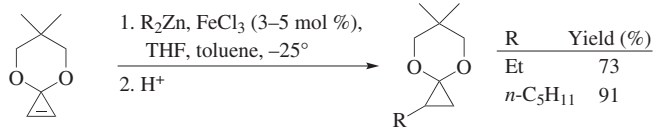
Additionally, some palladium-catalyzed Type II zinc-ene cyclizations have been described, but the products are obtained in low yields.[8] Prenylzinc bromide adds to

acrolein acetals in the presence of a nickel catalyst; interestingly, the reaction occurs without allylic transposition (Scheme 104).[138]



Scheme 104

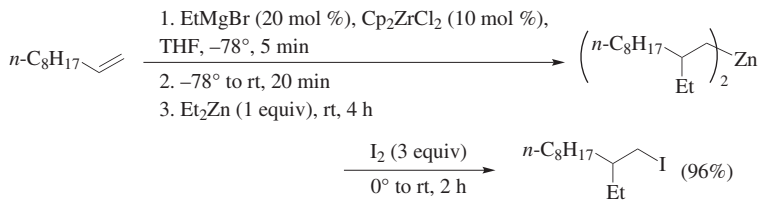
Iron-Catalyzed Carbozincation. The addition of diorganozinc reagents across the strained double bond of cyclopropenone ketals is also catalyzed by $FeCl_3$ and the corresponding alkylated cyclopropanone ketals are obtained in good yields (Scheme 105).[139] A ternary system including $FeCl_3$, a chiral phosphine, and TMEDA also catalyzes the enantioselective addition of Et_2Zn to a cyclopropene ketal.[139]



R	Yield (%)
Et	73
n-C_5H_{11}	91

Scheme 105

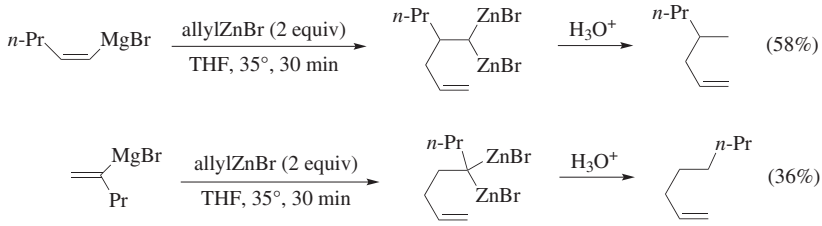
Zirconium-Catalyzed Ethylzincation. The addition of Et_2Zn to a variety of monosubstituted alkenes is catalyzed by a combination of Cp_2ZrCl_2 (10 mol %) and EtMgBr (20 mol %), affording the corresponding ethyl-substituted dialkylzincs (Scheme 106).[140]



Scheme 106

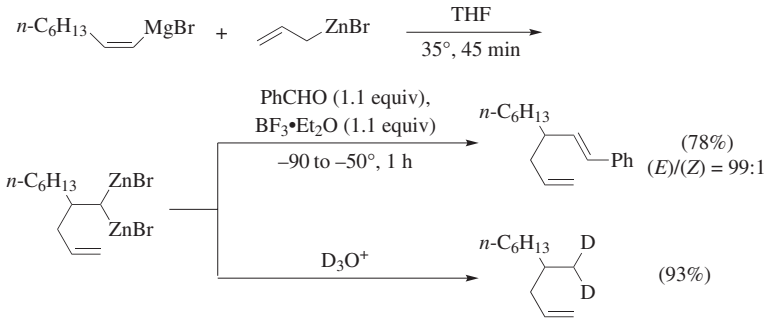
Carbozincation of Metalated Alkenes

The addition of allylzinc bromide to alkenylmagnesium reagents leads to organo-*gem*-dimetallic species (Scheme 107).[76] Although these organometallic compounds are obtained in moderate chemical yields, the reaction provides easy access to *gem*-dimetallic reagents via a carbometalation reaction. Subsequently, it was found that a wide range of 1,1-dimetallic compounds are available in high yields by carbometalation of alkenyl organometallics with allylzinc bromide using similar reaction conditions.[141] The mechanism is described in Scheme 5 in the "Mechanism and Stereochemistry" section. The bismetalated species are oligomeric but, for the sake of clarity, they are represented as monomers in the schemes. Various metals may be used as the alkenyl partners including Li, Mg, B, Al, and Cu, but the presence of zinc (or cadmium) is essential for the addition to proceed.

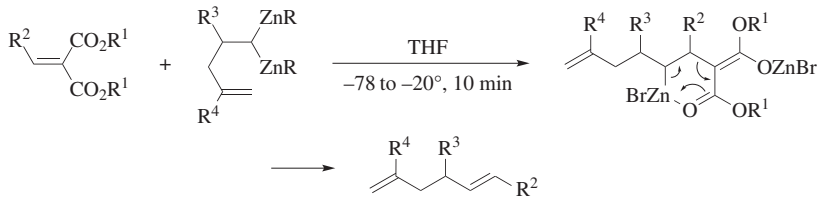


Scheme 107

Reactivity. Treatment of the dimetallic compounds with D_3O^+/D_2O or with aldehydes in the presence of $BF_3{\bullet}Et_2O$ gives the corresponding 1,1-dideuterated alkenes (100% D) and the 1,5-dienes, respectively, in good yields (Scheme 108).[141] The reaction is chemoselective in that ketones do not react. (*Z*)-Alkenes are also obtained with very high stereoselectivity and fairly rapidly by reaction of organo-*gem*-dimetallics with alkylidene malonates at −20° (Scheme 109).[142]



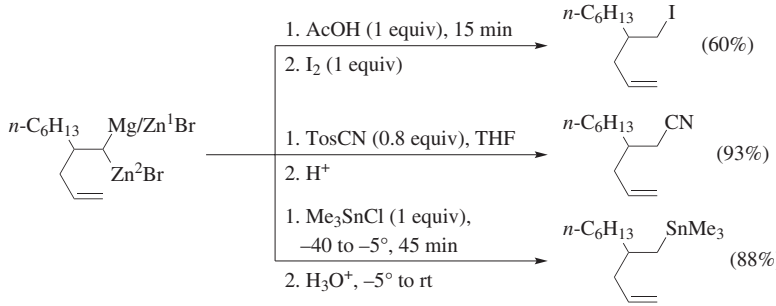
Scheme 108



R^1	R^2	R^3	R^4	Yield (%)	(*Z*)/(*E*)
Et	$EtO_2C(CH_2)_3$	*n*-C_6H_{13}	H	83	82:18
Et	$PhMe_2Si$	*n*-C_6H_{13}	H	83	14:86
Et	$EtO_2C(CH_2)_3$	H	*n*-Bu	81	45:55
i-Pr	$EtO_2C(CH_2)_3$	*n*-C_6H_{13}	H	60	84:16
c-C_6H_{11}	$EtO_2C(CH_2)_3$	*n*-C_6H_{13}	H	91	91:9

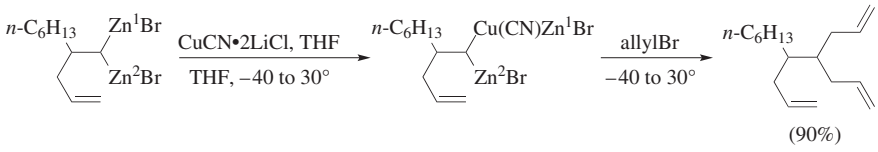
Scheme 109

The different nature of the two metals present in the bismetalated species, or their different stereotopicity, can be used to make two new bonds successively (Scheme 110).[15,88]



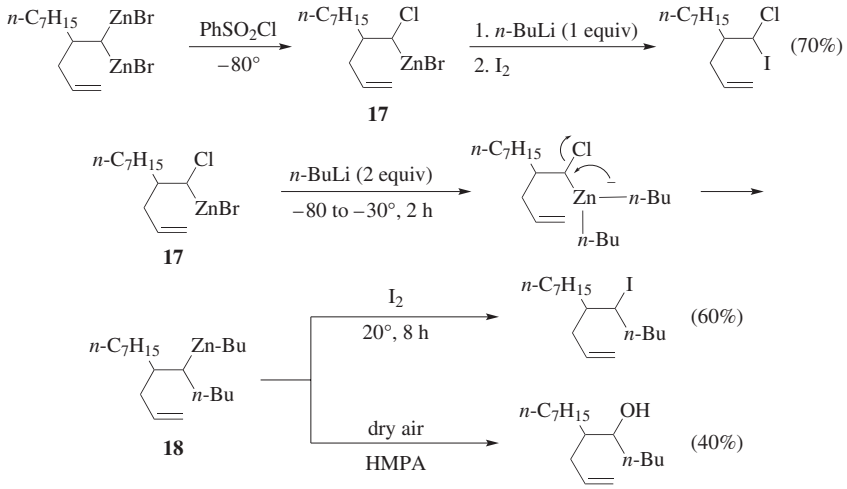
Scheme 110

The reactivity of bismetalated species toward alkylating or allylating electrophiles can be increased by a transmetalation reaction with copper cyanide to provide the corresponding zinc cyanocuprates.[15] These new dimetallic species react with an electrophile to give the monoalkylated or monoallylated derivatives, which, by a second transmetalation step with the same copper cyanide and reaction with the second electrophile, give the corresponding disubstituted products (Scheme 111).[143]



Scheme 111

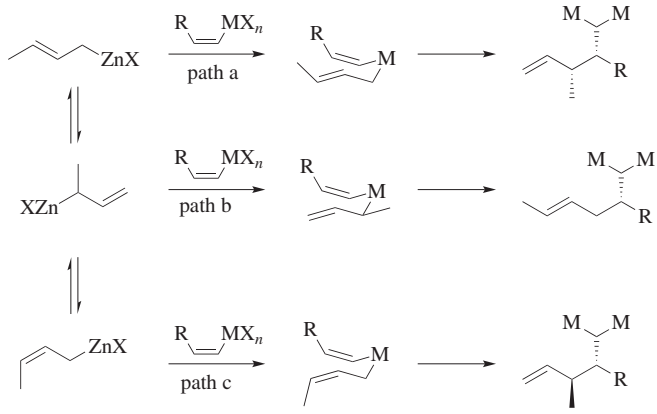
The direct monoalkylation of the organo-*gem*-dimetallic reagents is rather difficult because the second step is competitive with the first; thus, an intramolecular nucleophilic substitution was developed (Scheme 112).[87,144] Reaction of a dimetallic species with neat $PhSO_2Cl$ at −80° affords the α-chlorozinc carbenoid **17**, which is stable at low temperature (typically below −60° in Et_2O solution, or below −20° in THF). Addition of one equivalent of *n*-BuLi followed by quenching with iodine leads to the expected α-chloro-iodo compound. On the other hand, addition of two equivalents of an alkyllithium reagent to the chlorocarbenoid **17** produces the α-chloro-triorganozincate, which undergoes a 1,2-metalate rearrangement to compound **18**. The resulting organometallic species may further react with iodine to give the secondary alkyl iodide, or may be oxidized by a slow absorption of dry air to give the secondary alcohol.[144]



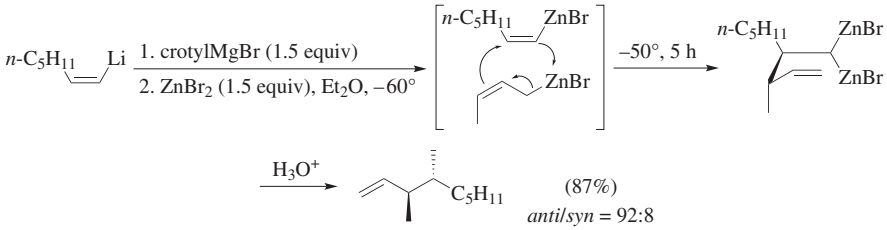
Scheme 112

Diastereoselectivity. The addition of substituted allylic systems to configurationally homogeneous alkenylmetals can generate at least three products by an intermolecular metallo-ene reaction (Scheme 113).[145] The diastereoselection is highly dependent on the temperature and on the nature of the solvent. Thus, decreasing the Lewis basicity of the solvent by changing from THF to ether speeds up the reaction considerably and allows it to be carried out at much lower temperature. For example, (*Z*)-1-heptenylithium reacts with crotylmagnesium bromide and zinc dibromide in ether at −50° to give the stable 1,1-dimetallic species within five hours. After acidic hydrolysis, the *anti* product, (3*S*,4*R*)–dimethylnonene, is obtained in 87% yield and 92:8 diastereomer ratio (Scheme 114).[145] The *syn* diastereomer is similarly obtained in high diastereomeric purity by using (*E*)-1-heptenyllithium as the substrate (Scheme 115).[145] By comparison, crotylzincation of 1-octene requires

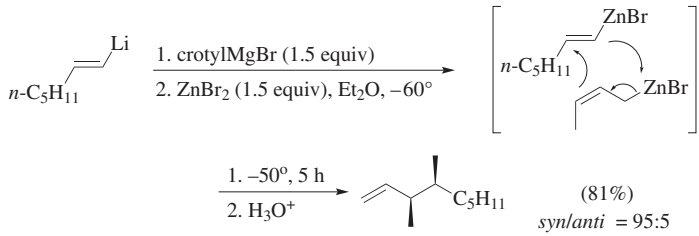
heating to 50° for 66–96 hours, with 1-octene being used as the solvent.[18] The high diastereoselectivity observed in the crotylmetalation of vinylmetals may be accounted for by a kinetically favored (*Z*)-configuration of the crotylmetal species in a chair-like transition state structure.[145]



Scheme 113

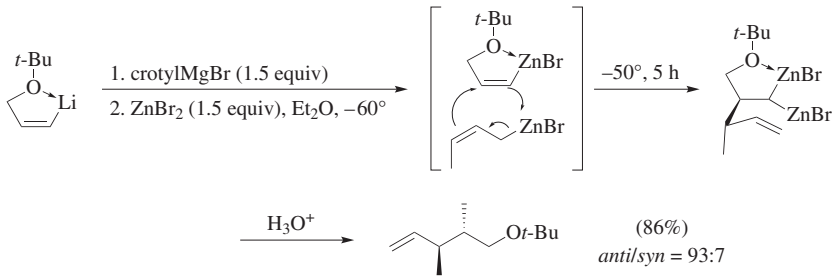


Scheme 114



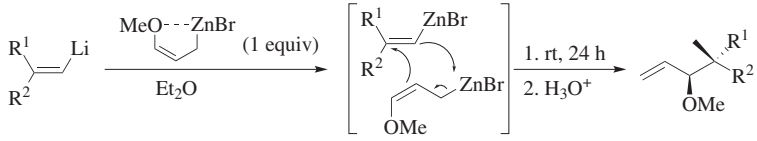
Scheme 115

Crotylmetalation of (*Z*)-3-lithio-1-propenyl *tert*-butyl ether, in which the zinc may be strongly coordinated by the *tert*–butoxy group, still proceeds at low temperature with high diastereoselectivity (Scheme 116).[145]



Scheme 116

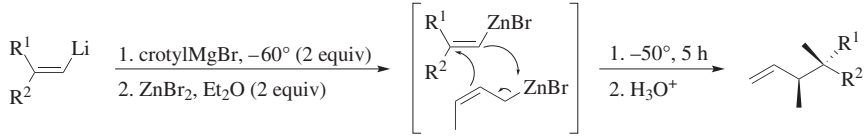
An allylzinc bromide bearing an alkoxy group may also be employed as shown in Scheme 117.[145]



R^1	R^2	Yield (%)	dr
t-BuOCH$_2$	H	80	95:5 *anti*
H	*t*-BuOCH$_2$	81	95:5 *syn*

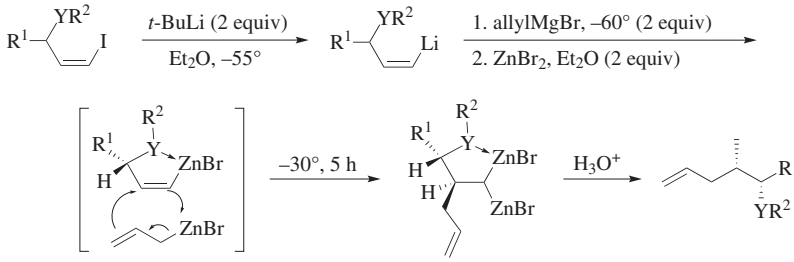
Scheme 117

This method has been extended to various γ–heterosubstituted vinylmetals (Scheme 118)[146] and to the allylmetalation of γ–alkyl–γ–heterosubstituted vinylmetals (Scheme 119).[146–148] In the latter reactions, the allyl reactant approaches the vinyl group from the side opposite to the alkyl group in the rigid five-membered ring formed by coordination of the zinc by the heteroatom. The same selectivity is obtained when the γ–trimethylsilylpropargylic alcohol is used directly as the starting material in a one-pot reaction (Scheme 120).[147]



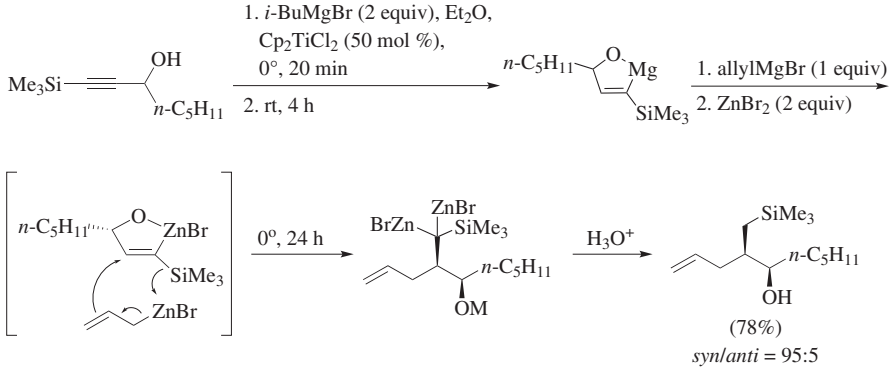
R^1	R^2	Yield (%)	*syn*/*anti*
H	$PhSCH_2$	65	95:5
H	Et_2NCH_2	60	92:8
Et_2NCH_2	H	65	9:91
$PhSCH_2$	H	56	5:95

Scheme 118



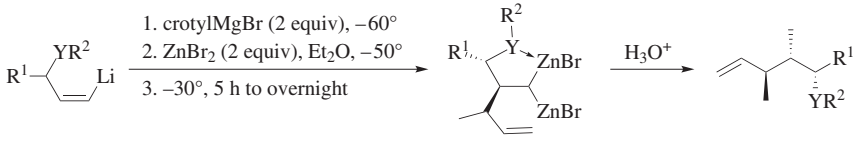
R^1	YR^2	Yield (%)	*syn/anti*
n-Pr	*t*-BuO	81	95:5
Me	Bn_2N	75	98:2
n-Bu	MeS	65	98:2

Scheme 119



Scheme 120

Combining this facial selectivity with the selectivity arising from use of a substituted allylzinc bromide creates three contiguous stereogenic centers (Scheme 121).[146,147]

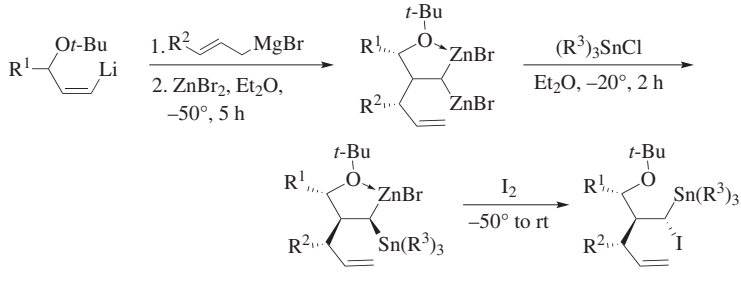


R^1	YR^2	Yield (%)	*anti/syn*
n-Pr	*t*-BuO	75	>95:5
Me	Bn_2N	72	>95:5
n-Bu	MeS	62	>95:5

Scheme 121

The chelated organo-*gem*-dimetallics react with one equivalent of R_3SnCl to give the [α-(trialkylstannyl)alkyl]zinc chlorides and then with one equivalent of iodine to

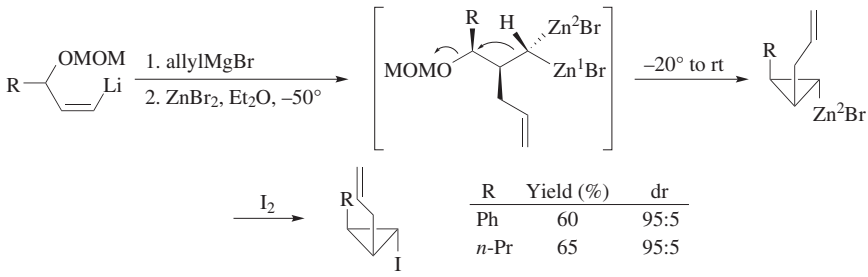
give the corresponding (α-iodoalkyl)trialkylstannanes with fair to good diastereoselectivity and good yield (Scheme 122).[15,149]



R^1	R^2	R^3	Yield (%)	*syn*/*anti*
H	H	Me	83	75:25
H	H	*n*-Bu	79	75:25
n-Pr	Me	*n*-Bu	80	95:5

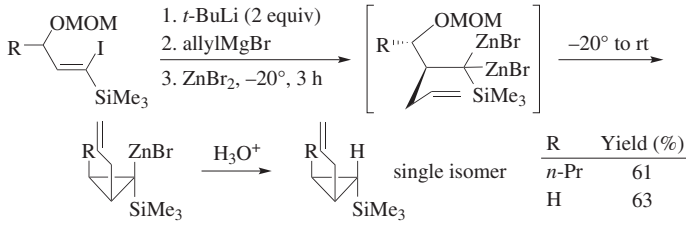
Scheme 122

As depicted in Scheme 121, the addition of substituted allylzinc bromides to γ-hetero-substituted vinyl metals (YR = OBu-*t*, NR_2, SR) allows the creation of stereogenic centers. However, if the coordinating group is a methoxymethyl (MOM) ether, the dimetallic species is not stabilized at higher temperature and becomes thermally labile. Warming the mixture to room temperature promotes an internal nucleophilic substitution, leading to a configurationally stable metalated cyclopropane, which can further react with electrophiles (Scheme 123).[150] Since the alkyl and allyl groups are *anti* to each other in the bismetalated intermediate and *cis* in the metalated cyclopropane, the internal nucleophilic substitution of the MOM group by one of the C–M bonds occurs with inversion of configuration at the electrophilic center. To explain the origin of the relative configuration of the metalated carbon observed in the product (*trans* to the alkyl and allyl groups), a mechanism involving an inversion–inversion at both centers through a W-shaped conformer is postulated.[151] The diastereoselective synthesis of a tetrasubstituted cyclopropane can also be achieved using the same procedure (Scheme 124).[151] In this case, a gauche interaction exists in the W-shaped transition state structure **19** between trimethylsilyl and the allyl moiety that is released in structure **20**; such an interaction is absent in the nonsubstituted structure **21**.

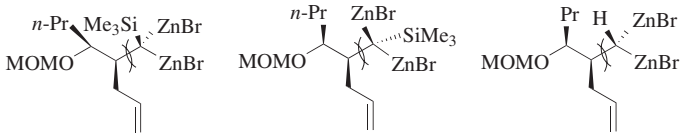


R	Yield (%)	dr
Ph	60	95:5
n-Pr	65	95:5

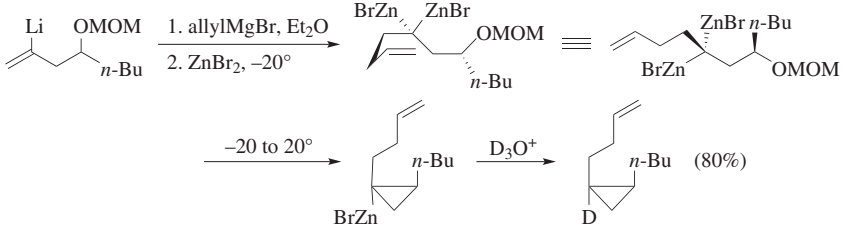
Scheme 123



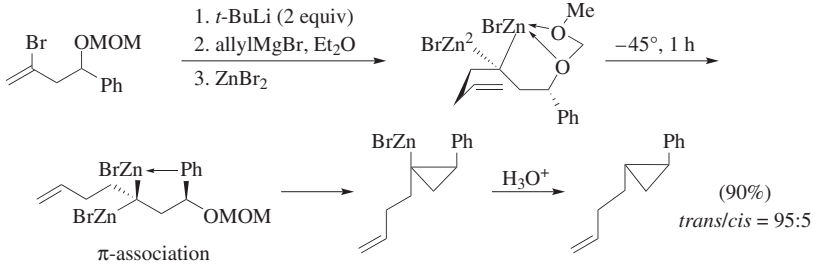
Scheme 124



An alternative strategy to prepare tertiary cyclopropylzinc derivatives is shown in Scheme 125).[151] Replacing the butyl group with a phenyl group changes the stereochemical outcome of the cyclization reaction. Although the carbometalation is performed at lower temperatures, the organo-*gem*-dimetallic reagent cyclizes immediately to afford the *trans*-cyclopropane with a diastereomer ratio of 95:5. This unexpected result led the authors to consider π-association between one metal and the phenyl group in the W-shaped transition state structure (Scheme 126).[151]



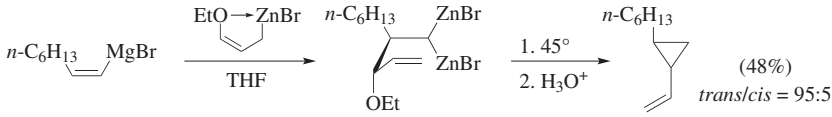
Scheme 125



Scheme 126

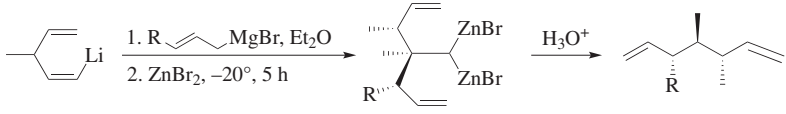
This situation holds true if a vinyl group replaces the phenyl group, whereas its replacement by a pentafluorophenyl group, which is less prone to π-association with the metal, results in a 1:1 mixture of *cis* and *trans* isomers. Also, the use of a more coordinating solvent (THF instead of ether) disrupts this association and lower diastereoselectivity is observed.[151]

Yet another approach to 1-alkyl-2-vinylcyclopropanes[152,153] involves addition of (3-ethoxyallyl)zinc bromide to an alkenylmagnesium reagent to afford an organo-*gem*-dimetallic species that undergoes a 1,3-elimination leading to the corresponding cyclopropane (Scheme 127).[152]



Scheme 127

A double bond is capable of a weak dipolar interaction with the zinc atom of an organozinc species as the result of the inherent polarity of the Zn^{+}–C^{-} bond and the partial negative charge on the terminal carbon of the double bond. Such an interaction has been identified by NMR investigations[15] and an X-ray structure determination.[154] A double bond thus may take the place of a heteroatom in reactions of the type discussed above. For example, treatment of 1-lithio-3-methyl-1,4-pentadiene with allylzinc bromide or crotylzinc bromide leads to the corresponding dienes with good diastereoselectivity (Scheme 128).[155] In these reactions, the terminal vinyl moiety coordinates the zinc atom to form a five-membered ring complex and the allyl or crotyl reagent approaches the vinylzinc moiety *anti* to the methyl group. Notably, when the vinyl group is replaced by an ethyl group, two diastereomers are obtained in equal amounts.[155]

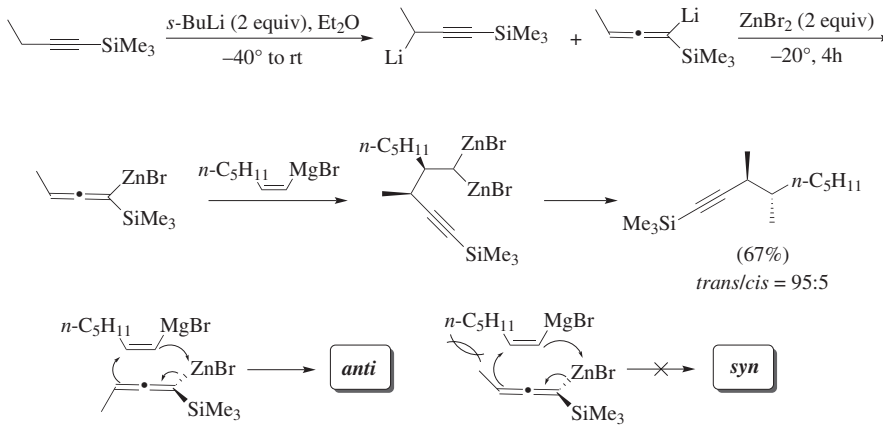


R	Yield (%)	dr
H	67	90:10
Me	77	>95:5

Scheme 128

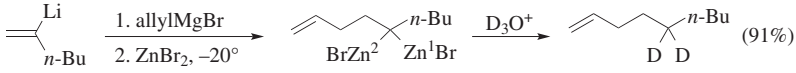
The carbometalation of alkenylmetals can also be carried out with substituted propargylzinc bromides (Scheme 129).[146] The addition of zinc salts to a propargyl/allenyl organolithium reagent leads quantitatively to the allenylzinc bromide.[146] Considering that the latter reacts with the alkenyl metal reagent via an S_E2' process, the stereochemical result is explained by minimizing steric interaction between the

methyl group located on an sp^2 carbon atom of the allenic system and the prochiral carbon atom of the alkenyl metal moiety. The transition state leading to the *syn* isomer is highly disfavored by the repulsion between the two alkyl groups. The same diastereomer is obtained from the (*E*)-alkenylmagnesium reagent, and the scope of the reaction is quite broad. The use of functionalized alkenyl metals, as well as the replacement of the alkyl group on the allenyl zinc bromide by other alkyl groups are possible without altering the diastereoselectivity.[146]

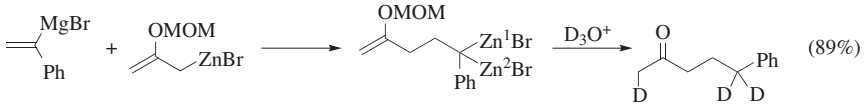


Scheme 129

Alkenes metalated at the internal carbon of the double bond may also be employed as illustrated in Scheme 130[156] and Scheme 131.[157] Of special interest in the latter reaction is the addition of a functionalized allylic zinc reagent such as [2-(methoxymethoxy)-2-propenyl]zinc bromide, since it allows a formal site-selective addition of an acetonyl moiety across the styrene double bond (Scheme 131). However, the reaction fails with β-substituted α-styrylmagnesium bromides such as (1-phenyl-1-pentenyl)magnesium even under forcing conditions.[157]



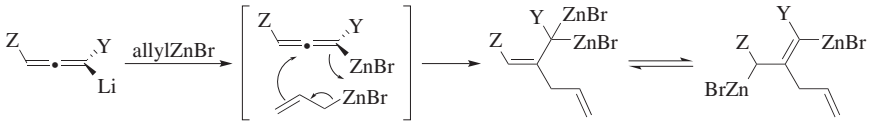
Scheme 130



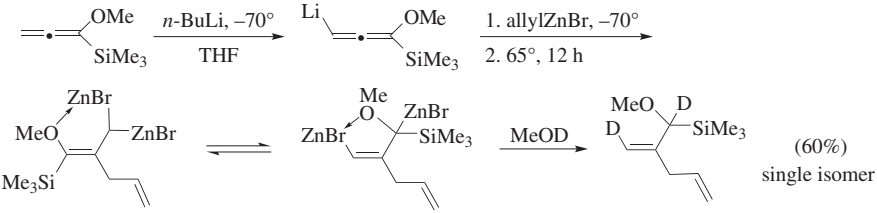
Scheme 131

Carbozincation of Metalated Allenes

Allylic 1,1-dimetallic reagents are easily obtained by addition of allylzinc bromide to metalated allenes. They may react as geminal dimetals or as vinylic-allylic 1,3-dimetallic species as a consequence of tautomerism (Scheme 132).[158] If an oxygen atom is present γ to the lithium atom, deuterolysis of the reaction mixture shows that the reaction is regioselective. Deuteration occurs exclusively on carbons 1 and 3 (Scheme 133).[158]

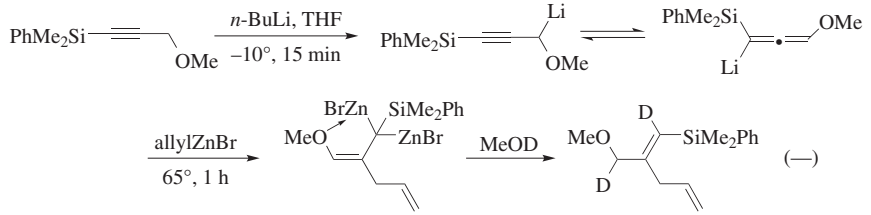


Scheme 132

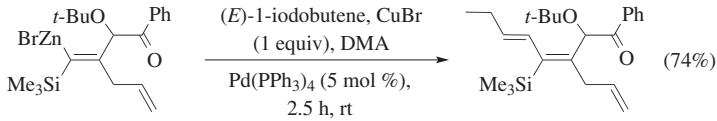


Scheme 133

The metalation of propargylic ethers also leads, via its metalotropic equilibrium, to the corresponding allenylmetal, which can react with allylzinc bromide. Again, a single isomer is obtained after deuterolysis (Scheme 134).[158] The high regio- and stereoselectivity is accounted for by a favorable coordination of the dimetallic reagent. The latter can also react with other electrophiles, such as acyl chlorides, ketones, aldehydes, phenyl isocyanate, alkyl halides, and imines to give the corresponding monofunctionalized vinyl metals.[159] These intermediates can then react with a second electrophile. The reactivity of the second metal is lower than the reactivity of the first due to the vinylic character of the remaining metal and the intramolecular coordination by the heteroatom. However, it can be deuterated, iodinated, or coupled with a vinyl iodide under palladium catalysis in the presence of a stoichiometric amount of a copper salt in DMA or DMF (Scheme 135).[159]

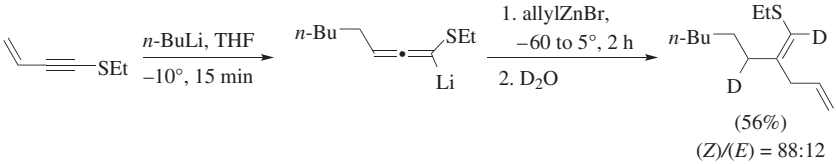


Scheme 134

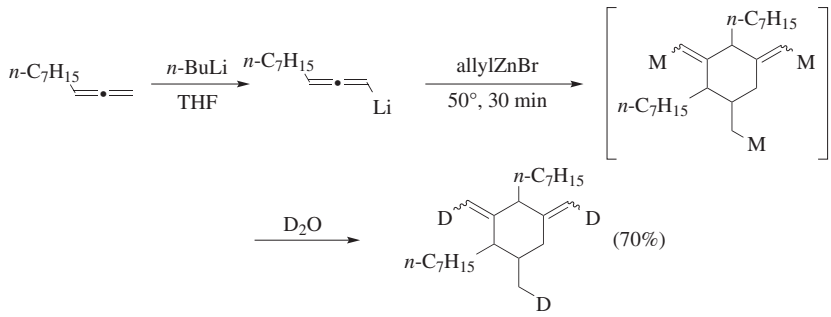


Scheme 135

Metalated allenes can also be prepared by carbolithiation of activated enynes. In this case, the subsequent addition of allylzinc bromide followed by an acidic deuterolysis produces an 88:12 mixture of geometric isomers (Scheme 136).[158] Performing the reaction with nonsilylated or nonoxygenated adducts causes the dimetallic reagent to be protonated nonregioselectively and undergo three consecutive rearrangements leading to cyclic polyorganometallic species with good stereoselectivity (Scheme 137).[160]



Scheme 136

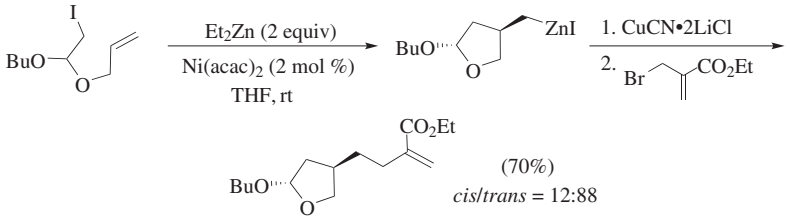


Scheme 137

APPLICATIONS TO SYNTHESIS

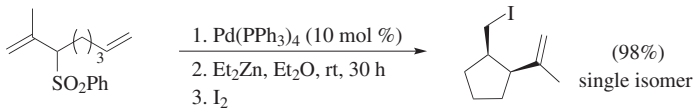
The Pd-catalyzed carbozincation reaction is not efficient for the preparation of five-membered ring oxygen or nitrogen heterocycles and a nickel-catalyst is required in such instances (Scheme 138).[133] This method has been applied to the synthesis

of several natural products, including (+)-methyl *epi*-jasmonate[135] and the antitumor antibiotic (−)-methylenolactocin.[161]

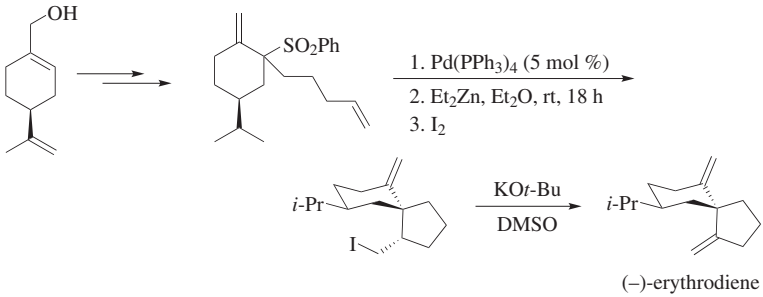


Scheme 138

A palladium-catalyzed Type I zinc-ene reaction has been used to prepare the carbon skeleton of the sesquiterpenoid (−)-erythrodiene;[139] however, the zinc-ene cyclization utilizing an allyl sulfone as precursor is even more efficient (Scheme 139).[39] The main advantage of this strategy is that substituted allyl sulfones are accessible by a wide range of simple procedures. One example is the concise total synthesis of (−)-erythrodiene in only six linear steps from (−)-perillyl alcohol in an overall 60% yield (Scheme 140).[39]

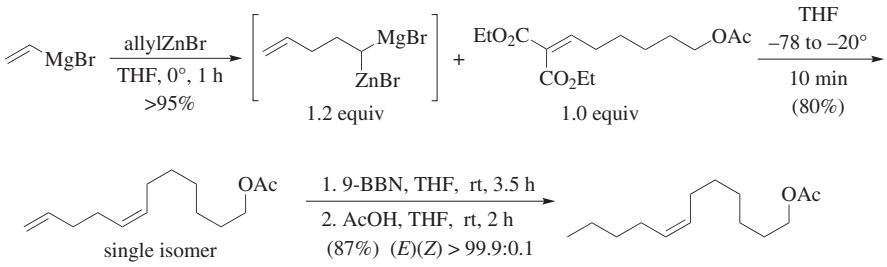


Scheme 139



Scheme 140

The cabbage looper moth pheromone is synthesized in only two steps by alkenylation of a functionalized alkylidenemalonate with a 1,1-dimetalloalkane (Scheme 141).[142]



Scheme 141

COMPARISON WITH OTHER METHODS

Carbometalation reactions in general, and carbozincation reactions in particular, critically depend on the nature of the initial nucleophilic organozinc derivative and on the electrophilicity of the carbon–carbon multiple bonds. Alkyl- and arylzinc derivatives exhibit a low intrinsic reactivity and only rarely undergo uncatalyzed intermolecular carbozincation reactions. The same is true for any carbometalation reaction. However, since one of the most distinguishing features of organozinc species is their ability to undergo transmetalation reactions with transition metal complexes, the metal-catalyzed carbozincation reaction has been widely exploited in addition reactions with alkenes and alkynes. Moreover, the carbon–zinc bond formed in the carbozincation reaction usually exhibits configurational stability, which may lead to a unique isomer after reaction with electrophiles. One additional major advantage of the carbozincation reaction is the possibility of using allylic organozinc reagents as nucleophilic species. Allylzinc reagents are much more reactive towards unsaturated carbon–carbon bonds than alkylzincs or any other allylmetal species. The use of an allylic organometallic reagent is also more attractive from a synthetic point of view as the allyl moiety can be easily converted into a variety of important functional groups.

The carbozincation of alkenes and alkynes by allylic organozinc reagents is generally considered to be a metallo-ene process involving a six-centered transition state and has found many important applications. Although still under investigation, most studies indicate that the zinc-ene reaction presents a wider scope than the well-known magnesium-ene reaction. A special feature unique to allylzinc species is their addition to metalated vinyl and alkynyl derivatives leading to bismetalated species. Here again, only the presence of zinc allows such transformations. The addition of substituted allylic systems with a stereochemically pure alkenylmetal proceeds with excellent diastereoselection creating two new sp^3 stereogenic centers. For example, the high diastereoselectivity observed in the crotylzincation has been attributed to the preferential (*Z*)-crotylzinc reagent reacting through a chair-like transition state.

The allylzincation reaction of a γ-heterosubstituted alkenylmetals also proceeds with very high diastereoselectivity. The resulting bismetalated species can be further used for polyfunctionalization of the carbon skeleton. Similarly, the propargylzincation of alkenyl metal reagents is a useful method for the introduction of an alkynyl residue on a substituted double bond.

Among the intramolecular carbometalation reactions, and particularly the 5-exo-trig cyclization reactions, carbozincation presents some advantages over the well-known carbo-lithiation and -magnesiation reactions. For instance, the most serious limitation of carbo-lithiation and -magnesiation methods is the highly reactive nature of the carbon–metal bond, which precludes the presence of many functional groups. Moreover, it is often difficult to prepare secondary and tertiary alkyllithium derivatives via iodine–lithium exchange, and still impossible to perform the carbolithiation reaction on α,β-unsaturated electrophilic alkenes. Such limitations are very easily overcome using the organozinc derivatives since they are easily prepared in the presence of functional groups, can be accessed by zinc insertion into primary, secondary, and even tertiary carbon–iodine bonds, and add across α,β-unsaturated carbonyl compounds, provided that the organozinc species is secondary. Notably, organozinc derivatives prefer to react with isolated double bonds rather than with a functional group such as an ester.

Finally, a unique feature of carbozincation reactions is the ability of delocalized organozinc species to add across double and triple bonds, including propargylic zinc halides (zinc-ene-allene and zinc-yne-allene carbocyclization reactions) and, more recently, zinc enolates of ester derivatives. Such transformations are exclusive to zinc and represent a carbon analog of the aldol addition reaction.

EXPERIMENTAL CONDITIONS

Caution: Extreme care should be taken in reactions involving pyrophoric (neat) diethylzincs, *trialkylaluminums*, *and alkyllithiums.* These organometallic reagents should be transferred with dry gas-tight syringes using standard procedures for handling air-sensitive reagents. Immediately after use, these syringes should be rinsed by purging them several times in an Erlenmeyer flask containing an anhydrous solvent such as acetone, dichloromethane, or hexane. Use of a cannula instead of a syringe is recommended for reactions involving pyrophoric reagents. Argon is recommended as the inert gas.

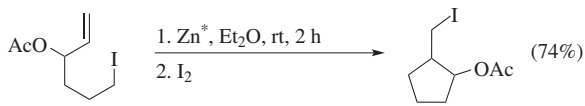
The form of zinc (dust, foil, shot) is important for the success of the formation of an organozinc halide by oxidative addition. Usually, zinc dust (325 mesh) gives the best results. Procedures for activation may involve removal of inert oxide by washing several times with 5% hydrochloric acid and washing in turn with water, methanol, and ether, followed by drying.[162] The preparation of functionalized alkylzinc halides is best performed by adding a THF solution of an alkyl iodide to 2–3 equivalents of zinc dust that has been successively activated with a solution of 1,2-dibromoethane (3–5 mol %) and TMSCl (1 mol %). It is important to add the alkyl iodide as a concentrated solution (2.5–3 M) in THF to obtain rapid zinc insertion. Under these conditions, primary alkyl iodides undergo zinc insertion between 30 and 40°, whereas secondary alkyl iodides react more readily (15° to room temperature). Organozinc halide formation is usually complete after a few hours. The organometallic solution is diluted with THF to a 1.0–1.5 M solution, and the excess zinc dust is allowed to settle. The clear, colorless supernatant liquid can be transferred with a syringe or cannula to a separate flask and used for further applications.

The analysis of organozinc halides can be conveniently performed by gas chromatography. This method is optimal for following formation of the zinc species. Thus, an internal standard (dodecane or other inert alkane) is added to the alkyl iodide before the addition to the zinc slurry in THF. The ratio of the two compounds is determined by GC analysis. At the end of the reaction, no alkyl iodide should be present. A small reaction aliquot is then treated with a THF solution of iodine and the new ratio of the reformed alkyl iodide to the internal standard is determined, allowing the precise evaluation of the yield of the organozinc reagent.

When a solution of highly reactive zinc is needed (Rieke zinc, see "Experimental Procedures"), a solution of freshly fused $ZnBr_2$ is prepared in Et_2O (usually 1 M solution) and treated with lithium naphthalenide. The preparation of allylic zinc reagents gives better yields if cut zinc foil or granular zinc (30 mesh) is used. The fragmentation reaction of homoallylic alcohols allows the preparation of highly substituted and functionalized allylic zinc reagents.[163]

Caution: When using diethylzinc for an iodine–zinc exchange, it is important to strictly maintain the absence of moisture and air, because of the high reactivity of this reagent toward water and oxygen. Special care must be taken during subsequent removal of the excess diethylzinc, which is a highly flammable liquid. Mixtures of diethylzinc and liquid oxygen are explosive. The condensation of oxygen into a trap containing diethylzinc must be absolutely avoided. However, dilution of diethylzinc with acetone, toluene, or THF (∼1 M solution) affords a solution that does not burn spontaneously in air.

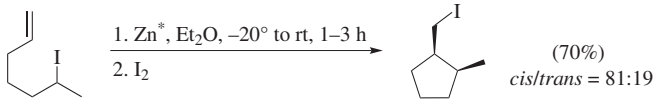
EXPERIMENTAL PROCEDURES



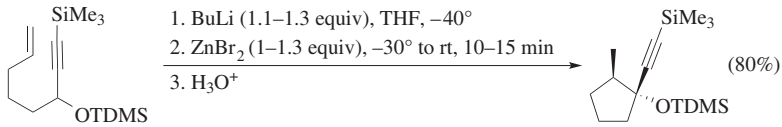
1-Acetoxy-2-iodomethylcyclopentane [General Procedure for the Cyclization Involving Rieke's Activated Zinc].[51] *Preparation of Rieke's activated zinc.* A 50-mL 2-necked flask, fitted with a magnetic stirrer, an inert gas inlet, and a septum cap was charged with naphthalene (1.62 g, 12.66 mmol) and freshly cut lithium (84.9 mg, 12.23 mmol). Anhydrous THF (5 mL) was added and the color of the reaction mixture immediately turned dark green. The mixture was stirred for 2 h at rt, and then cooled in an ice-water bath, while 1 M zinc bromide (Et_2O, 6.15 mL, 6.15 mmol) was added dropwise (2 drops per second). The black suspension was stirred for 10 min at rt and anhydrous Et_2O (20 mL) was added. The stirring was stopped and the activated zinc was allowed to settle. The supernatant was removed via cannula and anhydrous Et_2O (20 mL) was added. The suspension was stirred for 5 min and allowed to settle. The washing process was repeated twice and finally anhydrous Et_2O (15 mL) was added to the active zinc slurry, which was ready for use.

Intramolecular carbometalation of organozinc reagents. Neat 3-acetoxy-6-iodohexene (750 mg, 2.8 mmol) was added to the vigorously stirred suspension of

the active zinc. The consumption of the iodide as well as the formation of the cyclic products were followed by gas chromatographic analysis of hydrolyzed aliquots, and after 1 h at rt, the reaction mixture was treated with I_2 (770 mg, 3 mmol). The crude material was purified by silica gel chromatography (cyclohexane/EtOAc, 100:0– 4:1) to afford the product (532 mg, 74%) as a colorless oil (59/41 mixture of *cis*/*trans* diastereomers): IR (film) 2950, 2820, 1730, 1440, 1420, 1370, 1235, 1175, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.19 (m, 0.59H, C*H*OAc *cis*), 4.80 (m, 0.41H, C*H*OAc *trans*), 3.33 (dd, J = 9.3, 4.9 Hz, 0.41H, C*H*I trans), 3.26–3.13 (m, 1.59H C*H*I *cis* and *trans*), 2.32 (m, 0.59H, C*H*CH_2I *cis*), 2.20 (m, 0.41H, C*H*CH_2I *trans*), 2.05 (s, 1.77H, CH_3CO *cis*), 2.02 (s, 1.23H, CH_3CO *trans*), 2.00–1.30 (m, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.1, 80.1, 77.3, 47.7, 47.3, 32.5, 32.4, 31.7, 30.6, 22.5, 21.1, 10.3, 4.68. Anal. Calcd for $C_8H_{13}O_2I$: C, 35.48; H, 4.88. Found: C, 36.11; H, 4.97.

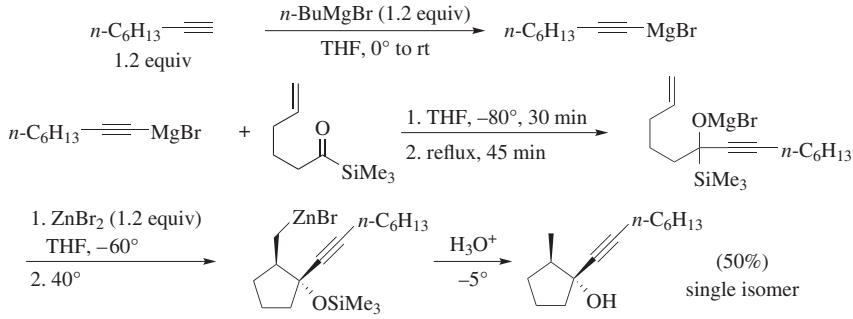


***cis*-1-Iodomethyl-2-methylcyclopentane [Carbocyclization of a Secondary Organozinc Reagent].[51]** Rieke's activated zinc was generated by addition of 1 M zinc bromide (Et_2O, 4.7 mL, 4.7 mmol) to a solution of lithium naphthalenide (9.38 mmol) prepared from lithium (65.1 mg, 9.38 mmol) and naphthalene (1.24 g, 9.69 mmol) in anhydrous THF (5 mL). It was then washed several times with anhydrous Et_2O as described in the general procedure. Neat 6-iodo-1-heptene (300 mg, 1.33 mmol) was added to the suspension of active zinc in Et_2O at −20°. After stirring for 40 min, gas chromatography of both hydrolyzed and iodinolyzed aliquots indicated a complete conversion to the corresponding organozinc reagent and that cyclization had only occurred to an extent of 5%. The reaction mixture was slowly warmed to rt, and the amount of cyclic products reached 50% at −5° and 100% at 10° (*cis*/*trans*, 81:19). The reaction mixture was then treated with iodine. The crude product was purified by silica gel chromatography (pentane) to give the major diastereomer (209 mg, 70%) as a colorless oil (*cis*/*trans*, 98:2): ^1H NMR ($CDCl_3$, 200 MHz) δ 3.12 (dd, J = 7.8, 1.6 Hz, 2H), 2.25 (m, 1H), 2.15 (m, 2H), 1.85–1.25 (m, 5H), 0.80 (d, J = 6.9 Hz); Anal. Calcd for $C_7H_{13}I$: C, 37.52; H, 5.85. Found: C, 37.69; H, 5.97.



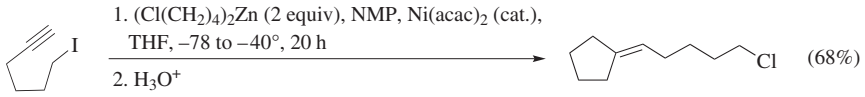
1-[(Thexyldimethylsilyl)oxy]-2-methyl-1-[(trimethylsilyl)ethynyl]cyclopentane [Intramolecular Metallo–Ene–Allene Reaction].[113] A solution of 1-(trimethylsilyl)-3-[(thexyldimethylsilyl)oxy]oct-7-en-1-yne (400 mg, 1.2 mmol)

in anhydrous THF (10–15 mL) was cooled to −40° while 1.6 M *n*-BuLi (hexanes, 1.1–1.3 equiv) was added dropwise. The color of the solution immediately turned yellow-orange. When the metalation was complete, 1 M zinc bromide (Et_2O, 1–1.3 equiv) was added dropwise at −30°, and the reaction mixture was allowed to warm to rt and stirred for an additional 10–15 min. The reaction mixture was cooled to −5° while 1 M aq HCl (10 mL) was added slowly. Et_2O was added, the layers were separated, and the aqueous layer was extracted with Et_2O. The combined extracts were washed with saturated aq $NaHCO_3$ and stirred for at least 3 h with a few crystals of $Na_2S{\bullet}9H_2O$, then filtered to remove all zinc salts before further purification (otherwise isolated yields are lower than those reported). The filtrate was washed with brine, dried over $MgSO_4$, and concentrated under vacuum. The crude product was purified by silica gel flash chromatography (pentane/EtOAc, 98:2) to afford the title product (318 mg, 80%) as a colorless liquid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.0–1.2 (m, 7H), 0.95 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.9 Hz, 3H), 0.95 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 6.9 Hz, 3H), 0.78 (s, 6H), 0.19 (s, 3H), 0.18 (s, 3H), 0.14 (9, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 108.3, 90.6, 79.7, 46.8, 41.6, 34.4, 30.2, 24.9, 20.6, 20.3, 18.8, 18.7, 16.3, 0.0, −0.9, −1.0.

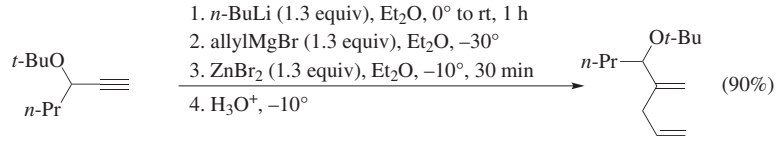


***trans*–2–Methyl-1-(1-octynyl)cyclopentanol [Tandem Zinc-Promoted Brook Rearrangement/Ene–Allene Carbocyclization Reaction].[33]** To a cold (0°) stirred solution of octyne (0.18 mL, 1.2 mmol) in THF was added 1 N *n*-BuMgBr (Et_2O, 1.2 mL, 1.2 mmol) dropwise. The mixture was first warmed to rt for 90 min and then cooled to −80° while adding trimethyl(1-oxo-5-hexenyl)silane (0.170 g, 1 mmol) over a period of 30 min. The mixture was heated at reflux for 45 min, cooled to −60°, and 1 N $ZnBr_2$ (THF, 1.2 mL, 1.2 equiv) was added. The reaction mixture was heated at 40° for a few hours and the progress of the reaction was followed by gas chromatography of hydrolyzed aliquots. The reaction mixture was cooled to −5° while 1 M aq HCl (10 mL) was added slowly. Et_2O was added, the layers were separated, and the aqueous layer was extracted with Et_2O. The combined extracts were washed with saturated aq $NaHCO_3$, stirred for at least 3 h with a few $Na_2S{\bullet}9H_2O$ crystals, then filtered to remove all zinc salts. The filtrate was washed with brine (2 x15 mL), dried over $MgSO_4$, and concentrated under vacuum. Purification by column chromatography on silica gel gave the title product (0.107 g, 50%) as a colorless liquid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.21 (t, J = 6.9 Hz, 2H),

2.05–1.85 (m, 4H), 1.69–1.66 (m, 2H), 1.48–1.45 (m, 2H), 1.45–1.23 (m, 7H + 1H, O*H*), 1.0 (d, $J = 6.6$ Hz, 3H), 0.88–0.83 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 114.5, 81.5, 78.6, 45.7, 41.0, 31.3, 31.0, 28.8, 28.5, 22.5, 20.4, 18.7, 16.4, 14.0.

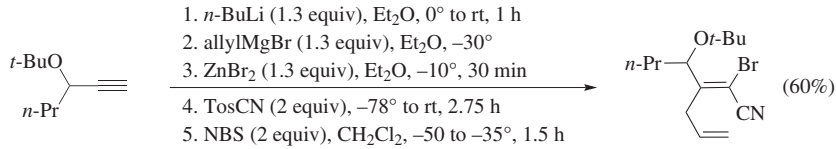


(5-Chloropentylidene)cyclopentane [Intramolecular Nickel-Catalyzed Carbozincation].[74] $Ni(acac)_2$ (116 mg, 0.45 mmol) was dissolved in THF (4.5 mL) and NMP (1.5 mL) at −40° under argon and 6-iodo-1-hexyne (1.24 g, 6 mmol) was added. The solution was cooled to −78° and bis(4-chlorobutyl)zinc (12 mmol) in THF (1 mL) was carefully added by syringe. The reaction mixture was stirred for 20 h at −40° and then was hydrolyzed with saturated aq NH_4Cl (5 mL). The aq phase was extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvents were evaporated. The crude residue was purified by silica gel chromatography (hexanes) to give the title product (0.70 g, 68%): IR (neat) 2935 (s), 1440 (m), 920 (w), 740 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.19–5.12 (m, 1H), 3.46 (t, $J = 6.8$ Hz, 2H), 2.16–2.07 (m, 4H), 1.93–1.91 (m, 2H), 1.74–1.69 (m, 2H), 1.62–1.23 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.6, 119.2, 44.9, 33.4, 32.1, 28.6, 28.5, 26.8, 26.3, 26.2; EIMS *m*/*z*: M^+ 172 (13), 95 (100), 82 (39), 67 (87), 41 (36); M^+ calcd for $C_{10}H_{17}Cl$, 172.09974; found, 172.10184.

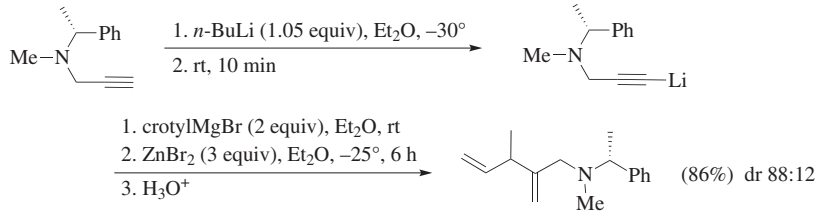


5-*tert*-Butoxy-4-methylen-oct-1-ene [Synthesis of an *sp*^{2} Organo-*gem*-bismetallic by Allylmetalation of an Alkenylmetal].[86] To a cooled (0°) solution of 3-(*tert*-butoxy)hex-1-yne (309 mg, 2 mmol) in anhydrous Et_2O (10 mL) was added dropwise 1.6 M *n*-BuLi (hexane, 1.6 mL, 2.6 mmol, 1.3 equiv). The mixture was allowed to warm to rt and was stirred for an additional 1 h after which a pale yellow suspension was obtained. The suspension was cooled to −30°, then 1.38 M allylmagnesium bromide (Et_2O, 1.9 mL, 2.6 mmol, 1.3 equiv) was added dropwise. The solution was warmed to −10°, 1 M $ZnBr_2$ (2.6 mL, 2.6 mmol, 1.3 equiv) was added, and the mixture was stirred at −10° for 0.5 h. The resulting yellow solution was then hydrolyzed with 1 M aq HCl at 0°, allowed to warm to rt, and the aqueous layer was extracted twice with Et_2O. The combined extracts were stirred for 4 h with aq Na_2S. The new aqueous layer was extracted twice with Et_2O. After usual work-up, flash chromatography on silica gel (cyclohexane/EtOAc, 98:2) of the crude product yielded the title product (353 mg, 90%) as a clear liquid: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.95–5.75 (m, 1H), 5.15–4.85 (m, 3H), 4.75 (d, $J = 1.6$ Hz, 1H), 3.87

(t, $J = 7.1$ Hz, 1H), 2.83 (dd, $J = 15.0$ Hz, 6.7 Hz, 1H), 2.70 (dd, $J = 15.0$ Hz, 7.4 Hz, 1H), 1.55–1.15 (m, 4H), 1.14 (s, 9H), 0.87 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 152.0, 136.9, 116.1, 110.4, 75.6, 74.1, 38.7, 35.7, 28.8, 19.5, 14.2. Anal. Calcd for $C_{13}H_{24}O$: C, 79.54; H, 12.32. Found: C, 79.40; H, 12.29.

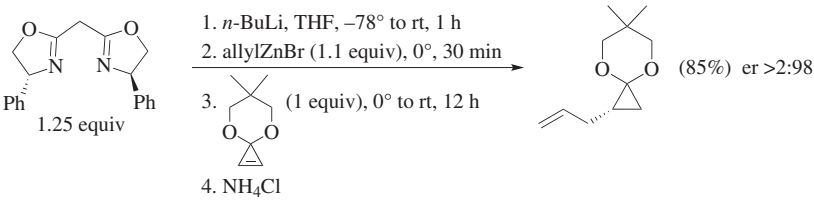


(*Z*)-2-Allyl-1-bromo-3-(*tert*-butoxy)-1-cyanohex-1-ene [Synthesis of a Polysubstituted Stereodefined Alkene via an sp^2 Organo-*gem*-bismetallic].[86] The typical procedure described for the preparation of 5-*tert*-butoxy-4-methylen-oct-1-ene (see above) was followed omitting the final hydrolysis. The mixture was cooled to −78° and TosCN (1 g, 4 mmol, 2 equiv) was introduced, after which it was allowed to warm to room temperature. After 2.75 h of further stirring at this temperature, the mixture was cooled to −50°, and a solution of NBS (0.75 g, 4 mmol, 2 equiv) in CH_2Cl_2 (20 mL) was added. After 1.5 h of further stirring at −35°, the mixture was hydrolyzed with aq $NaHCO_3$. Following the usual workup, flash chromatography of the crude product on silica gel (cyclohexane/EtOAc, 98:2) yielded the title product (360 mg, 60%) as a clear liquid: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.87–5.79 (m, 1H), 5.28 (dd, $J = 17.0$, 1.2 Hz, 1H), 5.16 (dd, $J = 10.0$, 1.2 Hz, 1H), 4.54–4.50 (m, 1H), 3.42 (dd, $J = 14.1$, 7.3 Hz, 1H), 3.21 (dd, $J = 14.1$, 6.6 Hz, 1H), 1.60–1.50 (m, 2H), 1.34–1.26 (m, 2H), 1.17 (s, 9H), 0.94 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.2, 133.2, 118.6, 115.1, 84.9, 75.0, 73.3, 37.1, 36.1, 28.2, 19.1, 14.0. Anal. Calcd for $C_{14}H_{22}BrNO$: C, 56.01; H, 7.39; N, 4.67. Found: C, 56.76; H, 7.40; N, 4.50.



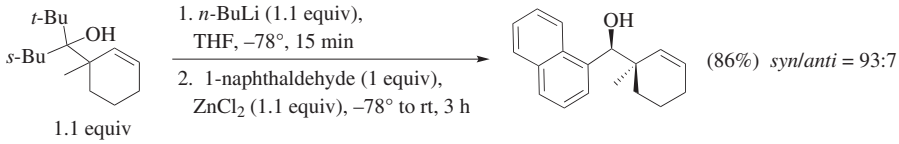
(*R*)-*N*-Methyl-*N*-(3-methyl-2-methylenepent-4-enyl)-1-phenylethylamine [Diastereoselective Carbozincation of a Propargyl Amine].[92] To a cooled (−30°) solution of (*R*)-(1)-*N*-methyl-*N*-propargyl-1-phenylethylamine (346 mg, 2 mmol) in anhydrous Et_2O (10 mL) was added dropwise 1.6 M *n*-BuLi (hexane, 1.3 mL, 2 mmol, 1.05 equiv). The reaction mixture was allowed to warm to rt. After 10 min of further stirring a pale yellow solution was obtained to which was added 1.2 M crotylmagnesium bromide (Et_2O, 3.3 mL, 2 equiv, the reaction mixture turned gray). The solution was cooled to −25°, and 1 M ethereal Et_2O zinc bromide

(6 mL, 3 equiv) was added. This mixture was stirred at −25° for 6 h resulting in a yellow paste. The reaction mixture was hydrolyzed with an aq NH_3/NH_4Cl (1:2), allowed to warm to rt, and 0.5 mL of ethanolamine was added. After stirring at rt for 30 min, the aqueous layer was extracted with Et_2O (2 x 20 mL). The combined organic layers were washed with saturated aq $NaHCO_3$, dried over $MgSO_4$, and the solvents were evaporated under vacuum. Flash chromatography of the crude product on SiO_2 (cyclohexane/EtOAc, 90:10) yielded the title product (394 mg, 86%, dr 88:12) as a clear liquid: IR (neat) 3090, 2980, 1640, 1645, 1010, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.24 (m, 5H), 5.57 (m, 1H), 4.97 (m, 4H), 3.06 (q, J = 6.9 Hz, 1H), 3.05 (m, 2H), 2.76 (d, J = 13.4 Hz, 1H), 2.10 (s, 3H), 1.37 (d, J = 6.8 Hz, 3H), 1.11 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 144.3, 143.1, 128.3, 127.9, 126.9, 113.3, 111.3, 63.5, 59.6, 40.6, 38.2, 19.0, 18.1. Anal. Calcd for $C_{16}H_{23}N$ (229.12): C, 83.78; H, 10.11. Found: C, 83.71; H, 10.15.

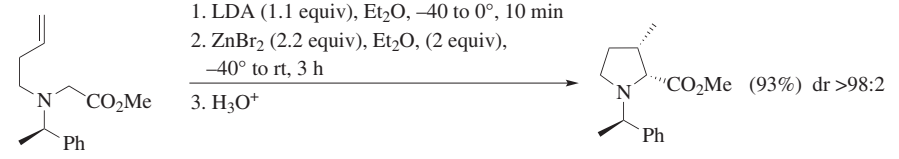


(*S*)-1-Allyl-6,6-dimethyl-4,8-dioxaspiro[2,5]octane [Carbometalation of a Cyclopropenone Ketal with a Chiral Allylzinc Reagent].[105] To a solution of the bisoxazoline (422 mg, 1.38 mmol) and 2,2′-dipyridyl (~1 mg) as an indicator in anhydrous THF (1.8 mL) was added a 1.6 M solution of *n*-BuLi in hexane at −78 to 0°. The colorless, clear solution changed to a red-brown suspension immediately after completion of the addition. The suspension was stirred at 0° for 30 min and at rt for 30 min. The brownish suspension was cooled to 0° and then 1 M allylzinc bromide (1 M THF, 1.25 mL, 1.25 mmol) was added. The reaction mixture turned to a clear red solution. After stirring at 0° for 30 min, the ketal (165 μL, 1.1 mmol) was added. The reaction mixture was allowed to warm to rt and the stirring continued for 12 h, at which time 50 μL of saturated aq NH_4Cl was added. The resulting white precipitate was removed by fitration and the solvent was evaporated under reduced pressure. The residual oil was chromatographed on 30 g of silica gel (hexanes/EtOAc/Et_3N, 95:3:2 to 60:38:2) yielding the allylation product as a colorless oil (169 mg, 85%): $[\alpha]_D^{20}$ – 3.8 (c 5.8, benzene); IR (neat) 3080, 2960, 2910, 2860, 1640, 1480, 1455, 1380, 1180, 1080, 920 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ ~1.1 (m, 1H), 5.92 (ddt, J = 6.1, 10.3, 17.3 Hz, 1H), 5.12 (ddt, J = 1.7, 2.1, 17.3 Hz, 1H), 5.02 (ddt, J =1.7, 2.1, 10.3 Hz, 1H), 3.51 (br s, 4H), 2.30 (m, 1H), 2.06 (m, 1H), 1.26 (m, 1H), 1.00 (s, 3H), 0.51 (dd, J = 5.9, 4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.4, 114.7, 90.4, 76.3, 75.8, 31.4, 30.6, 23.6, 22.5, 22.2, 17.3. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.19; H, 9.77.

A 2:1 white crystalline complex of the bisoxazoline and Zn(II) (416 mg, 0.62 mmol, 80% recovery) was also obtained.

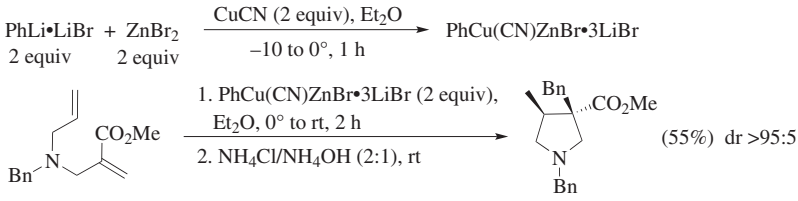


***syn*-3-[(Hydroxynaphthyl)methyl]-3-methylcyclohexene [Zinc-Ene Reaction of a Highly Substituted Allylzinc Derivative Followed by Addition of an Aldehyde].**[34] A two-necked flask equipped with an argon inlet was charged with the alcohol (0.30 g, 1.26 mmol) and THF (2 mL). This solution was cooled to −78° and 1.57 M *n*-BuLi (hexane, 0.80 mL, 1.26 mmol) was added. After stirring for 15 min, 1-naphthaldehyde (0.15 mL, 1.13 mmol) was added via a syringe followed by a solution of zinc chloride (0.17 g, 1.26 mmol) in THF (2 mL). The reaction mixture was slowly warmed to rt, stirred for 3 h, quenched with saturated aq NH_4Cl, and extracted with Et_2O. The combined organic layers were washed with brine and dried ($MgSO_4$). The solvents were evaporated and the crude residue was purified by flash chromatography (pentane/Et_2O, 90:10) to afford the title product (0.24 g, 0.97 mmol, 86%, *syn*/*anti* = 93:7) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 8.08–8.04 (m, 1H), 7.75–7.66 (m, 3H), 7.46–7.37 (m, 3H), 5.71 (dt, J = 10.2, 3.7 Hz, 1H), 5.45 (s, 1H, CH *syn*), 5.40 (s, 1H, CH *anti*), 5.32 (d, J = 10.2 Hz, 1H), 1.94–1.32 (m, 6H), 0.93 (s, 3H, CH_3 *syn*), 0.70 (s, 3H, CH_3 *anti*); HRMS (*m*/*z*): M^+ calcd for $C_{18}H_{20}O$, 252.1509; found, 252.1525.

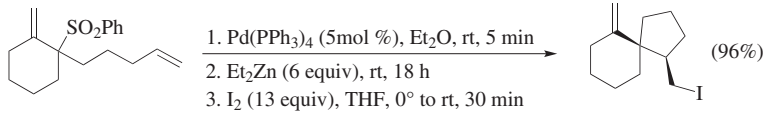


(2*R*,3*S*)-3-Methyl-2-carbomethoxy-*N*-(*R*)-1-phenylethyl)pyrrolidine [Diastereoselective Intramolecular Carbometalation of an Amino-Zinc Enolate].[120] A solution of methyl-*N*-(*R*)-1-(phenylethyl)-*N*-(but-3-enyl)glycinate (0.123 g, 0.5 mmol) in anhydrous Et_2O was cooled to −40° while 2 M LDA (THF/*n*-heptane, 0.275 mL, 0.55 mmol) was added dropwise. The reaction mixture was then allowed to warm to 0° for 10 min, then cooled to −40° while a solution of 1 M zinc bromide (Et_2O, 1.1 mL, 1.1 mmol) was added dropwise. The reaction mixture was allowed to warm to rt, stirred for 3 h, then cooled to 0° while a solution of NH_4Cl/NH_4OH (2:1) was added slowly. Et_2O was added, and the mixture was stirred for at least 3 h with a few $Na_2S{\bullet}9H_2O$ crystals. The layers were separated, and the aqueous layer was extracted with Et_2O. The combined Et_2O extracts were washed with brine, dried over $MgSO_4$, and concentrated. The crude material was purified by chromatography on silica gel (cyclohexane/Et_2O, 80:20) to give the title product (0.114 g, 93%): $[\alpha]_D^{25}$ + 79.4 (*c* 0.0507, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.23 (m, 5H), 3.71 (q, J = 6.6 Hz, 1H), 3.63 (s, 3H), 3.36 (d, J = 8.6 Hz, 1H), 3.03 (dt, J = 8.9, 2.9 Hz, 1H), 2.88–2.80 (m, 1H), 2.46–2.42 (m, 1H),

1.99–1.96 (m, 1H), 1.65–1.60 (m, 1H), 1.37 (t, $J = 6.7$ Hz, 3H), 0.92 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.1, 144.6, 128.4, 127.6, 127.2, 67.7, 62.1, 50.9, 50.7, 36.7, 32.1, 22.6, 15.8. Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.91; H, 8.55; N, 5.59.

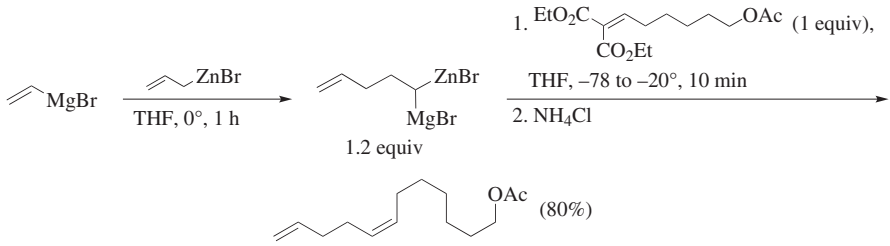


(Methyl (3*R,4*S**)1,3-Dibenzyl-4-methylpyrrolidine-3-carboxylate [Stereoselective Synthesis of a Substituted Pyrrolidine by a Domino Michael Addition/Carbocyclization Reaction].[126]** A solution of 1 M zinc bromide (Et_2O, 4 mL, 4 mmol) and a solution of PhLi (Et_2O, 4 mmol) were added dropwise and consecutively to a suspension of copper cyanide (360 mg, 4 mmol) in Et_2O (7 mL) at −10°. The reaction mixture was stirred at 0° for 1 h and a solution of methyl 2-[(*N*-allyl-*N*-benzyl amino)methyl]acrylate (490 mg, 2 mmol) in Et_2O was added dropwise at 0°. The cold bath was removed and the biphasic mixture was stirred at rt for 2 h. The product was hydrolyzed with aq NH_4Cl/NH_4OH (2:1). The layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvents were evaporated under reduced pressure. The crude material was purified by chromatography on silica gel (cyclohexane/EtOAc, 80:20) to give the product (356 mg, 55%) as a yellow oil: IR (neat) 3062, 3028, 2959, 2795, 1728, 1604, 1495, 1473, 1454, 1436, 1377, 1357, 1314, 1271, 1196, 1133, 1097, 1070, 1029, 910, 735, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.15 (m, 10H), 3.74 (s, 2H), 3.72 (s, 3H), 3.28 (d, $J = 13.4$ Hz, 1H), 3.24 (d, $J = 9.9$ Hz, 1H), 3.02 (t, $J = 8.6$ Hz, 1H), 2.86 (d, $J = 13.4$ Hz, 1H), 2.68 (m, 1H), 2.60 (d, $J = 9.9$ Hz, 1H), 2.44 (t, $J = 8.6$ Hz, 1H), 1.28 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.42, 139.13, 138.30, 129.66 (2C), 128.82 (2C), 128.35 (4C), 127.05, 126.59, 60.86, 60.27, 59.95, 55.58, 51.78, 40.88, 38.09, 14.06. Anal. Calcd for $C_{21}H_{25}NO_2$: C, 77.98; H, 7.79; N 4.33. Found: C, 78.12; H, 7.73; N, 4.26.

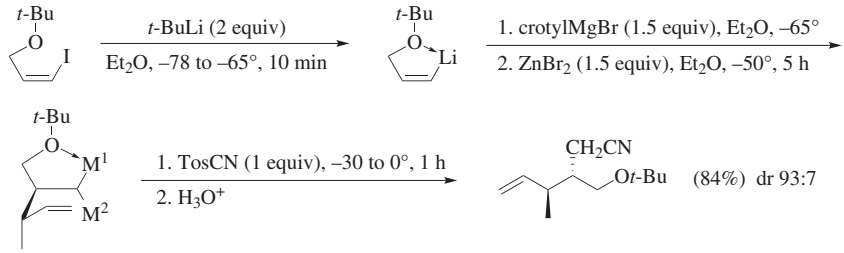


1-(Iodomethyl)-6-(methylene)spiro[4.5]decane [An Allyl Sulfone as a Precursor to an Allylzinc in the Palladium-Catalyzed Zinc-Ene Cyclization].[39] To a stirred solution of (2-methylene-1-(pent-4-enyl)cyclohexanesulfonyl)benzene

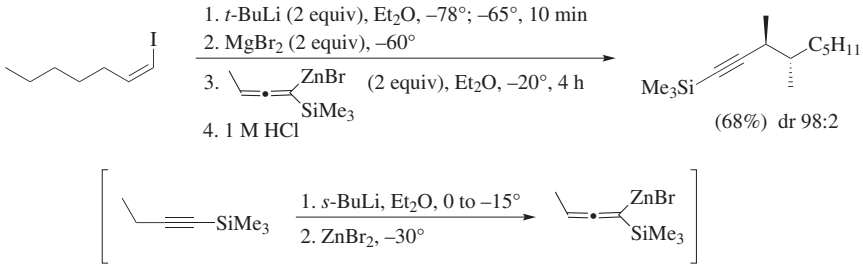
(113 mg, 0.37 mmol) in Et_2O (10 mL) at rt was added $Pd(PPh_3)_4$ (21 mg, 0.018 mmol). The resulting solution was stirred for 5 min before 1 M Et_2Zn (hexane 2.2 mL, 2.2 mmol) was added. The resulting mixture was stirred for 18 h at rt before it was cooled to 0° and quenched with a solution of I_2 (1.2 g, 4.7 mmol) in THF (5 mL). The resulting mixture was stirred at rt for 30 min, diluted with Et_2O (50 mL), washed with 20% aq $Na_2S_2O_3$ (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered through cotton, and evaporated under vacuum. The residue was purified by silica gel flash column chromatography to afford the title product (103 mg, 96%): IR (neat) 3081, 2931, 2855, 1638, 1445, 1183, 895 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.79 (s, 1H), 4.63 (s, 1H), 3.16 (ddd, J = 9.6, 2.8, 1.6 Hz, 1H), 2.70 (dd, J = 12.5, 9.6 Hz, 1H), 2.52 (m, 1H), 2.28 (m, 1H), 2.30–1.90 (m, 2H), 1.90–1.48 (m, 5H), 1.39–1.20 (m, 3H), 1.12–1.02 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 152.2, 108.2, 53.9, 45.6, 38.2, 35.5, 33.8, 29.6, 28.8, 22.7, 19.7, 14.2; EIMS m/z: M^+ 290 (18), 163 (100), 121 (71), 109 (63), 95 (85), 81 (87), 67 (62), 55 (37); HRMS–EI (m/z): M^+ calcd for $C_{12}H_{19}I$, 290.0532; found 290.0533.



(*Z*)-1-Acetoxy-7,11-Dodecadiene [Synthesis of a Functionalized (*Z*)-Alkene by Reaction of a 1,1-Dimetalloalkane with a Functionalized Alkylidenemalonate].[142] A solution of 1.5 M allylzinc bromide (THF, 12 mmol) was added at 0° to a solution of 0.5 M vinylmagnesium bromide (THF, 12 mmol). An exothermic reaction occurred and the resulting mixture was stirred for 1 h at this temperature. The resulting solution of the bimetallic species was cooled to −78° and a solution of the alkylidenemalonate (10 mmol) in THF (3 mL) was added. The mixture was warmed to −20°, stirred for 10 min, and quenched with saturated aq NH_4Cl. The mixture was diluted with Et_2O (100 mL). The resulting organic layer was then washed with aq NH_4Cl (100 mL) followed by water (100 mL), dried over $MgSO_4$, and the solvents were evaporated under vacuum. The crude oil obtained after evaporation of the solvents was purified by silica gel flash chromatography (hexane), affording the pure functionalized alkene in 80% yield: IR (neat) 2929, 1741, 1650, 1366 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.86–5.76 (m, 1H), 5.41–5.35 (m, 2H), 5.04–4.92 (m, 2H), 4.07–4.02 (t, J = 6.7, 2H), 2.15–1.94 (m, 9H), 1.63–1.57 (m, 2H), 1.39–1.27 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 138.6, 130.8, 129.7, 114.6, 64.6, 33.9, 32.4, 29.4, 28.7, 27.2, 26.7, 25.8, 20.9; EIMS m/z: 109 (21), 135 (8), 165 (10), 181 (2), 224 (1). (The isomeric purity was determined by ^1H NMR and capillary gas chromatography.)

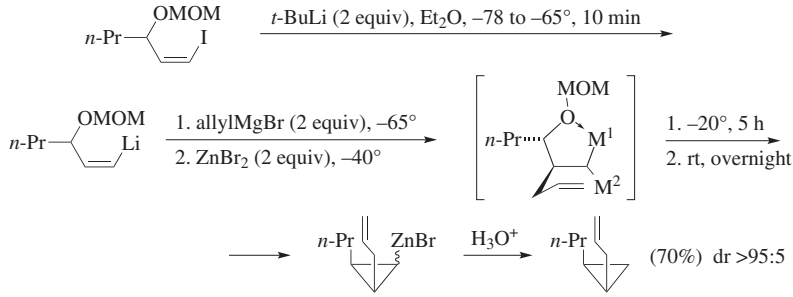


(2*S)-(Cyanomethyl)-(3*S**)-methyl-1-*tert*-butoxypent-4-ene [Diastereoselective Carbometalation of a Vinylmetal].**[145] To a solution of (Z)-1-iodo-3-*tert*-butoxyprop-1-ene (500 mg, 2.1 mmol) in Et_2O (30 mL) at −78° was added a solution of 1.6 M *t*-BuLi (hexane, 2.8 mL, 4.4 mmol, 2 equiv). The solution was warmed to −65° for 10 min to complete the lithium–iodine exchange, and then 1 M crotylmagnesium bromide (Et_2O, 3.3 mL, 3.3 mmol, 1.5 equiv) was added at −65°, followed by 1 M $ZnBr_2$ (Et_2O, 3.3 mL, 3.3 mmol, 1.5 equiv). The reaction mixture was stirred at −50° for 5 h, and the formation of the adduct was monitored by gas chromatography. Once the formation of the bismetallic species was quantitative, *p*-toluenesulfonyl cyanide (380 mg, 2.1 mmol) was added at −30°, the mixture was warmed to 0° for 1 h, and aq 1 M HCl (20 mL) was added. The aqueous phase was extracted with Et_2O (2 x 20 mL), and the combined organic phases were washed with 1 M aq HCl (2 x 20 mL). The organic layer was treated overnight with aq Na_2S and then washed with $NaHCO_3$ (2 x 20 mL), dried over $MgSO_4$, and concentrated under vacuum. The residue was chromatographed on SiO_2 (cyclohexane/EtOAc, 90:10) to give the title product (340 mg, 84%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.65 (m, 1H), 5.1 (dd, J = 12, 16 Hz, 2H), 3.55 (dd, J = 11.8, 6 Hz, 1H), 3.4 (dd, J = 8.8, 11.8 Hz, 1H), 2.5 (dd, J = 16, 8.5 Hz, 2H), 2.3 (m, 1H), 1.7 (m, 1H), 1.2 (s, 9H), 1.05 (d, J = 7.5 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.2, 119.0, 115.4, 72.7, 60.1, 40.7, 38.5, 27.3, 17.5. Anal. Calcd for $C_{12}H_{21}NO$: C, 73.79; H, 10.83. Found: C, 74.08; H, 11.42.



(*S,*S**)-3,4-Dimethyl-1-trimethylsilyl-non-1-yne [Propargylmetalation of an Alkenylmetal].**[146] To a solution of (*Z*)-1-iodohept-1-ene (448 mg, 2 mmol) in Et_2O (20 mL) was added a solution of 1.6 M *t*-BuLi (hexane, 2.5 mL, 4 mmol, 2 equiv) at −78°. The solution was warmed to −65° for 10 min to complete the lithium–iodine exchange, and then $MgBr_2$ was added (4 mmol, 2 equiv) at −60°,

followed by (1-(trimethylsilyl)buta-1,2-dien-1-yl)zinc(II) bromide (2 equiv) in Et_2O. [(1-(Trimethylsilyl)buta-1,2-dien-1-yl)zinc(II) bromide was prepared by treatment of but-1-yn-1-yltrimethylsilane (504 mg, 4 mmol) in Et_2O (20 mL) with 1.3 M *s*-BuLi (hexane, 4 mL, 4 mmol, 1.3 equiv). The solution was allowed to warm to rt, then 1 M $ZnBr_2$ (Et_2O, 5.2 mL, 1.3 equiv) was added at −30° to give the allenylzinc bromide.] The reaction mixture was stirred at −20° for 4 h and quantitative formation of the adduct was confirmed by gas chromatography. Protonation was accomplished using aq 1 M HCl (20 mL). The aqueous phase was extracted twice with Et_2O (2 x 20 mL) and the combined organic phases were washed with 1M HC1 (2 x 20 mL). The organic layer was treated overnight with aq $Na_2S{\bullet}9H_2O$, washed with aq $NaHCO_3$ (2 x 20 mL), dried over $MgSO_4$, and then concentrated under vacuum. The residue was chromatographed on silica gel (cyclohexane/EtOAc, 98:2) to yield the title product (304.7 mg, 68%, dr >95:5): IR 2950, 2920, 2860, 2850, 2160, 1450, 1375, 1430, 1245, 900, 840, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.51 (m, 1H), 1.43 (m, 2H), 1.18–1.36 (m, 7H), 1.14 (d, $J = 6.9$ Hz, 3H), 0.93 (d, $J = 6.2$ Hz, 3H), 0.91 (t, $J = 7.0$ Hz, 3H), 0.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.7, 85.1, 37.7, 35.0, 32.1, 31.8, 26.9, 22.7, 18.7, 15.5, 14.2, 0.4. Anal. Calcd for $C_{14}H_{28}Si$: C, 74.57; H, 12.57. Found: C, 74.28; H, 12.72.



1(*S)-(Prop-2-enyl)-2(*S**)-propylcyclopropane [Synthesis of a Stereodefined Substituted Cyclopropylzinc Reagent from a *gem*-Bismetallic Compound].**[151] To a solution of (*Z*)-1-iodo-3-(methoxymethoxy)hex-1-ene (1.35 g, 5 mmol) in Et_2O (30 mL) was added a solution of 1.6 M *t*-BuLi (hexane, 6.25 mL, 10 mmol, 2 equiv) at −78°. The solution was warmed to −65° for 10 min to complete the lithium–iodine exchange, and then 1 M allylmagnesium bromide (Et_2O, 10 mL, 10 mmol, 2 equiv) was added, followed by 1 M $ZnBr_2$ (Et_2O, 10 mL, 10 mmol, 2 equiv) at −40°. The reaction mixture was stirred at −20° for 5 h, was then allowed to warm to rt, and stirred overnight. The protonation was carried out with 1 M aq HCl (20 mL). The aqueous phase was extracted with Et_2O (2 x 20 mL), and the combined organic phases were washed with 1 M aq HCl (2 x 20 mL). The organic layer was stirred overnight with aq $Na_2S{\bullet}9H_2O$, washed with aq $NaHCO_3$ (2 x 20 mL), dried over $MgSO_4$, and concentrated under vacuum. Purification by silica gel flash chromatography afforded the product (434 mg, 70%) as a liquid: ^1H NMR (400 MHz, $CDC1_3$) δ 5.85 (ddt, $J = 17.15$, 10.25, 7.10 Hz, 1H, CH=), 5.00 (ddd, $J_{trans} = 17.15$ Hz, $J_{cis} = 10.25$ Hz, $J_{gem} = 1.62$ Hz, 2H, CH_2=), 2.15

(m, 2H, CH_2C=), 1.40 (m, 4H, $(CH_2)_2$), 0.70–0.80 (m, 2H, CH_2), 0.55–0.60 (dd, J = 4.4, 3.7 Hz, 1H, CH), −0.30 (dd, J = 5.5, 4.4 Hz, 1H, CH); ^{13}C NMR ($CDC1_3$, 100 MHz) δ 140.2 (HC=), 114.5 (=CH_2), 34.4 (CH_2C=), 28.7, 22.7 ($(CH_2)_2$), 15.8, 15.3, 10.9, ($C_{cyclopr}$), 14.1 (CH_3).

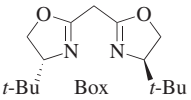
TABULAR SURVEY

Within each Table the entries are arranged primarily in order of increasing carbon count of the acceptor, and secondarily by substrate type. Protecting groups, chiral auxiliaries, and simple substituents on heteroatoms are excluded from the carbon count.

A dash enclosed in parentheses [(—)] signifies that the product was isolated but no yield was reported.

The following abbreviations (not included in "*The Journal of Organic Chemistry* Standard Abbreviations and Acronymns") are used in the Tabular Survey:

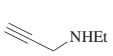
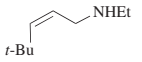
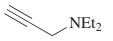
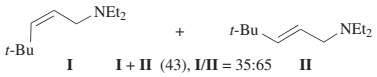
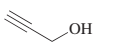
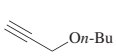
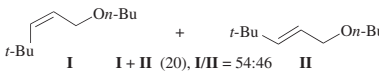
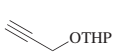
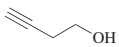
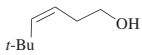
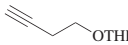
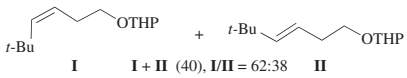
Ad	adamantyl
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthalene
Boc	*tert*-butyloxycarbonyl
Box	2,2′-methylenebis[(4S)-4-*tert*-butyl-2-oxazoline]



dba	dibenzylideneacetone
dpp	2,3-bis(2-pyridyl)pyrazine
dppe	1,2-bis(diphenylphosphino)ethane
dppp	1,3-bis(diphenylphosphino)propane
dppb	1,4-bis(diphenylphosphino)butane
dppbz	1,2-bis(diphenylphosphino)benzene
GPa	gigapascal
Np	neopentyl or naphthyl
PMP	*p*-methoxyphenyl
PTSA	p-toluenesulfonic acid
Red-Al	sodium bis(2-methoxyethoxy)aluminum hydride
TBDPS	*tert*-butyldiphenylsilyl
Thex	thexyl; 2,3-dimethylbutyl

TABLE 1. CARBOZINCATION OF ALKYNES

A. UNCATALYZED ADDITION OF ALKYLZINC DERIVATIVES

Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3			
	1. *t*-Bu_2Zn (3 eq), THF, 65°, 48 h 2. H^+	 (40) (*Z*)/(*E*) = 60:40	50
	1. *t*-Bu_2Zn (3 eq), THF, 65°, 48 h 2. H^+	 **I** **I + II** (43), **I/II** = 35:65 **II**	50
	1. *t*-Bu_2Zn (3 eq), THF 2. H^+	 Temp (°) Time (h) (*Z*)/(*E*) 35 72 (5) 15:85 65 24 (30) 15:85 65 48 (65) 12:88	50
	1. *t*-Bu_2Zn (3 eq), THF, 65°, 48 h 2. H^+	 **I** **I + II** (20), **I/II** = 54:46 **II**	50
	1. *t*-Bu_2Zn (3 eq), THF, 65°, 48 h 2. H^+	 **I** **I + II** (30), **I/II** = 35:65 **II**	50
C_4			
	1. *t*-Bu_2Zn (3 eq), THF, 65°, 48 h 2. H^+	 (40) (*Z*)/(*E*) = 60:40	50
	1. *t*-Bu_2Zn (3 eq), THF, 65°, 48 h 2. H^+	 **I** **I + II** (40), **I/II** = 62:38 **II**	50

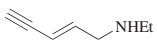
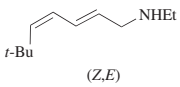
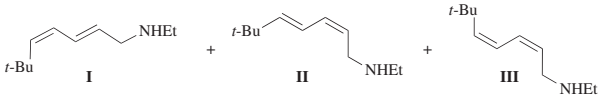
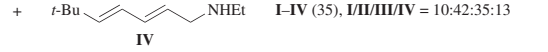
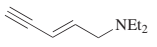
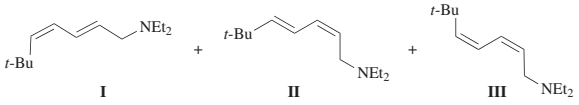
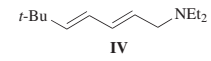
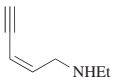
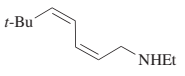
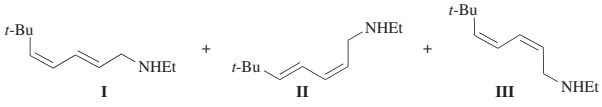
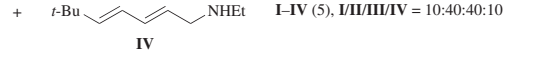
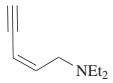
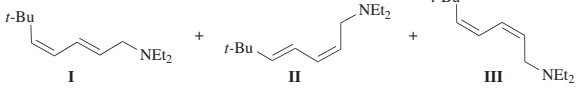
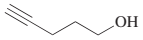
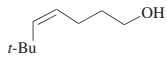
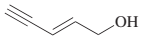
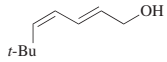
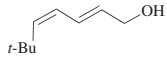
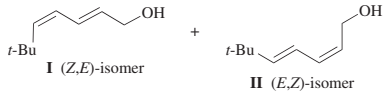
C_5			
	1. *t*-Bu_2Zn, Et_2O, 35°, 24 h 2. H^+	 (40) (*Z*,*E*)	53
	1. *t*-Bu_2Zn, THF, 65°, 48 h 2. H^+	 **I** **II** **III**  **IV** **I–IV** (35), **I/II/III/IV** = 10:42:35:13	52
	1. *t*-Bu_2Zn (3 eq), solvent, temp, time 2. H^+	 **I** **II** **III**  **IV** Solvent Temp (°) Time (h) **I–IV** **I/II/III/IV** Et_2O 35 24 (37) 100:0:0:0 THF 65 48 (40) 20:35:30:15	52
	1. *t*-Bu_2Zn, Et_2O, 35°, 24 h 2. H^+	 (10)	52
	1. *t*-Bu_2Zn, THF, 65°, 48 h 2. H^+	 **I** **II** **III**  **IV** **I–IV** (5), **I/II/III/IV** = 10:40:40:10	52

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

A. UNCATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	1. *t*-Bu_2Zn (3 eq), solvent, temp, time 2. H^+	 **I** + **II** + **III** + **IV**	52
		Solvent / Temp (°) / Time (h) / **I–IV** / **I/II/III/IV** Et_2O / 35 / 24 / (42) / 0:0:100:0 THF / 65 / 48 / (35) / 24:31:35:10	
	1. *t*-Bu_2Zn (3 eq), THF, 65°, 48 h 2. H^+	 (42) (*Z*)/(*E*) = 65:35	50
	1. *t*-Bu_2Zn (3 eq), Et_2O, 35°, 24 h 2. H^+	 (45) (*Z*)/(*E*) = —	53
	1. *t*-BuZnCl (3 eq), Et_2O, 35°, 24 h 2. H^+	 (43)	53
	1. *t*-Bu_2Zn, solvent, temp, time 2. H^+	 **I** (*Z*,*E*)-isomer + **II** (*E*,*Z*)-isomer	52

Solvent	Temp (°)	TIme (h)	**I + II**	**I/II**
Et_2O	35	24	(45)	100:0
THF	20	24	(50)	100:0
THF	35	24	(55)	100:0
THF	65	3	(45)	100:0
THF	65	24	(60)	45:55
THF	65	48	(70)	20:80
THF	65	80	(65)	20:80
Et_2O/toluene	65	48	(40)	100:0

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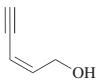
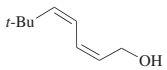
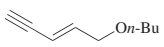
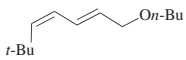
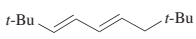
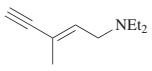
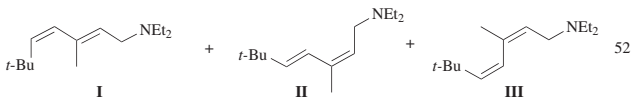
	1. *t*-Bu_2Zn, Et_2O, 35°, 24 h 2. H^+	 (15)	52
	1. *t*-Bu_2Zn, THF, 65°, 48 h 2. H^+	 **I** + **II** (5), **I/II** = 50:50	52
	1. *t*-Bu_2Zn (3 eq), Et_2O, 35°, 24 h 2. H^+	 (41)	53
	1. *t*-Bu_2Zn (3 eq), THF, 65°, 48 h 3. H^+	 (35)	52
C_6			
	1. *t*-Bu_2Zn, conditions 2. H^+	 **I** + **II** + **III** + **IV**	52

Solvent	Temp (°)	Time (h)	**I–IV**	**I/II/III/IV**
Et_2O	35	24	(40)	100:0:0:0
THF	65	48	(50)	24:22:46:8

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TABLE 1. CARBOZINCATION OF ALKYNES
A. UNCATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

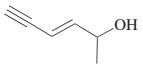
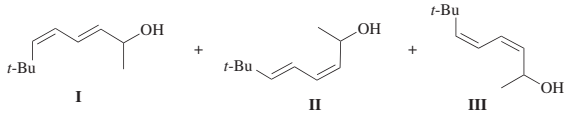
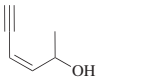
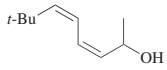
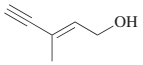
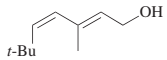
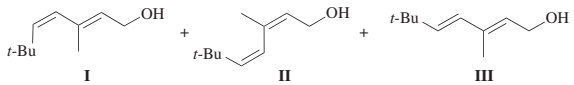
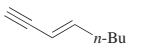
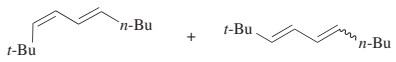
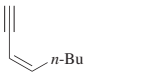
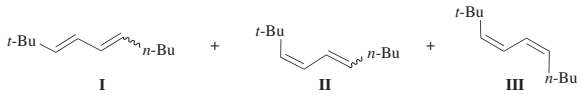
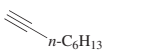
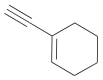
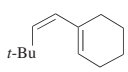
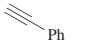
Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	1. *t*-Bu_2Zn, solvent, temp, time 2. H^+	 **I** + **II** + **III**	52
		Solvent / Temp (°) / Time (h) / **I + II + III** / **I/II/III** Et_2O / 35 / 24 / (60) / 100:0:0 THF / 35 / 24 / (75) / 80:0:20 THF / 65 / 3 / (70) / 53:20:27 THF / 65 / 24 / (75) / 45:22:33 THF / 65 / 48 / (72) / 23:35:42 THF / 65 / 80 / (70) / 27:32:41	
	1. *t*-Bu_2Zn, Et_2O, 35°, 24 h 2. H^+	 (40)	52
	1. *t*-Bu_2Zn, THF, 65°, 48 h 2. H^+	 **I** + **II** (30), **I/II** = 50:50	52
	1. *t*-Bu_2Zn, Et_2O, 35°, 24 h 2. H^+	 (50)	52
	1. *t*-Bu_2Zn, THF, 65°, 48 h 2. H^+	 **I** **II** **III** **I + II + III** (65), **I/II/III** = 16:32:52	52
C_8			
 (*E*)/(*Z*) = 45:55	1. *t*-Bu_2Zn, solvent, temp, time 2. H^+	 **I** (*Z*)-isomer **II** (*E*)/(*Z*) = 55:45	52
		Solvent / Temp (°) / Time (h) / **I + II** / **I/II** Et_2O / 35 / 24 / (40) / 100:0 THF / 65 / 48 / (65) / 75:25	
	1. *t*-Bu_2Zn, solvent, temp, time 2. H^+	 **I** **II** **III**	52
		Solvent / Temp (°) / Time (h) / **I + II + III** / **I/II/III** Et_2O / 35 / 24 / (30) / 0:0:100 THF / 65 / 48 / (70) / 50:50:0	
	1. *t*-Bu_2Zn (3 eq), THF, 65°, 48 h 2. H^+	 **I** **I + II** (40), **I/II** = 55:45 **II**	50
	1. *t*-Bu_2Zn, Et_2O, 35°, 24 h 2. H^+	 (55)	53
	1. *t*-Bu_2Zn, Et_2O, temp, time 2. H^+	 Temp / Time (h) / (55) 30° / 24 reflux / 48 / (70)	53

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
HC≡CH	ZnBr, 2.5 eq	1. THF, 35°, 30 min 2. H^+	(30)	77
Me_3Si≡	MgBr, 1.2 eq + $ZnBr_2$ 1.2 eq	1. "Allylzinc", Et_2O 2. 0°, 1 h; then 20°, 1 h 3. H^+	Me_3Si (85) (*E*)/(*Z*) = 100:0	155
Cl≡Li	ZnBr, 2.5 eq	1. THF, 40°, 2 h 2. H^+	(16)	78
C_3				
Cl	ZnBr, 3.0 eq	1. THF, 20°, 3 h 2. H^+	(72)	164
Br	ZnBr, *n* eq	1. THF, temp, time 2. H^+		

n	Temp (°)	Time (h)		
2	20	3	(36)	164
2	20	8	(35)	164
3	20	24	(31)	164
3	20	3	(83)	165
3	40	1.5	(54)	166
4	65	5	(72)	164
4	65	3	(74)	164

	ZnBr, 4 eq	1. THF, 20°, 3 h 2. D^+	D, D (73)	164
	ZnBr, *x* eq	1. THF, temp, time 2. H^+	**I** + **II** + **III**	164

x	Temp (°)	Temp (h)	**I + II + III**	**I/II/III**
2	20	24	(59)	92:8:0
3	20	3	(93)	93:7:0
3	20	24	(73)	89:11:0
3	65	3	(68)	91:8<1
3	65	24	(71)	65:32:3

	ZnBr, 3 eq	1. THF, 40°, 2 h 2. H^+	(68)	166
	ZnBr, *x* eq	1. THF, temp, 3 h 2. H^+	**I** + **II**	

x	Temp (°)	**I + II**	**I/II**	
3	20	(69)	100:0	165
3	40	(64)	100:0	166
3	65	(69)	100:0	165
4	20	(65)	92:8	164
4	65	(75)	92:8	164

Ph	ZnBr, 3 eq	1. THF, temp, 24 h 2. H^+	Ph, Ph **I** + Ph, Ph **II**	165, 164

Temp (°)	**I + II**	**I/II**
20	(62)	77:23
65	(35)	47:53

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

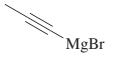
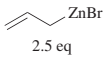
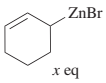
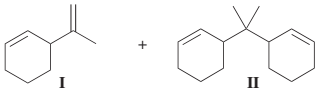
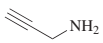
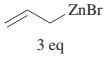
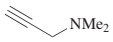
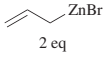
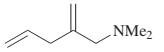
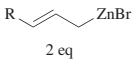
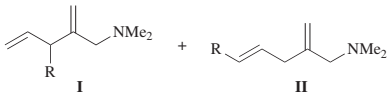
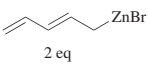
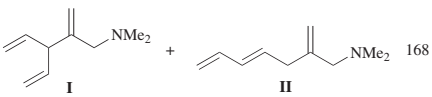
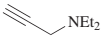
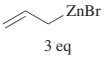
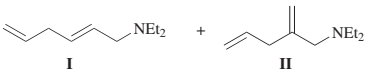
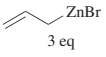
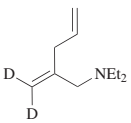
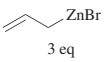
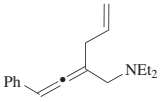
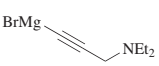
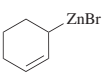
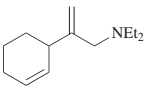
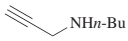
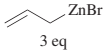
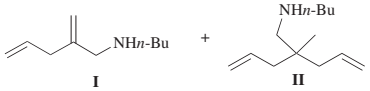
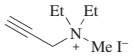
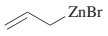
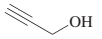
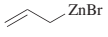
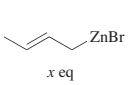
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 2.5 eq	1. THF, 66°, 3 h 2. H^+	 (45)	77
	 *x* eq	1. THF, 40°, 3 h 2. H^+	 **I** + **II** *x* | **I + II** | **I/II** 1.25 | (45) | 100:0 2 | (47) | 49:51	78
	 3 eq	1. THF, 65°, 23 h 2. H^+	 **I** + **II** **I + II** (32), **I/II** = 22:78	56
	 2 eq	1. THF, 20°, 24 h 2. H^+	 (70)	165
	 2 eq	1. THF, temp, time 2. H^+	 **I** + **II** R | Temp (°) | Time (h) | **I + II** | **I/II** Me | 20 | 24 | (65) | 100:0 Me | 65 | 8 | (30) | 90:10 Ph | 20 | 24 | (69) | 81:19 Ph | 65 | 24 | (34) | 22:78	165 168 165, 168 165, 168
	 2 eq	1. THF, temp, 24 h 2. H^+	 **I** + **II** Temp (°) | **I + II** | **I/II** 20 | (22) | 66:34 65 | (36) | 14:86	168
	 3 eq	1. THF, 65°, time 2. H^+	 **I** + **II** Time (h) | **I + II** | **I/II** 23 | (70) | 0:100 69 | (16) | 13:87	56 55
	 3 eq	1. THF, 65°, 23 h 2. D^+	 (65)	56
	 3 eq	1. THF, 65°, 23 h 2. Benzaldehyde (4 eq) 3. H^+	 (45)	56
	 *x* eq	1. THF, 40°, 3 h 2. H^+	 *x* | (30) | (49) 1.25 | 2	78

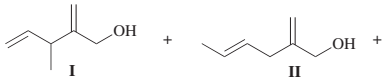
TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 3 eq	1. THF, 65°, 23 h 2. H^+	 **I** + **II** (43), **I/II** = 58:42	56
	 3 eq	1. THF, 65°, 8 h 2. H^+	 (50)	164
	 *x* eq	1. THF, temp, time 2. H^+	 **I** + **II**	

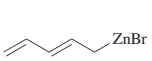
x	Temp (°)	Time (h)	**I + II**	**I/II**	
2.5	40	1	(77)	100:0	77
3	20	24	(62)	68:32	76
3	20	3	(74)	100:0	165
3	65	3	(94)	93:7	165
4	40	1	(87)	88:12	169


x eq

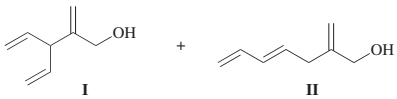
1. THF, temp, time
2. H^+


I + **II** + **III**

x	Temp (°)	Time (h)	**I + II + III**	**I/II/III**	
2.5	40	1	(46)	100:0:0	77
3	20	3	(93)	100:0:0	165, 168
3	20	24	(75)	93:0:0	165
3	65	3	(86)	100:0:0	165
3	65	24	(69)	99:1:0	168
4	40	3	(80)	0:100:0	169


3 eq

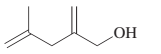
1. THF, 24 h
2. H^+

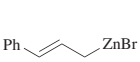

I + **II**

Temp (°)	**I + II**	**I/II**	
20	(77)	72:28	168
65	(66)	66:34	

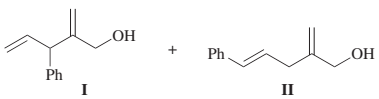

4 eq

1. THF, 40°, 1 h
2. H^+

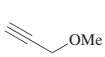
 (79) 169

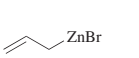

3 eq

1. THF, temp, time
2. H^+

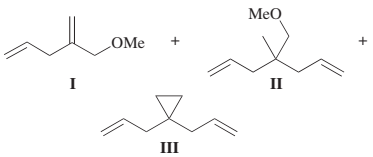

I + **II**

Temp (°)	Time (h)	**I + II**	**I/II**	
20	3	(26)	93:7	165, 168
65	3	(35)	84:16	168
20	24	(92)	82:18	165
65	24	(67)	74:26	168




x eq

1. THF, temp, time
2. H^+


I + **II** + **III**

x	Temp (°)	Time (h)	**I + II + III**	**I /II/III**	
2	20	8	(75)	80:20:0	164
2	20	24	(60)	100:0:0	165
2	65	8	(73)	79:21:0	164
3	65	8	(72)	44:38:18	164
3.75	0	63	(45)	0:100:0	169

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

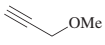
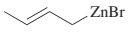
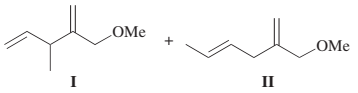
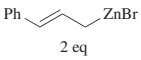
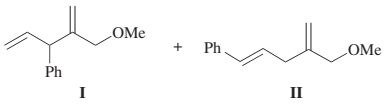
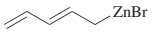
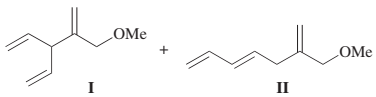
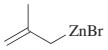
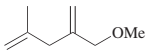
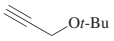
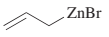
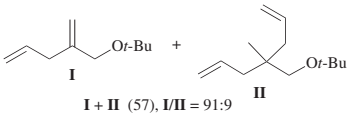
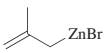
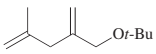
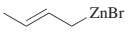
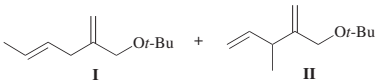
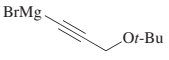
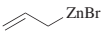
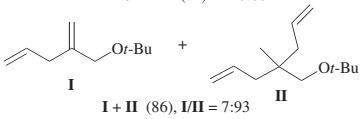
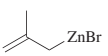
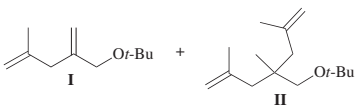
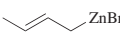
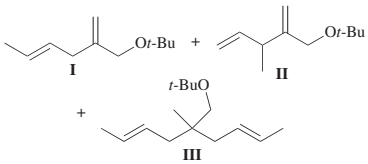
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 2 eq	1. THF, temp, time 2. H^+	 **I** **II**	
			Temp (°) / Time (h) / **I + II** / **I /II**: 20 / 24 / (82) / 100:0	165
			35 / 45 min / (25) / 77:23	169
			40 / 2 / (68) / 7:93	169
			65 / 8 / (46) / 92:8	168
			65 / 15 / (52) / 85:15	165, 168
	 2 eq	1. THF, temp, 24 h 2. H^+	 **I** **II**	168
			Temp (°) / **I + II** / **I/II**: 20 / (88) / 74:26	
			65 / (58) / 64:36	
	 3 eq	1. THF, temp, 24 h 2. H^+	 **I** **II**	168
			Temp (°) / **I + II** / **I/II**: 20 / (89) / 65:35	
			65 / (81) / 53:47	
	 2.5 eq	1. THF, 35°, 1.5 h 2. H^+	 (68)	169
590				
	 1.25 eq	1. THF, 35°, 1.5 h 2. H^+	 **I** **II**	169
			I + II (57), **I/II** = 91:9	
	 2.5 eq	1. THF, 35°, 1.5 h 2. H^+	 (77)	169
	 2.5 eq	1. THF, 35°, time 2. H^+	 **I** **II**	169
			Time / **I + II** / **I/II**: 45 min / (49) / 5:95	
			1.5 h / (74) / 20:80	
	 2.5 eq	1. THF, 65°, 2.5 h 2. H^+	 **I** **II**	169
			I + II (86), **I/II** = 7:93	
	 2.5 eq	1. THF, 65°, 3 h 2. H^+	 **I** **II**	169
			I + II (82), **I/II** = 73:27	
	 2.5 eq	1. THF, 65°, 16.5 h 2. H^+	 **I** **II** **III**	169
			I + II + III (66), **I/II/III** = 8:6:86	
591				

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

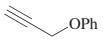
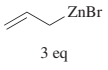
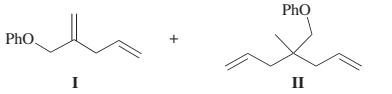
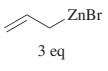
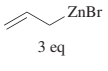
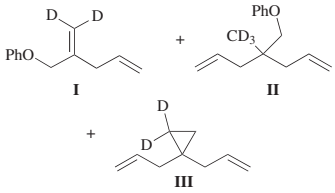
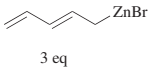
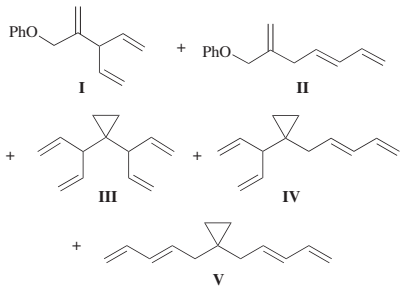
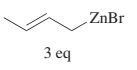
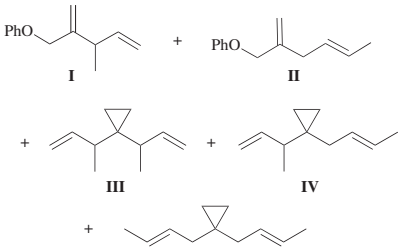
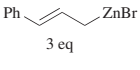
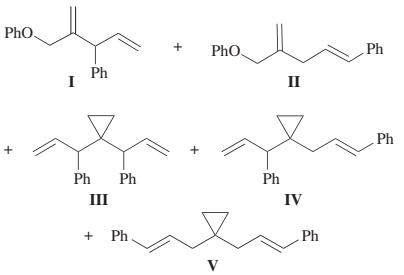
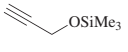
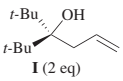
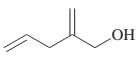
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 3 eq	1. THF, temp, 8 h 2. H^+	 **I** + **II** Temp (°) / **I + II + III** (91) / **I/II/III** 65:2:33 (20°); 16:1:83 (65°) + **III**	164
	 3 eq	1. THF, 65°, 4 h 2. H^+	 (56)	166
	 3 eq	1. THF, 65°, 8 h 2. D^+	 **I** + **II** + **III** **I + II + III** (81), **I/II/III** = 16:1:83	164
	 3 eq	1. THF, temp, time 2. H^+	 **I** + **II** + **III** + **IV** + **V** Temp (°) / Time (h) / **I–V** / **I/II/III/IV/V** 20 / 24 / (83) / 57:43:0:0:0 65 / 8 / (80) / 46:28:1:4:21 65 / 24 / (61) / 47:17:1:8:27	164
	 3 eq	1.THF, temp, time 2. H^+	 **I** + **II** + **III** + **IV** + **V** Temp (°) / Time (h) / **I–V** / **I/II/III/IV/V** 20 / 8 / (93) / 100:0:0:0:0 65 / 8 / (91) / 77:5:4:<1:13 65 / 24 / (77) / 55:6:12:<1:26	164
	 3 eq	1. THF, temp, time 2. H^+	 **I** + **II** + **III** + **IV** + **V** Temp (°) / Time (h) / **I–V** / **I/II/III/IV/V** 20 / 24 / (70) / 55:45:0:0:0 65 / 8 / (78) / 23:27:5:14:31	164
	 **I** (2 eq) + BuLi, $ZnCl_2$	1. **I**, THF 2. BuLi (2 eq), THF, 0°, 15 min 3. $ZnCl_2$ (2 eq), THF, rt, 2 h 4. H^+	 (74)	163

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

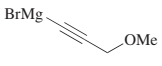
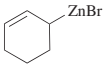
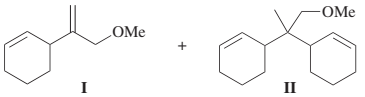
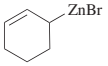
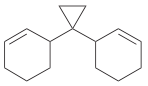
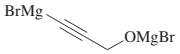
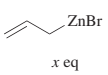
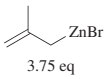
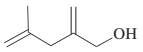
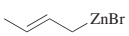
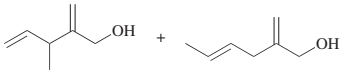
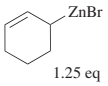
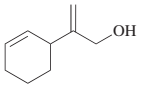
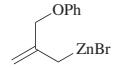
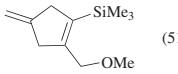
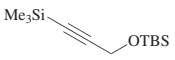
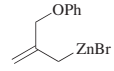
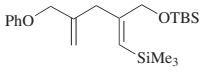
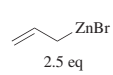
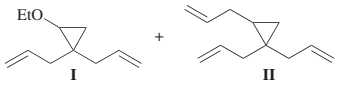
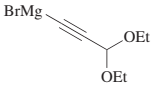
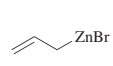
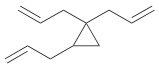
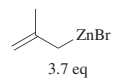
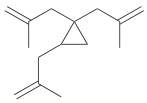
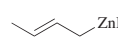
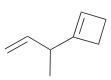
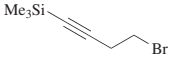
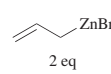
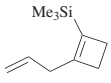
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 2.5 eq	1. THF, 40°, 17 h 2. H^+	 **I** + **II** (64), **I/II** = 81:19	78
	 4 eq	1. THF, 65°, 24 h 2. H^+	 (56)	78
	 *x* eq	1. THF, temp, 2 h 2. H^+		169
			x Temp (°) **I + II** **I/II** 2.5 65 (87) 45:55 3.75 35 (74) 16:84	
	 3.75 eq	1. THF, 65°, 15 h 2. H^+	 (74)	169
	 3.75 eq	1. THF, 65°, 15 h 2. H^+	 **I** **II** **I** + **II** (56), **I/II** = 70:30	169
	 1.25 eq	1. THF, 40°, 3 h 2. H^+	 (50)	78
	 1.2 eq	1. THF, Carius tube, 100°, 30 h 2. $Pd(PPh_3)_4$ (10 mol %), 65°, 24 h 3. H^+	 (51)	170, 60
	 1.2 eq	1. THF, Carius tube, 100°, 35 h 2. H^+	 (—)	170, 60
	 2.5 eq	1. 65°, 3 h 2. H^+	 **I** **II** **I** + **II** (52), **I/II** = 29:71	166
	 2.5 eq	1. THF, 65°, 3 h 2. H^+	 (37)	166
	 3.7 eq	1. THF, 65°, 1.5 h 2. H^+	 (55)	166
C_4				
		1. THF 2. H^+	 (69)	58
	 2 eq	1. THF, 60°, 24 h 2. H^+	 (84)	59

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

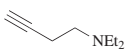
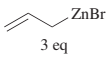
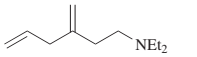
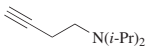
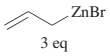
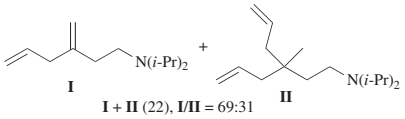
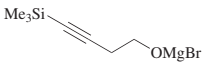
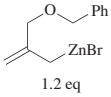
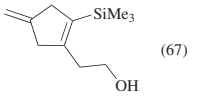
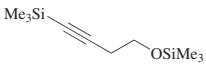
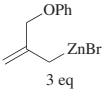
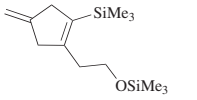
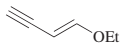
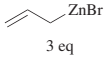
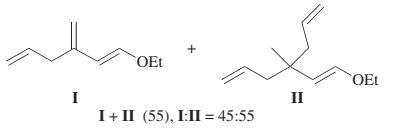
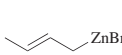
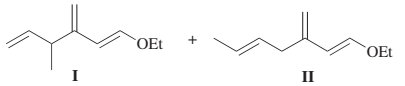
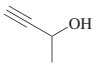
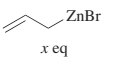
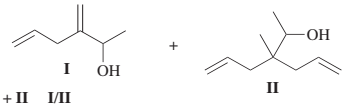
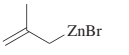
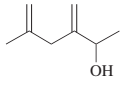
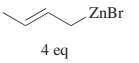
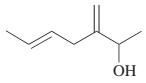
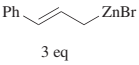
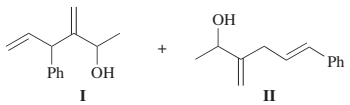
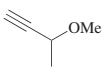
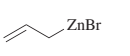
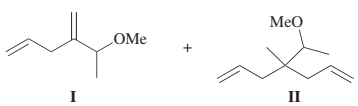
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
	 3 eq	1. THF, 65°, 23 h 2. H^+	 (60)	55, 56
	 3 eq	1. THF, 65°, 23 h 2. H^+	 **I** **II** **I + II** (22), **I/II** = 69:31	56
	 1.2 eq	1. THF, Carius tube, 100°, 55 h 2. $Pd(PPh_3)_4$ (10 mol %), 65°, 24 h 3. H^+	 (67)	170, 60
	 3 eq	1. THF, Carius tube, 100°, 30 h 2. $Pd(PPh_3)_4$ (5 mol %), 65°, 24 h 3. H^+	 (78)	170
	 3 eq	1. THF, rt, 6 h 2. H^+	 **I** **II** **I + II** (55), **I**:**II** = 45:55	82
	 3 eq	1. THF, temp, 6 h 2. H^+	 **I** **II** Temp / **I + II** / **I/II**: rt (78) 96:4; 50° (53) 75:25	82
	 *x* eq	1. MBr_2, (*y* eq), THF, temp, time 2. H^+ *x* / M / *y* / Temp (°) / Time (h) / **I + II** / **I/II**: 4 none 0 rt 3 (76) 100:0; 4 Zn 2 40 2 (79) 100:0; 4 Mg 2 40 2 (71) 86:14; 8 Zn 2 40 2 (77) 100:0; 8 Mg 2 40 2 (54) 24:76	 **I** **II**	169
	 4 eq	1. THF, 40°, 1 h 2. H^+	 (85)	169
	 4 eq	1. THF, 40°, 3 h 2. H^+	 (80)	169
	 3 eq	1. THF, temp, 24 h 2. H^+	 **I** **II** Temp (°) / **I + II** / **I/II**: 20 (63) 42:58; 65 (57) 37:63	165, 168
	 2 eq	1. THF, rt, 3 h 2. H^+	 **I** **II** **I + II** (45), **I**:**II** = 51:49	169

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

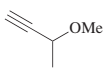
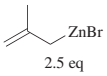
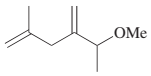
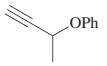
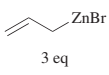
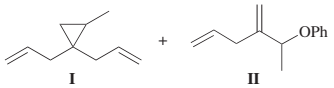
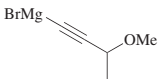
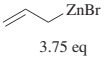
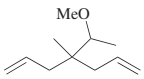
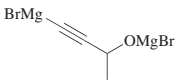
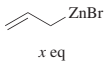
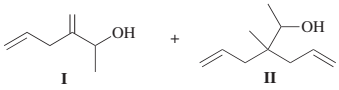
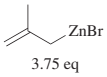
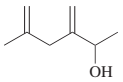
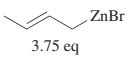
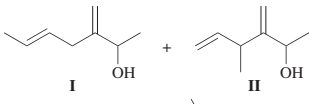
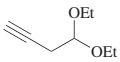
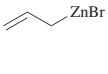
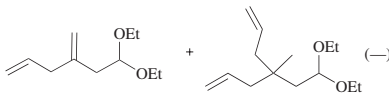
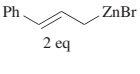
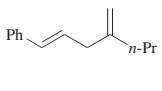
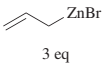
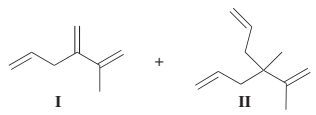
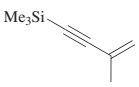
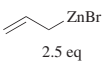
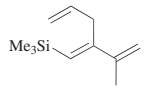
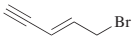
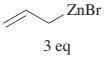
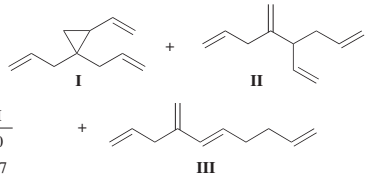
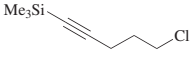
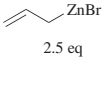
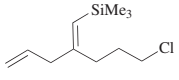
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
	 2.5 eq	1. THF, 35°, 1.5 h 2. H^+	 (58)	169
	 3 eq	1. THF, 40°, 1.5 h 2. 65°, 3 h 3. H^+	 **I** **II** **I + II** (76), **I/II** = 80:20	166
	 3.75 eq	1. THF, 40°, 15 h 2. H^+	 (75)	169
	 *x* eq	1. THF, temp, 2 h 2. H^+ *x* Temp (°) **I + II** **I/II** 2.5 65 (80) 46:54 3.75 35 (78) 19:81	 **I** **II**	169
	 3.75 eq	1. THF, 65°, 15 h 2. H^+	 (76)	169
	 3.75 eq	1. THF, 65°, 3 h 2. H^+	 **I** **II** **III** **I + II + III** (73), **I/II/III** = 50:12:38	169
		1. — 2. H^+	 (—)	166
C_5				
	 2 eq	1. THF, temp, time 2. H^+	 Temp (°) Time (h) 20 24 (10) 65 8 (28) 65 24 (57)	168
	 3 eq	1. THF, rt, 6 h 2. H^+	 **I** **II** **I + II** (50), **I/II** = 58:42	82
	 2.5 eq	1. THF, 65°, 16–25 h 2. H^+	 (57)	57
	 3 eq	1. THF, temp, 15 h 2. H^+ Temp (°) **I + II + III** **I/II/III** 20 (52) 44:6:50 65 (31) 13:10:77	 **I** **II** **III**	164
	 2.5 eq	1. THF, 65°, 16–25 h 2. H^+	 (63)	57

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

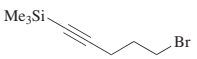
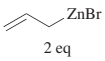
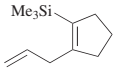
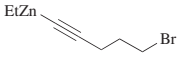
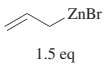
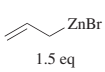
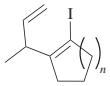
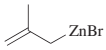
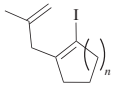
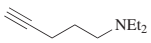
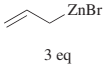
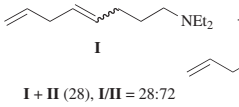
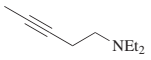
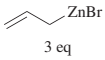
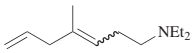
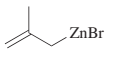
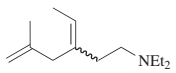
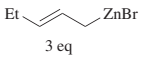
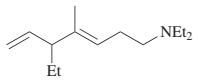
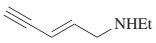
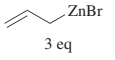
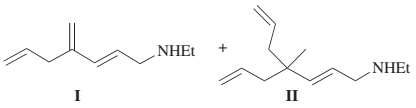
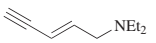
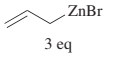
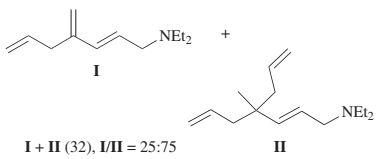
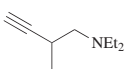
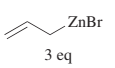
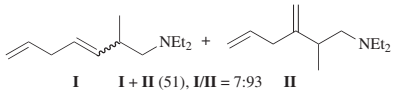
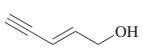
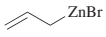
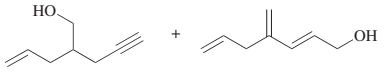
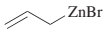
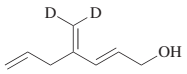
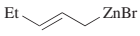
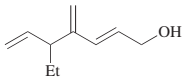
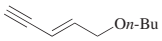
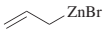
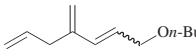
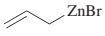
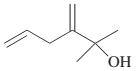
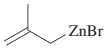
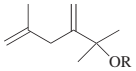
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
	 2 eq	1. THF, 60°, 24 h 2. CuBr (2 eq) 3. H^+	 (64)	59
	 1.5 eq	1. THF, rt, 12 h 2. –78° to rt 3. I_2 (1.5 eq), –78° 4. H^+	 (65)	84
C_{5-6}				
	 1.5 eq	1. THF, rt, 12 h 2. I_2, -78^o to rt	 *n*: 1 (86); 2 (75)	84
		1. THF 2. I_2	 *n*: 1 (77); 2 (64)	84
		1. THF 2. I_2	 *n*: 1 (80); 2 (82)	84
C_5				
	 3 eq	1. THF, 65°, 46 h 2. H^+	 **I** + **II** (28), **I/II** = 28:72	55, 56
	 3 eq	1. THF, 65°, 23 h 2. H^+	 (65)	55, 56
	 3 eq	1. THF, 65°, 23 h 2. H^+	 (75)	55, 56
	 3 eq	1. THF, 65°, 23 h 2. H^+	 (30)	55, 56
	 3 eq	1. THF, temp, time 2. H^+	 **I** + **II** Temp (°) / Time (h) / **I** + **II** / **I/II**: rt / 24 / (29) / 52:48 65 / 8 / (58) / 69:31	56, 167 167
	 3 eq	1. THF, 65°, 8 h 2. H^+	 **I** + **II** (32), **I/II** = 25:75	56
	 3 eq	1. THF, 65°, 23 h 2. H^+	 **I** **I** + **II** (51), **I/II** = 7:93 **II**	55, 56

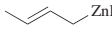
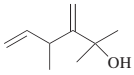
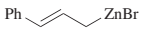
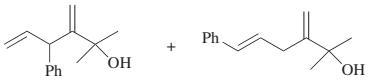
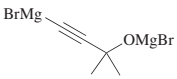
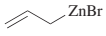
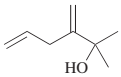
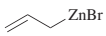
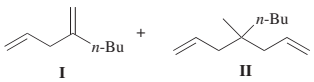
TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
	 3 eq	1. THF, temp, time 2. 20°, 15 h 3. H^+	 **I** + **II**	

Temp (°)	Time	**I + II + III**	**I/II/III**	
20	30 min	(73)	0:80:20	81
rt	24 h	(77)	0:82:18	167
65	1 h	(69)	14:72:14	81
65	1 h	(77)	0:82:18	81
65	23 h	(56)	29:66:5	81

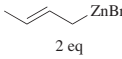
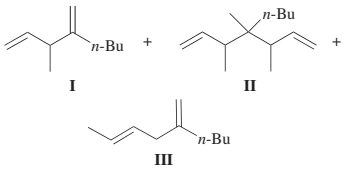
III

	 3 eq	1. THF, TMEDA, 65°, 1 h 2. 20°, 15 h 3. D^+		(63)	81
	 3 eq	1. THF, rt, 24 h 2. H^+		(74)	167
	 3 eq	1. THF, rt, 24 h 2. H^+		(57)	167
	 4 eq	1. THF, 35°, 15 h 2. H^+		(71)	169
	 *x* eq	1. THF, temp, time 2. H^+		R *x* Temp (°) Time (h) H 4 40 3 (80) Me 2.5 35 1.5 (50)	169

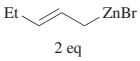
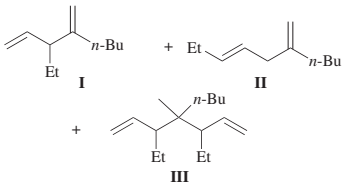
	 4 eq	1. THF, 40°, 15 h 2. H^+		(47)	169
	 3 eq	1. THF, 65°, 24 h 2. H^+	 **I** **I + II** (34), **I/II** = 30:70 **II**		168
	 2.5 eq	1. THF, 65°, 2 h 2. H^+		(65)	169
C_6					
	 *x* eq	1. THF, temp, time 2. H^+	 **I** **II**		

x	Temp	Time (h)	**I + II**	**I/II**	
1.5[a]	rt	3	(46)	100:0	79
1.5	rt	3	(58)	90:10	79
2	20°	3	(66)	79:21	165
2	20°	24	(70)	71:29	165
2	65°	7	(60)	57:43	165
3	rt	3	(71)	69:31	79
4	rt	3	(63)	59:41	79
4	rt	15 min	(38)	76:24	79
4	65°	7	(60)	57:43	79

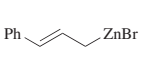
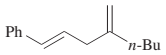
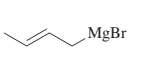
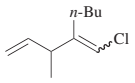
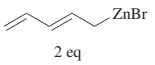
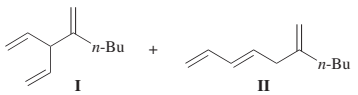
TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 2 eq	1. THF, temp, time 2. H^+	 **I** **II** **III**	

Temp (°)	Time (h)	**I + II + III**	**I/II/III**	
20	3	(46)	90:0:10	79, 168
20	24	(56)	86:0:14	79, 168
65	3	(63)	59:0:41	165
65	24	(65)	51:0:49	168
100	24	(50)	40:0:60	168

	 2 eq	1. THF, temp, time 2. H^+	 **I** **II** **III**	168

Temp (°)	Time (h)	**I + II + III**	**I/II/III**
20	3	(43)	85:15:0
20	24	(55)	80:20:0
65	3	(52)	57:43:0
65	24	(64)	52:48:0

	 2 eq	1. THF, temp, 24 h 2. H^+		Temp (°): 20 (10); 65 (55)	165
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –10°, 30 min 4. $PhSO_2Cl$ (4 eq), –20°, 15 h 5. H^+, –20°		(75) (*E*)/(*Z*) = 50:50	85
	 2 eq	1. THF, temp, 24 h 2. H^+	 **I** **II**		165

Temp (°)	**I + II**	**I/II**
20	(12)	28:72
65	(56)	3:97

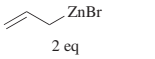
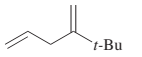
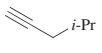
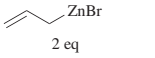
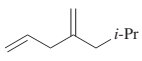
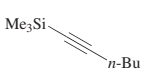
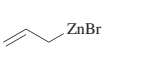
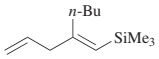
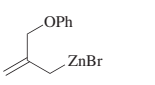
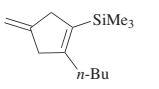
	 2 eq	1. THF, rt, 3 h 2. H^+		(35)	79
	 2 eq	1. THF, rt, 3 h 2. H^+		(57)	79
	 2.5 eq	1. THF, 65°, 16–25 h 2. H^+		(70)	57
	 1.2 eq	1. THF, Carius tube, 100°, 30 h 2. $Pd(PPh_3)_4$ (10 mol %), 65°, 24 h 3. H^+		(72)	60, 170

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

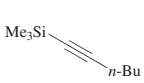
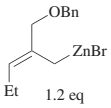
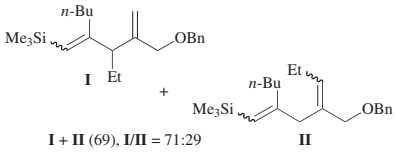
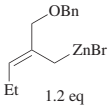
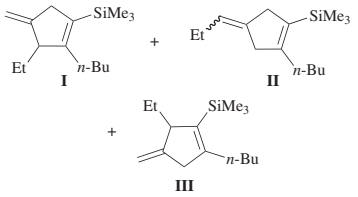
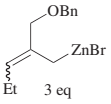
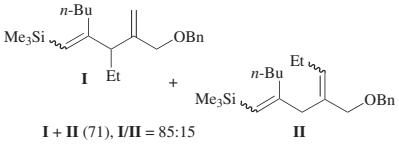
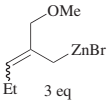
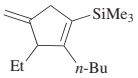
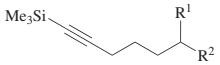
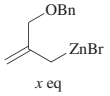
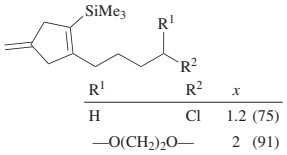
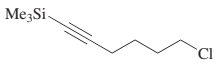
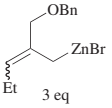
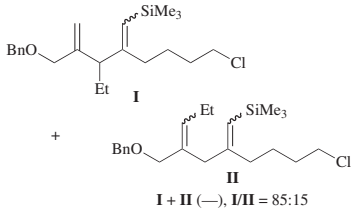
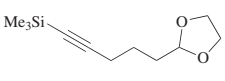
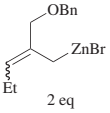
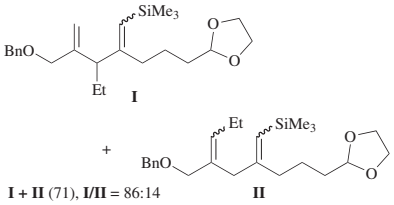
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 1.2 eq	1. THF, Carius tube, 100°, 30 h 2. H^+	 **I** + **II** (69), **I/II** = 71:29	60
	 1.2 eq	1. THF, Carius tube, 100°, 30 h 2. $Pd(PPh_3)_4$ (5 mol %), 65°, 30 h 3. H^+	 **I** + **II** + **III** (37), **I/II/III** = 51:38:11	60
	 3 eq	1. THF, 95°, 30 h 2. H^+	 **I** + **II** (71), **I/II** = 85:15	60
	 3 eq	1. THF, 75°, 24 h 2. $Pd(PPh_3)_4$ (5 mol %), 75°, 1.5 h 3. H^+	 (84)	60
	 *x* eq	1. THF, Carius tube, 100°, 30 h 2. $Pd(PPh_3)_4$ (10 mol %), 65°, 24 h 3. H^+		60, 170
	 3 eq	1. THF, Carius tube, 95°, 8 h 2. H^+	 **I** + **II** (—), **I/II** = 85:15	60
	 2 eq	1. THF, Carius tube, 95°, 30 h 2. H^+	 **I** + **II** (71), **I/II** = 86:14	60

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

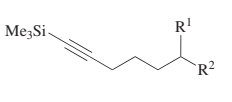
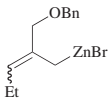
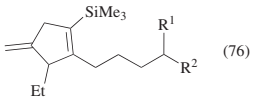
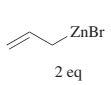
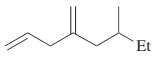
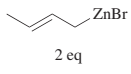
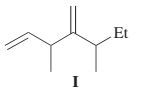
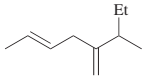
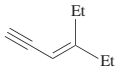
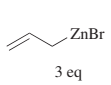
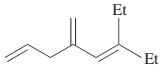
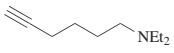
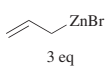
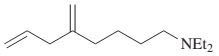
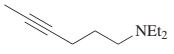
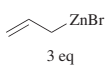
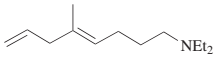
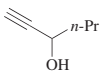
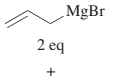
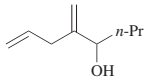
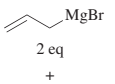
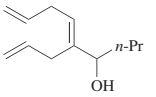
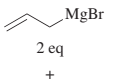
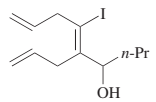
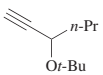
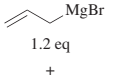
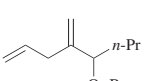
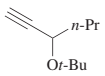
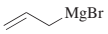
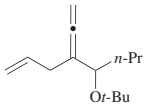
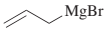
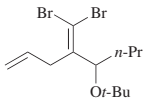
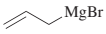
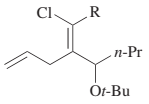
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 3 eq	1. THF, 95°, Carius tube, 30 h 2. $Pd(PPh_3)_4$ (5 mol %), 65°, 8 h 3. H^+	 (76) R^1 R^2 H Cl (76) —$O(CH_2)_2O$— (71)	60
	 2 eq	1. THF, rt, 3 h 2. H^+	 (50)	79
	 2 eq	1. THF/toluene, temp, time 2. H^+	 +  **I** **II** Temp (°) Time (h) **I + II** **I/II** 20 24 (10) 95:5 65 3 (17) 67:33 65 24 (30) 62:38	168
	 3 eq	1. THF, temp, 6 h 2. H^+	 Temp rt (20) 50° (28)	82
	 3 eq	1. THF, 65°, 46 h 2. H^+	 (25)	55, 56
	 3 eq	1. THF, 65°, 46 h 2. H^+	 (25)	55, 56
	 2 eq + $ZnBr_2$ 2 eq	1. BuLi (2 eq), Et_2O, 0°, 1 h 2. "Allylzinc", –30° 4. 0°, 4 h 5. H^+	 (62)	86
	 2 eq + $ZnBr_2$ 2 eq	1. BuLi (2 eq), Et_2O, 0°, 1 h 2. "Allylzinc", –30° 3. $Me_2CuCNLi_2$ (2 eq), THF, –40 to –20°, 15 min 4. Allyl-Br (2 eq), $P(OEt)_3$ (10 mol %), –40°, 16 h 5. H^+	 single isomer (56)	86
	 2 eq + $ZnBr_2$ 2 eq	1. BuLi (2 eq), Et_2O, 0°, 1 h 2. "Allylzinc", –30° 3. $Me_2CuCNLi_2$ (2 eq), THF, –40 to –20°, 15 min 4. Allyl-Br (2 eq), $P(OEt)_3$ (10 mol %), –40°, 16 h 5. I_2, –50° to rt, 30 min 6. H^+	 (25)	86
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. H^+	 (90)	85, 86

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. PhCHO (1.5 eq), –80° 5. BF_3 (1.5 eq), –80° 6. –80° to rt, 1 h 7. H^+	 (53) dr 68:32	85, 86
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. NBS (2.5 eq), –80°, 3 h 5. –80 to 0°, 1 h 6. H^+	 (65)	85, 86
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. TosCl (4 eq), –20°, 15 h 5. See table. 6. See table.	 single isomer	85, 86

Step 5	Step 6	R	
H^+, 20°	—	H	(87)
D^+, –20°	–20° to rt	D (>98%)	(60)
I_2, THF, –30°	H^+	I	(63)
NBS (1.5 eq), CH_2Cl_2, –20°, 2 h	H^+	Br	(63)

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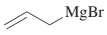
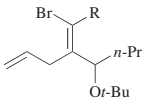
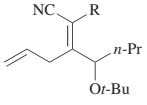
 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. TosBr (2 eq), Et_2O, –50°, 15 min 5. See table. 6. See table.	 single isomer		85, 86

Step 5	Step 6	R	
H^+, –20°	—	H	(63)
NCS (1.5 eq), CH_2Cl_2, –50°; –50 to –20°, 1 h	H^+	Cl	(60)

 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. TosCN (2 eq), Et_2O, –50° 5. See table. 6. rt, 2 h 7. See table. 8. See table.	 single isomer		85, 86

Step 5	Step 7	Step 8	R	
–50° to rt	H^+, –20°	—	H	(63)
–50° to rt, 1 h	NBS (2 eq), CH_2Cl_2, –30°, 1 h	H^+	Br	(60)
–50° to rt	$Me_2CuCNLi_2$ (1.5 eq), THF, –20°, 15 min	allyl-Br (1.5 eq), $P(OEt)_3$ (10 mol %), –40°, 12 h; H^+	allyl	(65)

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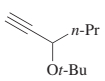
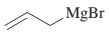
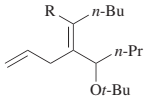
TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. TosCl (4 eq), Et_2O, –20°, 15 h 5. BuLi (2 eq), –78°, 1.5 h 6. See table.		85, 86

Step 6	R		(*Z*)/(*E*)
H^+	H	(53)	90:10
I_2, –78°; –78° to rt, 2 h; H^+	I	(57)	10:90

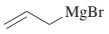
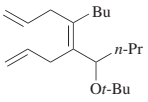
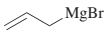
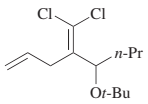
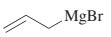
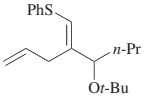
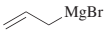
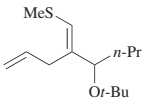
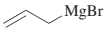
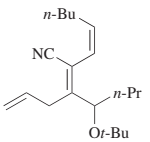
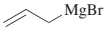
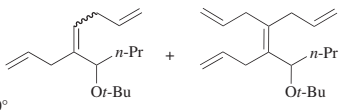
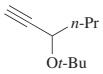
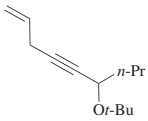
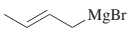
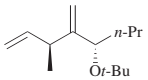
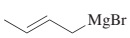
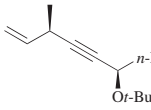
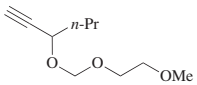
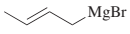
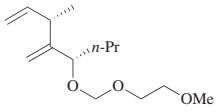
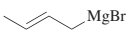
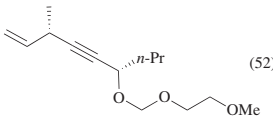
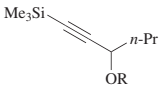
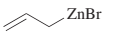
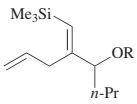
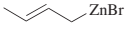
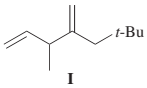
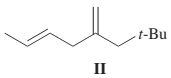
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. TosCl (4 eq), –20°, 15 h 5. BuLi (2 eq), –78°, 1.5 h 6. $Me_2CuCNLi_2$, THF, –20°, 15 min 7. Allyl-Br (1.5 eq), $P(OEt)_3$ (10 mol %), –40°, 16 h 8. H^+	 (50) (*E*)/(*Z*) = 90:10	16, 85, 86
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. NCS (3 eq), –30°, 3 h 5. H^+	 (56)	86
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. $PhSSO_2Ph$ (2 eq), –45°, 16 h 5. H^+	 (88)	86
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. $MeSSO_2Me$ (2 eq), –20° 5. –20° to rt, 16 h 6. H^+	 (42)	86
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. TosCN (2 eq), Et_2O, –50° 5. –50° to rt 6. rt, 2 h 7. (*Z*)-ICH=CH$(CH_2)_3CH_3$ (2 eq), $Pd(PPh_3)_4$ (10 mol %), –40° 8. –40 to 40° 9. H^+	 (35)	86
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –10°, 30 min 2. "Allylzinc", –20° 3. –10°, 30 min 4. Me_2CuLi (1.5 eq), THF, –40° 5. –40 to –20°, 30 min 6. Allyl-Br (1.5 eq), $P(OEt)_3$ (10 mol %), –40°, 2 h 7. H^+	 (80)	86

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

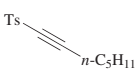
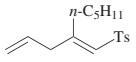
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –20°, 10 min 2. "Allylzinc", Et_2O, –20° 3. –10°, 30 min 4. $PhSO_2Cl$ (4 eq), –20°, 15 h 5. –20° to rt 6. H^+	 (70)	89
	 **I** 1.2 eq + $ZnBr_2$ 1.2 eq **II**	1. BuLi (1 eq), Et_2O, –20°, 10 min 2. **I**, Et_2O, –20°, 5 h 3. **II**, Et_2O, –20° 4. –20°, 1 h 5. H^+	 (75) dr 70:30	89
	 **I** 1.2 eq + $ZnBr_2$ 1.2 eq **II**	1. BuLi (1 eq), Et_2O, –20°, 10 min 2. **I**, Et_2O, –20°, 5 h 3. **II**, Et_2O, –20° 4. $PhSO_2Cl$ (4 eq), –20°, 1 h 5. –20° to rt, 15 h 6. H^+	 (71) dr 70:30	89
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –20°, 10 min 2. "Allylzinc", –30° 3. –20°, 4 h 4. H^+	 (60) dr 92:8	89
	 1.2 eq + $ZnBr_2$ 1.2 eq	1. BuLi (1 eq), Et_2O, –20°, 30 min 2. "Allylzinc", –30° 3. –20°, 4 h 4. $PhSO_2Cl$ (4 eq), –20° 5. –20° to rt, 16 h 6. H^+	 (52) dr 92:8	89
	 2.5 eq	1. THF, 65°, 16–25 h 2. H^+		57

R	
TMS	(52)
Bn	(74)

C_7

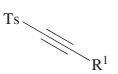
	 3 eq	1. THF, temp, time 2. H^+	 **I** +  **II**	168

Temp (°)	Time (h)	I + II	I/II
20	24	(6)	87:13
65	3	(18)	21:79
65	24	(26)	20:80

		1. THF, reflux 2. H^+		61

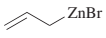
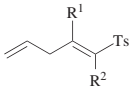
Allylzinc/Alkyne	Conc. (M)	Time (h)	
60:40	0.5	1.5	(92)
55:45	0.5	2.0	(90)

$C_{7–8}$

	R^2ZnBr 1.2 eq	1. THF, 0°, then reflux, time 2. H^+		172

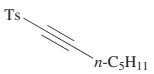
R^1	R^2	Time (h)	
n-C_5H_{11}	allyl	2	(92)
n-C_5H_{11}	Bn	12	(88)
Ph	allyl	2	(96)
Ph	Bn	24	(90)

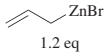
TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{7-8} 	 1.2 eq	1. THF, 0°, then reflux, 2 h 2. R^2X (1.0 eq), $Ni(PPh_3)_2Cl_2$ (10 mol %), 50°		

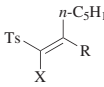
R^1	R^2	X		
n-C_5H_{11}	allyl	Br	(74)	61, 172
n-C_5H_{11}	4-$OHCC_6H_4$	Br	(60)	61, 172
n-C_5H_{11}	4-$MeOC_6H_4$	I	(45)	61, 172
n-C_5H_{11}	4-AcC_6H_4	I	(51)	61, 172
n-C_5H_{11}	4-NCC_6H_4	Br	(57)	61, 172
n-C_5H_{11}	4-$MeO_2CC_6H_4$	I	(42)	61, 172
n-C_5H_{11}	5-Cl-2-pyridinyl	I	(65)	61, 172
Ph	allyl	Br	(83)	61, 172
Ph	Ph	Br	(47)	61, 172
Ph	4-FC_6H_4	I	(61)	172
Ph	4-ClC_6H_4	Br	(54)	61
Ph	4-$MeOC_6H_4$	I	(55)	61, 172
Ph	4-$Me_2NC_6H_4$	Br	(63)	61, 172
Ph	Bn	Br	(40)	61, 172
Ph	4-$BrCH_2C_6H_4$	I	(41)	172
Ph	3-MeC_6H_4	Br	(57)	61
Ph	4-MeC_6H_4	Br	(60)	61, 172
Ph	4-$OHCC_6H_4$	Cl	(55)	61
Ph	4-$OHCC_6H_4$	Br	(63)	61, 172
Ph	4-AcC_6H_4	I	(61)	61, 172
Ph	4-NCC_6H_4	Br	(57)	61, 172
Ph	4-$MeO_2CC_6H_4$	I	(40)	61, 172
Ph	4-EtC_6H_4	Br	(43)	61
Ph	5-Cl-2-pyridinyl	I	(51)	61, 172

C_7

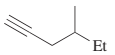


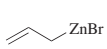

1.2 eq

1. THF, 0° to reflux
2. E^+ (1.5 eq), rt

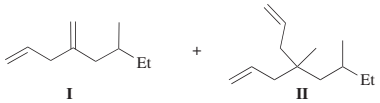


E^+	X		
I_2	I	(92)	173
NBs	Br	(89)	




2.5 eq

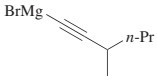
1. THF, temp, time
2. H^+

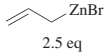


I + **II**

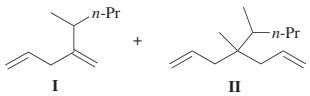
Temp (°)	Time	**I** + **II**	**I**/**II**
40	30 min	(40)	88:12
66	3 h	(78)	9:91

77




2.5 eq

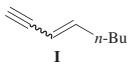
1. THF, 66°, 3 h
2. H^+

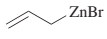


I + **II** (41), **I**/**II** = 7:93

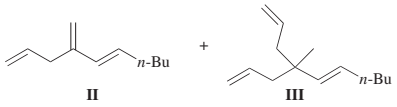
77

C_8


I

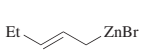

x eq

1. THF, temp, 6 h
2. H^+

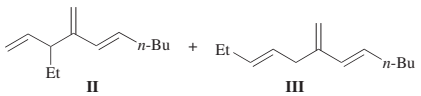


II + **III**

(*E*)/(*Z*) **I**	*x*	Temp	**II** + **III**	**II**/**III**	(*E*)/(*Z*) **II**	
60:40	2	—	(59)	100:0	60:40	79, 167
45:55	3	rt	(65)	66:34	45:55	82
45:55	4	20°	(55)	78:22	45:55	83


x eq

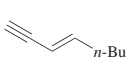
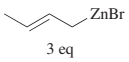
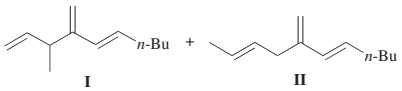
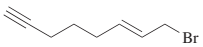
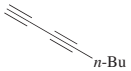
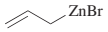
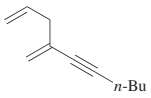
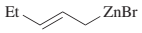
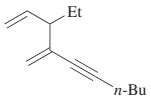
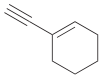
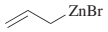
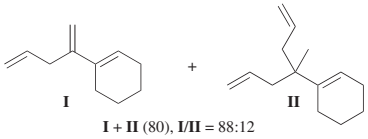
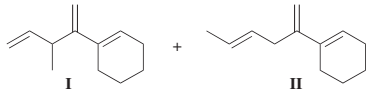
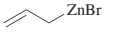
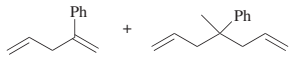
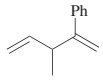
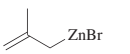
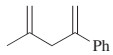
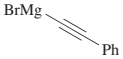
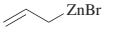
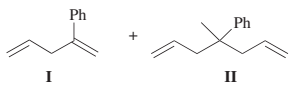
1. THF, temp, time
2. H^+



II + **III**

(*E*)/(*Z*) **I**	*x*	Temp (°)	**II** + **III**	**II**/**III**	(*E*)/(*Z*) **II**	t(*hr*)	
60:40	2	rt	(55)	95:5	60:40	3	79
60:40	2	65	(53)	70:30	60:40	2	79
60:40	2	65	(50)	66:34	60:40	8	79
45:55	4	20	(55)	95:5	45:55	6	83
45:55	4	65	(53)	70:30	45:55	2	83
45:55	4	65	(50)	65:35	45:55	8	83

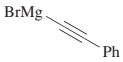
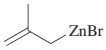
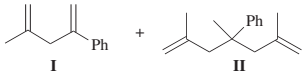
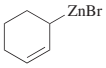
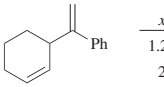
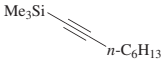
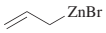
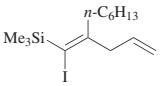
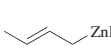
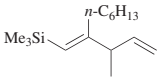
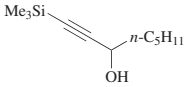
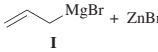
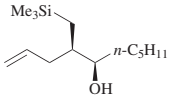
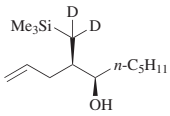
TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 3 eq	1. THF, temp, 6 h 2. H^+	 **I** + **II** (40), **I/II** = 91:9 (rt); 75:25 (50°)	82
	Intramolecular	1. Zn, THF, 20°, 2 h 2. 40°, 1 h 3. H^+	 (43)	62
	Intramolecular	1. Zn, THF, 20°, 2 h 2. 40°, 1 h 3. D^+	 (42) configuration not determined	62
	 4 eq	1. THF, 20°, 24 h 2. H^+	 (67)	83
	 4 eq	1. THF, temp, time 2. H^+	 Temp (°) / Time (h): 20 / 24 / (60); 65 / 65 / (55)	83
	 3 eq	1. THF, rt, 6 h 2. H^+	 **I** + **II** (80), **I/II** = 88:12	82
	 3 eq	1. THF, temp, 6 h 2. H^+	 Temp: **I** + **II** (45), **I/II** 48:52 (rt); **I** + **II** (51), **I/II** 30:70 (50°)	82
	 2.5 eq	1. THF, temp, time 2. H^+	 Temp (°) / Time / **I** + **II** / **I/II**: 0 / 24 h / (73) / 92:8; 35 / 30 min / (73) / 92:8	76
	 2.5 eq	1. THF, 35°, 45 min 2. H^+	 (52)	76
	 2.5 eq	1. THF, 35°, 1.5 h 2. H^+	 (66)	77
	 2.5 eq	1. THF, temp, time 2. H^+	 Temp (°) / Time / **I** + **II** / **I/II**: 35 / 30 min / (87) / 25:75; 35 / 3 h / (79) / 5:95; 66 / 3 h / (79) / 5:95	77

819

619

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 2.5 eq	1. THF, temp, 3 h 2. H^+	 **I** + **II** Temp (°) / **I + II** / **I/II** 35 (50) 92:8 66 (67) 73:27	77
	 *x* eq	1. THF, 40°, 3 h 2. H^+	 *x*: 1.25 (30); 2 (43)	78
		1. THF, 60°, 18–24 h 2. I_2	 (83) (*Z*)/(*E*) = 85:15	72
		1. THF, 60°, 18–24 h 2. H^+	 (68) (*Z*)/(*E*) = 90:10	72
	 **I**	1. *i*-BuMgBr (2 eq), Et_2O, 0° 2. Cp_2TiCl_2 (5 mol %), 0°, 3 h 3. **I** (2 eq), –10° 4. $ZnBr_2$ (2 eq), Et_2O, 0°, 4 h 5. H^+	 (78) dr 95:5	148
	 **I**	1. *i*-BuMgBr (2 eq), Et_2O, 0° 2. Cp_2TiCl_2 (5 mol %), 0°, 3 h 3. **I** (2 eq), –10° 4. $ZnBr_2$ (2 eq), Et_2O, 0°, 4 h 5. D^+	 (74) dr 95:5 D >98%	148

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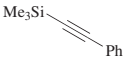
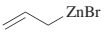
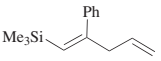
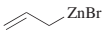
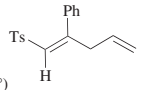
Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
	 2.5 eq	1. THF, rt, 12 h 2. H^+	 (78)	57
		1. THF, temp, time 2. H^+		61

Allylzinc/Alkyne	Conc (M)	Time (h)	Temp (°)	
1.0	0.5	3	50	(54)
1.2	0.5	5	50	(83)
1.5	0.5	3	50	(91)
1.5	0.5	7	30	(48)
1.5	0.5	2	reflux	(96)
1.5	0.1	5	reflux	(80)
1.5	0.25	2	reflux	(91)
1.5	1.0	2	reflux	(90)
2.0	0.5	1	reflux	(89)

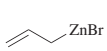
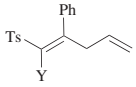
	 1.2 eq	1. THF, 0° to reflux 2. E^+ (1.5 eq), rt		E^+ / Y	
				I_2 I (93)	173
				NBS Br (90)	
				NCS Cl (80)	

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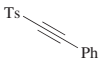
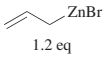
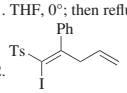
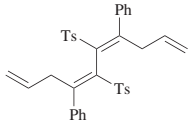
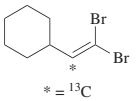
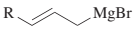
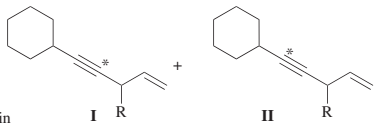
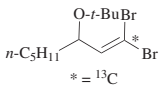
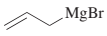
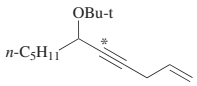
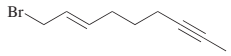
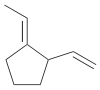
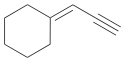
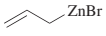
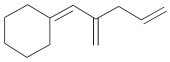
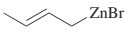
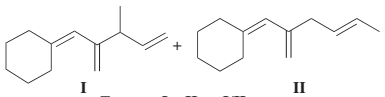
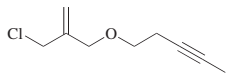
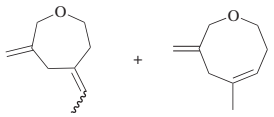
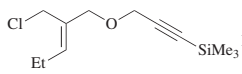
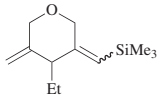
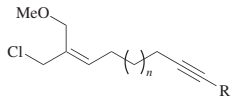
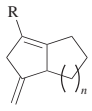
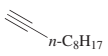
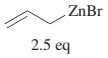
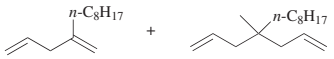
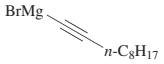
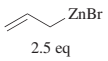
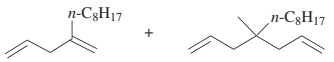
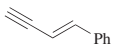
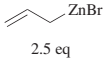
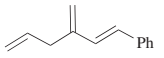
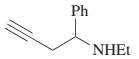
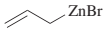
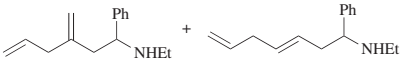
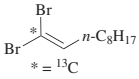
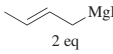
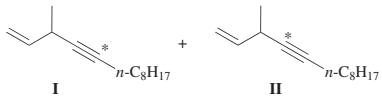
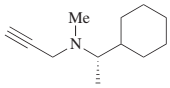
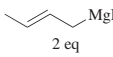
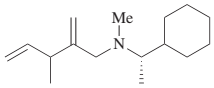
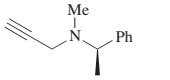
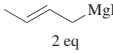
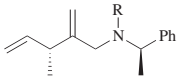
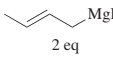
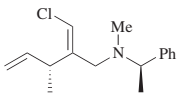
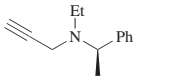
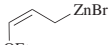
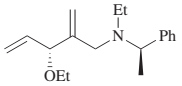
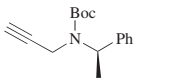
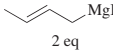
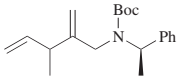
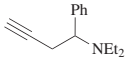
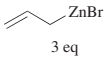
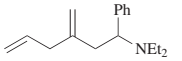
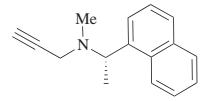
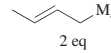
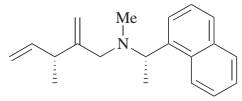
TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	 1.2 eq	1. THF, 0°; then reflux, 2 h 2.  (0.8 eq), 50°, $Ni(PPh_3)_2Cl_2$ (8 mol %)		173
 * = ^{13}C	 2 eq + $ZnBr_2$ 2 eq	1. BuLi (2 eq), Et_2O, –80° 2. –80° to rt, 30 min 3. "Allylzinc", Et_2O, –10° 4. 0°, time 4. $PhSO_2Cl$ (2 eq), –20°, 30 min 6. –20° to rt, 15 h 7. H^+	 **I** **II** R Time (h) **I + II** **I/II** H 2.5 (47) 92:8 Me 5 (67) 86:14	174
 * = ^{13}C	 2 eq + $ZnBr_2$ 2 eq	1. BuLi (2 eq), Et_2O, –80° 2. –80 to 0°, 1 h 3. "Allylzinc", Et_2O, –20° 4. $PhSO_2Cl$ (2 eq), –20° 5. –20° to rt, 15 h 6. H^+	 (74)	174
C_9 	Intramolecular	1. Zn, THF, 20°, 2 h 2. 60°, 24 h 3. H^+	 (50)	62
	 3 eq	1. THF, temp, 6 h 2. H^+	 Temp rt (35) 50° (33)	82
	 3 eq	1. THF, temp, 23 h 2. H^+	 **I** **II** Temp **I + II** **I/II** rt (23) 65:35 50° (30) 47:53	82
	Intramolecular	1. Mg, THF 2. $ZnBr_2$, Carius tube, 130°, 24 h	 **I** (*E*)/(*Z*) = 56:44 **II** **I + II** (44), **I/II** = 90:10	171
	Intramolecular	1. Mg, THF, 0° 2. $ZnBr_2$ (1.5 eq), Carius tube, 100°, 24 h 3. H^+	 (74)	171
C_{9-13} 	Intramolecular	1. Mg (4 eq) 2. 1,2-dibromoethane (2 eq), THF, time 2 3. $ZnBr_2$ (1.5 eq), solvent 4. Step 4 5. $Pd(PPh_3)_4$ (5 mol %), temp 5, time 5 6. Step 6		175, 171

n	R	Time 2 (h)	Solvent	Step 4	Temp 5, Time 5	Step 6	
1	TMS	—	—	rt, 2 h	rt, 3.5 h	—	(84)
2	TMS	10	THF	65°, 2 h	65°, 2 h	H^+	(67)
3	TMS	10	THF	65°, 8 h	rt, 4 h	H^+	(75)
1	*n*-Bu	10	THF	65°, 24 h	65°, 2 h	H^+	(44)

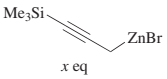
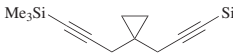
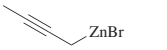
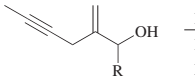
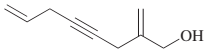
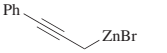
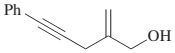
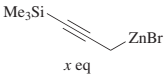
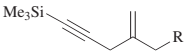
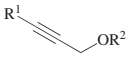
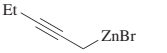
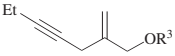
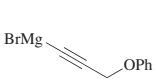
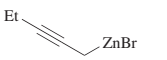
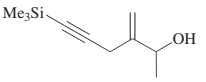
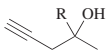
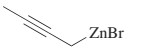
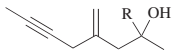
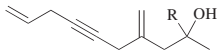
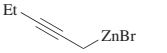
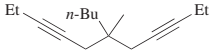
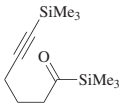
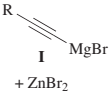
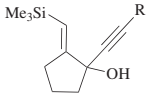
TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
B. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

	Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}		 2.5 eq	1. THF, 35°, 30 min 2. H^+	 **I** **II** **I + II** (72), **I/II** = 61:39	77
		 2.5 eq	1. THF, 66°, 3 h 2. H^+	 **I** **II** **I + II** (81), **I/II** = 9:97	77
		 2.5 eq	1. THF, rt, 6 h 2. H^+	 (40)	82
		 3 eq	1. THF, 65°, 1 h 2. rt, 8 h 3. H^+	 **I** **II** **I + II** (28), **I/II** = 91:9	56
	 $* = {}^{13}C$	 2 eq + $ZnBr_2$ (2 eq)	1. BuLi (2 eq), Et_2O, –80° 2. –80° to rt, 30 min 3. "Allylzinc", Et_2O, –10° 4. 0°, 5 h 5. $PhSO_2Cl$ (2 eq), Et_2O, –20°, 30 min 6. –20° to rt, 10 h 7. H^+	 **I** **II** **I + II** (55), **I/II** = 66:33	174
C_{11}		 2 eq + $ZnBr_2$ (3 eq)	1. BuLi (1 eq), Et_2O, –20°, 30 min 2. "Allylzinc", Et_2O, –25°, 6 h 3. H^+	 (69) dr 50:50	92
		 2 eq + $ZnBr_2$ (3 eq)	1. BuLi (1 eq), Et_2O, –20°, 30 min 2. "Allylzinc", Et_2O, –25°, time 2 3. H^+		92
				R Time 2 dr Me (62) 6 88:12 Et (68) 8 90:10 *i*-Pr (57) 6 75:25	
		 2 eq + $ZnBr_2$ (3 eq)	1. BuLi (1 eq), Et_2O, –20°, 30 min 2. "Allylzinc", Et_2O, –25° 3. $PhSO_2Cl$ (3 eq), –20°, 1 h 4. H^+	 (82) dr 88:12	92
		 2 eq	1. BuLi (1 eq), Et_2O, –20°, 30 min 2. "Allylzinc", Et_2O, –10°, 8 h 3. H^+	 (60) dr 93:7	92
		 2 eq + $ZnBr_2$ (3 eq)	1. BuLi (1 eq), Et_2O, –20° 2. –20 to 0°, 30 min 3. "Allylzinc", Et_2O 4. H^+	 (—) dr 50:50	92
		 3 eq	1. THF, 65°, 1 h 2. 20°, 8 h 3. H^+	 (52)	56
C_{15}		 2 eq + $ZnBr_2$ (3 eq)	1. BuLi (1 eq), Et_2O, –20°, 30 min 2. "Allylzinc", Et_2O, 15°, 5 h 3. H^+	 (60) dr 87:13	92

[a] The reaction was performed using inverse addition.

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

C. UNCATALYZED ADDITION OF PROPARGYL/ALLENYLZINC DERIVATIVES

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	 *x* eq	1. THF, 20°, 15 h 2. H^+		95
C_{3-4} 	 3 eq	1. THF, 30°, 24 h 2. H^+		94
C_3 	 3 eq	1. THF, 30°, 24 h 2. H^+	 (50)	94
	 3 eq	1. THF, 30°, 24 h 2. H^+	 (56)	94
	 *x* eq	1. THF, 20°, 15 h 2. H^+		95
	 2 eq	1. THF, 35°, time 2. H^+		93
	 2 eq	1. THF, 40°, 3 h 2. THF, 65°, 20 h 3. H^+	 (46)	93
C_4 	 4 eq	1. THF, 20°, 15 h 2. H^+	 (55)	95
C_{5-6} 	 4 eq	1. THF, temp, 24 h 2. H^+		94
	 3 eq	1. THF, temp, 24 h 2. H^+		94
C_6 	 2 eq	1. THF, 35°, 15 h 2. H^+	 (45)	93
	 + $ZnBr_2$	1. **I**, THF, –80°; reflux, 45 min 2. $ZnBr_2$, –60° to rt 3. H^+		33

R	*x*	
H	2	(41)
	3	(80)

R	
H	(70)
Me	(58)

R	*x*	
TMS	2	(68)
Me_2N	2	(20)
PrHN	3	(25)
HO	3	(62)
MeO	3	(60)
PhO	2	(75)

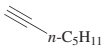
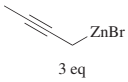
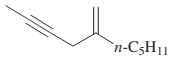
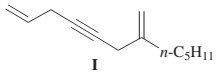
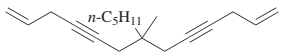
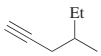
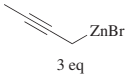
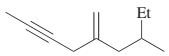
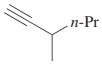
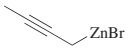
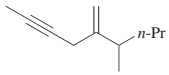
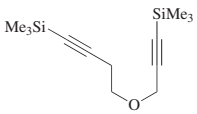
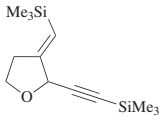
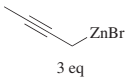
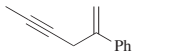
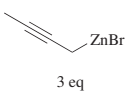
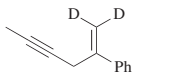
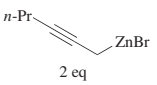
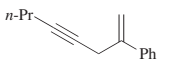
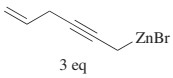
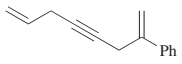
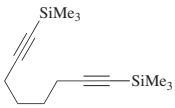
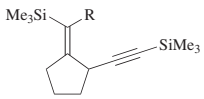
R^1	R^2	R^3	Time (h)	
H	*t*-Bu	*t*-Bu	23	(57)
BrMg	BrMg	H	4	(46)

R	Temp (°)	
H	30	(35)
Me	35	(60)

R	Temp (°)	
H	30	(39)
Me	35	(62)

R	
TMS	(75)
Ph	(65)

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
C. UNCATALYZED ADDITION OF PROPARGYL/ALLENYLZINC DERIVATIVES (*Continued*)

Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
	 3 eq	1. THF, 35°, 24 h 2. H^+	 (70)	94
	 3 eq	1. THF, 35°, 24 h 2. H^+	 **I** +  **II** **I + II** (48), **I/II** = 75:25	94
	 3 eq	1. THF, 35°, 24 h 2. H^+	 (67)	94
	 2 eq	1. THF, 35°, 24 h 2. H^+	 (43)	94
	Generated in situ from alkyne	1. *s*-BuLi (1.1 eq), Et_2O, –90°, 5 min 2. $ZnBr_2$ (1.5 eq), –80°, 15 min 3. –80° to rt, 1 h 4. H^+	 (57)	64
C_8				
	 3 eq	1. THF, 35°, 24 h 2. H^+	 (68)	94
	 3 eq	1. THF, 35°, 24 h 2. D^+	 (65)	94
	 2 eq	1. THF, 35°, 23 h 2. H^+	 (67)	93
	 3 eq	1. THF, 35°, 24 h 2. H^+	 (52)	94
	Generated in situ from alkyne	1. *s*-BuLi (1.1 eq), THF, –45°, 30 min 2. $ZnBr_2$ (1.5 eq), –45 to –30°, 10 min 3. –30 to 20°, 10 min 4. Steps 4–6		63

Steps 4–6	R	
H^+	H	(85)
I_2 (1.5 eq), 0°, 30 min; H^+	I	(78)
CuCN•2LiCl (1 eq), –20 to 0°, 30 min; allyl-C1 (1.5 eq), –20 to 0°, 30 min; H^+	allyl	(67)

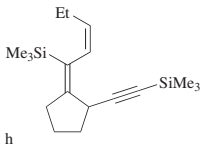
Generated in situ from alkyne	1. *s*-BuLi (1.1 eq), THF, –45°, 30 min 2. $ZnBr_2$ (1.5 eq), –45 to –30°, 10 min 3. *cis*-1-iodobutene (1.3 eq), –30 to 20°, 10 min 4. $Pd(PPh_3)_4$ (5 mol %), 30°, 1 h 5. H^+	 (65)	63

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
C. UNCATALYZED ADDITION OF PROPARGYL/ALLENYLZINC DERIVATIVES (*Continued*)

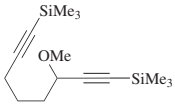
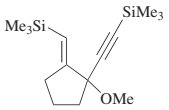
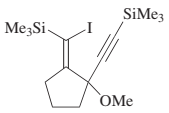
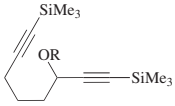
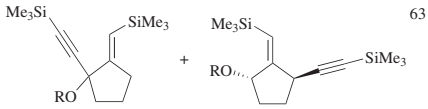
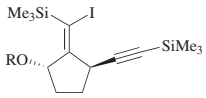
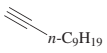
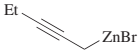
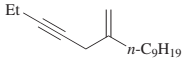
	Alkyne	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			1. *s*-BuLi (1.1 eq), THF, –80°, 1 h 2. $ZnBr_2$ (1.5 eq), –70°, 20 min 3. –70 to 20°, 2 h 4. H^+	 (89)	63
		Generated in situ from alkyne	1. *s*-BuLi (1.1 eq), THF, –80°, 1 h 2. $ZnBr_2$ (1.5 eq), –70°, 20 min 3. –70 to 20°, 12 h 4. I_2 (1.5 eq), 0°, 1 h 5. H^+	 (85)	63
	 R = ThexMe$_2$Si	Generated in situ from alkyne	1. *s*-BuLi (1.1 eq), THF, –45°, 1 h 2. $ZnBr_2$ (1.5 eq), –40°, 20 min 3. –40 to 20°, 1 h 4. H^+	 **I** **II** **I + II** (85), **I/II** = 14:86	63
		Generated in situ from alkyne	1. *s*-BuLi (1.1 eq), THF, –45°, 1 h 2. $ZnBr_2$ (1.5 eq), –40°, 10 min 3. –40 to 20°, 1 h 4. I_2 (1.5 eq), 0°, 30 min 5. H^+	 (63)	63
C_{11}			1. THF, 35°, 23 h 2. H^+	 (45)	93

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

D. UNCATALYZED ADDITION OF ZINC ENOLATE DERIVATIVES

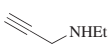
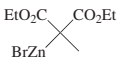
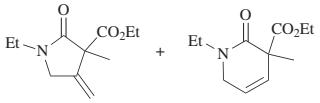
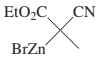
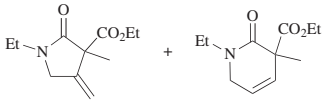
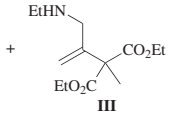
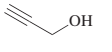
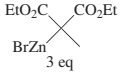
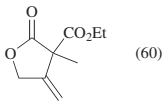
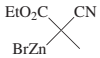
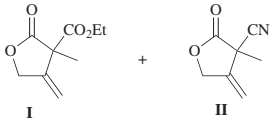
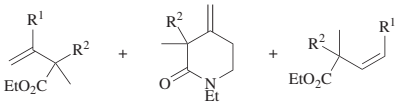
Alkyne	Zinc Enolate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 3 eq	1. $CH_2(OMe)_2$, 42°, time 2. H_2O Time (h) **I + II** **I/II** 4 (30) 63:35 23 (60) 70:30	 **I** + **II**	17
	 3 eq	1. $CH_2(OMe)_2$, 42°, 23 h 2. H_2O	 **I** + **II**  **III** **I + II + III** (21) **I/II/III** = 35:15:50	67
	 3 eq	1. $CH_2(OMe)_2$, 42°, 4 h 2. H_2O	 (60)	17
	 3 eq	1. $CH_2(OMe)_2$, 42°, 23 h 2. H_2O	 **I** + **II** **I + II** (35), **I/II** = 65:35	67

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
D. UNCATALYZED ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

Alkyne	Zinc Enolate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{3-6} 	 *x* eq	1. $CH_2(OMe)_2$, 42°, time 2. H_2O	 **I** **II** **III**	

R^1	R^2	*x*	Time (h)	**I + II + III**	**I/II/III**	Refs.
Et_2NCH_2	CN	3	23	(47)	100:0:0	67
Et_2NCH_2	EtO_2C	3	4	(20)	49:0:51	17
Et_2NCH_2	EtO_2C	3	23	(50)	48:0:52	17
n-$BuOCH_2$	EtO_2C	3	4	(42)	70:0:30	17
n-$BuOCH_2$	EtO_2C	3	23	(59)	67:0:33	17
n-$BuOCH_2$	CN	3	23	(41)	100:0:0	67
$EtHN(CH_2)_2$	EtO_2C	3	4	(30)	85:15:0	176
$EtHN(CH_2)_2$	EtO_2C	3	23	(45)	80:20:0	176
$EtO(CH_2)_2$	EtO_2C	2	4	(25)	100:0:0	67
$EtO(CH_2)_2$	EtO_2C	2	23	(56)	100:0:0	67
n-Bu	CN	2	4	(12)	100:0:0	67
n-Bu	CN	2	23	(18)	100:0:0	67

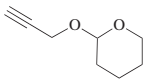
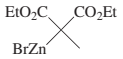
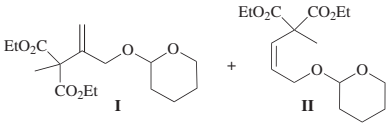
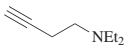
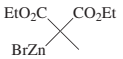
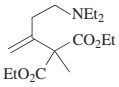
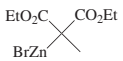
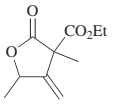
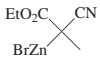
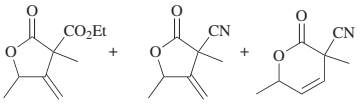
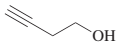
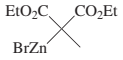
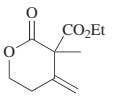
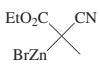
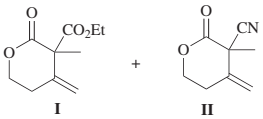
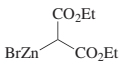
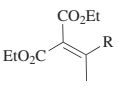
C_3 	 3 eq	1. $CH_2(OMe)_2$, 42°, 23 h 2. H_2O	 **I** **II** **I + II** (43), **I/II** = 72:28	17
C_4 	 2 eq	1. $CH_2(OMe)_2$, 42°, time 2. H_2O	 Time (h): 4 (41); 23 (40)	176
	 3 eq	1. $CH_2(OMe)_2$, 42°, time 2. H_2O	 Time (h): 4 (22); 23 (40)	17
	 3 eq	1. $CH_2(OMe)_2$, 42°, 23 h 2. H_2O	 **I** **II** **III** **I + II + III** (39), **I/II/III** = 9:23:68 *cis*/*trans* = 55:45	67
	 3 eq	1. $CH_2(OMe)_2$, 42°, time 2. H_2O	 Time (h): 4 (38); 23 (40)	176
	 3 eq	1. $CH_2(OMe)_2$, 42°, 23 h 2. H_2O	 **I** **II** **I + II** (14), **I/II** = 55:45	67
C_{5-14} 		1. Xylene 2. H^+	 R: *n*-Pr (51); *n*-C_6H_{13} (49); Ph (52); *p*-Tol (30); PMP (14); *n*-$C_{12}H_{25}$ (56)	66

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
D. UNCATALYZED ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

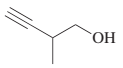
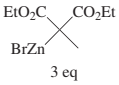
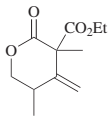
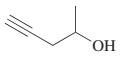
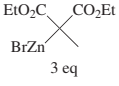
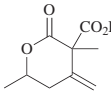
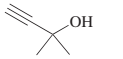
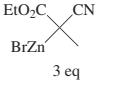
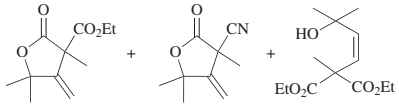
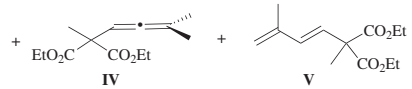
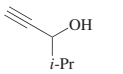
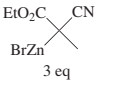
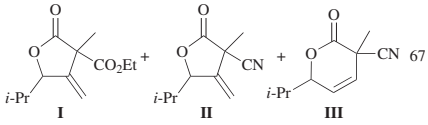
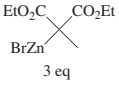
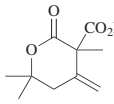
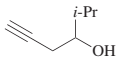
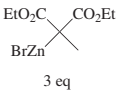
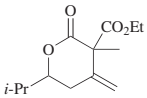
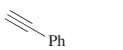
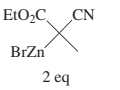
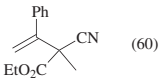
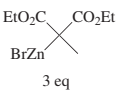
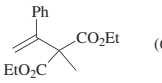
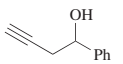
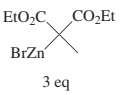
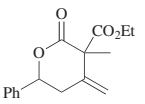
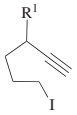
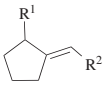
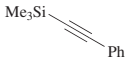
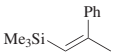
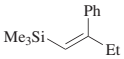
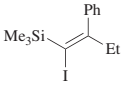
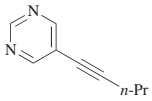
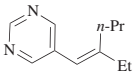
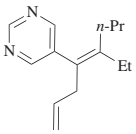
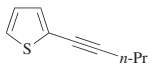
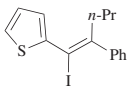
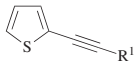
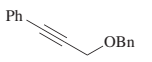
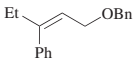
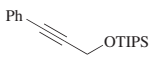
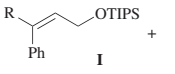
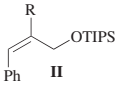
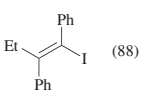
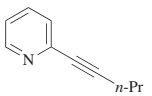
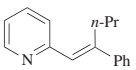
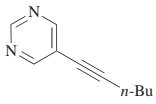
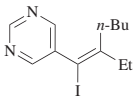
Alkyne	Zinc Enolate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
	 3 eq	1. $CH_2(OMe)_2$, 42°, time 2. H_2O	 Time (h): 4 (60); 23 (50)	176
	 3 eq	1. $CH_2(OMe)_2$, 42°, time 2. H_2O	 Time (h): 4 (53); 23 (52)	176
	 3 eq	1. $CH_2(OMe)_2$, 42°, 23 h 2. H_2O	 **I** + **II** + **III**	67
			 **IV** + **V** **I–V** (25), **I/II/III/IV/V** = 8:31:27:17:17	
C_6				
	 3 eq	1. $CH_2(OMe)_2$, 42°, 23 h 2. H_2O	 **I** + **II** + **III** (35), **I/II/III** = 7:25:68 *cis/trans* = 55:45	67
	 3 eq	1. $CH_2(OMe)_2$, 42°, time 2. H_2O	 TIme (h): 4 (70); 23 (79)	176
C_7				
	 3 eq	1. $CH_2(OMe)_2$, 42°, time 2. H_2O	 TIme (h): 4 (62); 23 (60)	176
C_8				
	 2 eq	1. $CH_2(OMe)_2$, 42°, 23 h 2. H_2O	 (60)	67
	 3 eq	1. Xylene 2. H^+	 (63)	66
C_{10}				
	 3 eq	1. $CH_2(OMe)_2$, 42°, 4 h 2. H_2O	 Time (h): 4 (70); 23 (68)	176

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

E. NICKEL-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES

Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{6–12}$ 	$R^2{}_2Zn$	1. THF, NMP, Ni(acac)$_2$ (cat.), –40°, 20 h 2. H_2O		73, 74
C_8 	Me_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), 0°, 10 h 2. H_2O	 (64) (*E*)/(*Z*) > 98:23	74
	Et_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 20 h 2. H_2O	 (82) (*E*)/(*Z*) = 99:1	74
	Et_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 20 h 2. I_2	 (61) (*E*)/(*Z*) = 97:3	74
C_9 	R_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 20 h 2. H_2O		74
	Et_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 48 h 2. H_2O	 (77) (*Z*)/(*E*) > 99:1	74
	Et_2Zn	1. THF, NMP, Ni(acac)$_2$ cat, –35°, 48 h 2. CuCN•2LiCl, –78 to 0° 3. Allyl-Br, –78° to rt, 5 min 4. H^+	 (35) (*Z*)/(*E*) > 99:1	74
	Ph_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 24 h 2. I_2	 (58) (*Z*)/(*E*) > 99:1	74
$C_{9–10}$ 	$(R^2)_2Zn$	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, time 2. H_2O		74
C_9 	Et_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 1 h 2. H_2O	 (56)	74
	R_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 1 h 2. H_2O	 **I** +  **II**	74
C_{10} 	Ph_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 3 h 2. I_2	 (88) (*Z*)/(*E*) > 99:1	74
	Ph_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 20 h 2. H_2O	 (67) (*E*)/(*Z*) > 99:1	74
	Et_2Zn	1. THF, NMP, Ni(acac)$_2$ (cat.), –35°, 48 h 2. I_2	 (64) (*E*)/(*Z*) > 99:1	74

R	(*E*)/(*Z*)	
Et	(73)	>99:1
n-C_5H_{11}	(67)	>99:1

R^1	R^2		(*E*)/(*Z*)	
H	n-C_5H_{11}	(65)	—	73
H	$Cl(CH_2)_4$	(68)	—	73, 74
Ph	n-C_5H_{11}	(62)	>99:1	74
Ph	Et	(59)	99:1	74

R^1	R^2	Time (h)		(*E*)/(*Z*)
n-Pr	Et	7.5	(63)	>1:99
n-Pr	Ph	24	(64)	>99:1
n-Bu	Ph	18	(67)	>99:1

R	**I + II**	**I/II**
Et	(73)	95:5
i-Pr	(68)	90:10
Ph	(64)	90:10

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
E. NICKEL-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES (*Continued*)

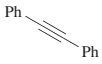
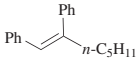
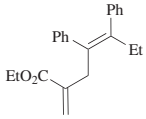
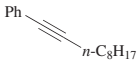
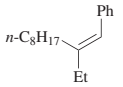
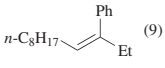
Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}				
	Et_2Zn	1. THF, NMP, $Ni(acac)_2$ (cat.), –35°, 3 h 2. H_2O	 (79) $(Z)/(E) > 98:2$	74
	Et_2Zn	1. THF, NMP, $Ni(acac)_2$ (cat.), –35°, 3 h 2. I_2	 (71) $(Z)/(E) > 99:1$	74
	$(n\text{-}C_5H_{11})_2Zn$	1. THF, NMP, $Ni(acac)_2$ (cat.), –35°, 18 h 2. H_2O	 (76) $(Z)/(E) > 99:1$	74
	Et_2Zn	1. THF, NMP, $Ni(acac)_2$ (cat.), –35°, 1 h 2. CuCN•2LiCl 3. RCOCl, –10° 4. H^+	 R (*E*)/(*Z*) Ph (55) >99:1 Me (58) >99:1	74
	Et_2Zn	1. THF, NMP, $Ni(acac)_2$ (cat.), –35°, 1 h 2. CuCN•2LiCl 3. Ethyl2-(bromomethyl)acrylate 4. H^+	 (71) $(Z)/(E) > 98:2$	74
C_{16}				
	Et_2Zn	1. THF, NMP, $Ni(acac)_2$ (cat.), –35°, 20 h 2. H_2O	 (69) +  (9) $(Z)/(E) > 98:2$	74

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

F. COPPER-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES

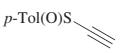
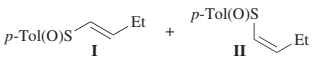
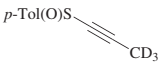
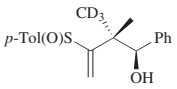
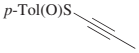
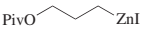
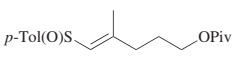
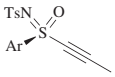
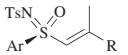
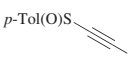
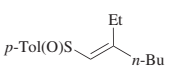
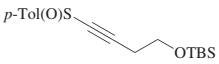
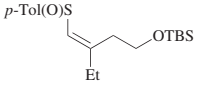
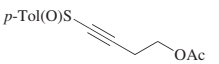
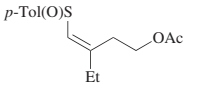
	Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2		Et_2Zn	1. CuI (2 mol %), THF, –78° to rt 2. H^+	 **I** + **II** (45), **I/II** = 53:47	177
C_3		Me_2Zn	1. CuI (10 mol %), THF, –78° to rt 2. PhCHO, 15 min, –25° 3. Et_2Zn, CH_2I_2, –25° 4. H^+	 (82) dr 25:1	178, 179
			1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (94)	180
		$RZnX^1$ 1.6 eq	1. CuX^2 (10 mol %), THF, 0°, 3 h 2. HCl	 $RZnX^1$ / CuX^2: Et_2Zn / CuI (90); *n*-BuZnBr / CuI (80); *n*-Bu_2Zn / CuCN•2LiCl (92)	181
C_4		*n*-BuZnBr or *n*-BuZnI 2 eq	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (74)	177
		Et_2Zn	1. CuI (2 mol %), THF, –78° to rt 2. H^+	 (78)	177
		Et_2Zn	1. CuI (2 mol %), THF, –78° to rt 2. H^+	 (84)	177

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

F. COPPER-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES (*Continued*)

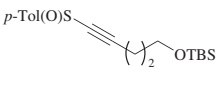
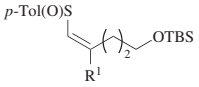
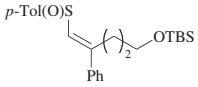
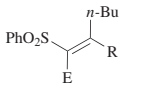
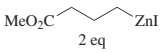
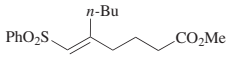
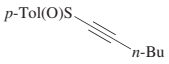
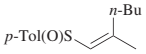
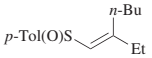
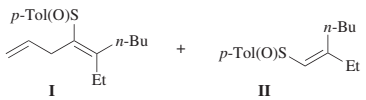
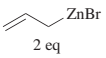
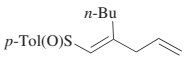
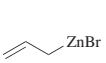
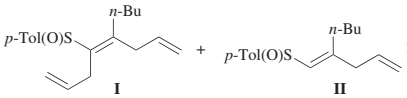
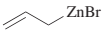
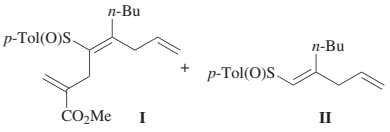
Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5				
	R^1R^2Zn	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 R^1 R^2 Me Me (73) *n*-Bu I (86)	180
	PhZnBr	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (87)	180
C_6				
	R_2Zn 1.6 eq	1. CuI (10 mol %), THF, 0°, 3 h 2. EX	 R E X Et H Cl (72) *i*-Pr H Cl (92) *n*-Bu H Cl (70) Et I I (65) Et allyl Br (60)	181
		1. CuI (10 mol %), THF, 0°, 3 h 2. HCl	 (55)	181
	Me_2Zn	1. CuI (2 mol %), THF, –78 to 0° 2. H^+	 (67)	177
	Et_2Zn *x* eq	1. CuX (*y* mol %), THF (*z* M), –78° to rt 2. H^+	 CuX *x* *y* *z* CuI 1 2 0.1 (15) CuI 2 2 0.1 (72) CuI 4 2 0.1 (57) CuI 2 0.5 0.1 (35) CuI 2 10 0.1 (46) CuI 2 2 1 (97) CuCN 2 2 1 (86) $Cu(OTf)_2$ 2 2 1 (69)	180 180 180 180 180 177 177 177
	Et_2Zn	1. CuX (2 mol %), THF, –78° to rt 2. AllylBr	 **I** **II** CuX **I + II** **I/II** CuCN•2LiCl (81) 79:21 CuI (76) 87:13 CuCN (69) 77:23 $Cu(OTf)_2$ (75) 71:29 CuI (75) 91:9	180
		1. CuX (2 mol %), THF, –78° to rt 2. H^+	 CuX CuI (72) CuCN (73) $Cu(OTf)_2$ (81)	177
		1. CuX (2 mol %), THF, –78° to rt 2. allylBr (5 eq)	 **I** **II** CuX **I + II** **I/II** CuCN•2LiCl (76) 97:3 $Cu(OTf)_2$ (74) 89:11	180
		1. CuI (2 mol %), THF, –78° to rt 2.  (5 eq)	 **I** **II** **I + II** (84), **I/II** = 70:30	180

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
F. COPPER-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES (*Continued*)

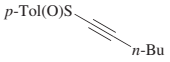
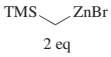
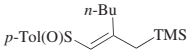
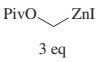
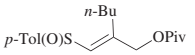
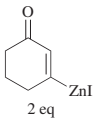
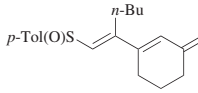
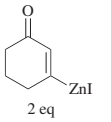
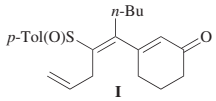
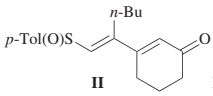
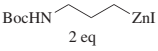
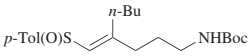
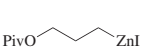
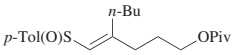
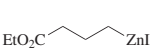
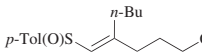
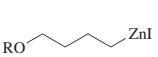
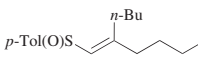
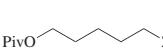
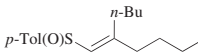
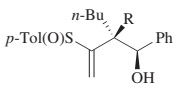
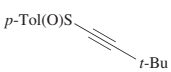
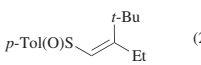
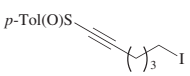
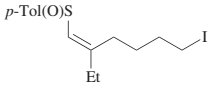
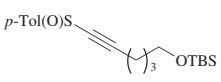
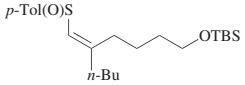
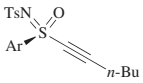
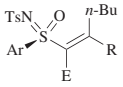
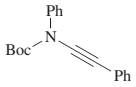
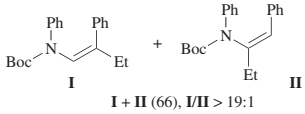
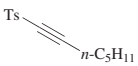
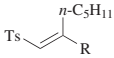
Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 2 eq	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (94)	177
	 3 eq	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (75)	177
	 2 eq	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (87)	177
	 2 eq	1. CuI (2 mol %), THF, –78° to rt 2. allyl-Br (5 eq)	 **I** +	180
			 **II** **I** + **II** (86), **I/II** = 84:16	
	 2 eq	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (84)	177
		1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (90)	180
	 3 eq	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (70)	177
	 2 eq	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 R: Ac (28); Bz (23); Piv (88)	180
		1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (100)	180
	R_2Zn	1. CuI (10 mol %), THF, –78° to rt 2. PhCHO, 15 min, –25° 3. Et_2Zn, CH_2I_2, –25° 4. H^+	 R: Me (88) dr 20:1; Et (75) dr 20:1	178, 179
	Et_2Zn	1. CuI (2 mol %), THF, –78° to rt 2. H^+	 (21)	177
	Et_2Zn	1. CuX (2 mol %), THF, –78° to rt 2. H^+	 CuX: CuI (71); CuI, ultrasound (79); CuCN (86)	177 180 180
	*n*-BuZnI	1. $Cu(OTf)_2$ (2 mol %), THF, –78° to rt 2. H^+	 (87)	180

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

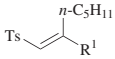
F. COPPER-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES (*Continued*)

	Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6		RZnX *x* eq	1. CuI (10 mol %), solvent, temp, time 2. E-X		181

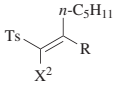
RZnX	*x*	Solvent	Temp (°)	Time (h)	E-X	E	
Me_2Zn	1.6	THF	0	3	HCl	H	(83)
EtZnI	1.6	THF	0	3	HCl	H	(90)
EtZnBr	1.6	THF	0	3	HCl	H	(75)
i-PrZnBr	1.6	THF	0	3	HCl	H	(80)
Et_2Zn	1.6	THF	0	2	HCl	H	(82)
Et_2Zn	1.6	Et_2O	rt	6	HCl	H	(80)
Et_2Zn	1.6	THF	0	3	I_2	I	(78)
Et_2Zn	1.6	THF	0	3	allyl-Br	allyl	(65)
$MeO_2C(CH_2)_3ZnI$	2	THF	0	3	HCl	H	(55)
PhZnBr	1.6	THF	0	3	HCl	H	(85)
n-$C_8H_{17}ZnI$	2	THF	0	3	HCl	H	(55)
n-C_6H_{13}—≡—ZnBr	1.6	THF	0	3	HCl	H	(18)
n-$C_6H_{13}C(Et)$=CHZnBr	1.8	THF	0	3	HCl	H	(72)

		Et_2Zn *x* eq	1. Cu(acac)$_2$ (10 mol %), Et_2O, 0° to rt, 16 h 2. H^+	 **I** + **II** (66), **I/II** > 19:1	182
C_7		RZnX 1.2 eq	1. CuI (10 mol %), THF, 0°; then reflux, time 2. H^+		172

R	X	Time (h)	
Ph	Cl	4	(89)
Bn	Br	2	(91)

		R^1ZnX 1.2 eq	1. CuI (10 mol %), THF, 0°; then reflux, time 2. R^2Br (1 eq), 50°, $NiPPh_3Cl_2$ (10 mol %)		172

R^1	X	Time (h)	R^2	
n-Bu	Cl	4	allyl	(69)
n-Bu	Cl	4	4-NCC_6H_4	(62)
Bn	Br	2	4-$OHCC_6H_4$	(57)
Bn	Br	2	Bn	(66)

		$RZnX^1$ 1.2 eq	1. CuI (12 mol %), THF, 0° to reflux 2. E^+ (1.5 eq), rt		173

R	X^1	E^+	X^2	
Ph	Cl	I_2	I	(83)
Ph	Cl	NBS	Br	(85)
Bn	Br	I_2	I	(89)
Bn	Br	NBS	Br	(81)

C_8

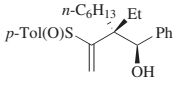
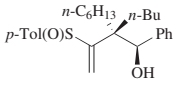
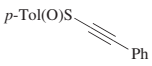
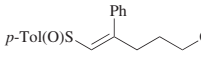
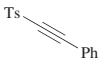
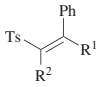
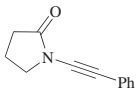
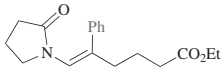
		Et_2Zn	1. CuI (10 mol %), THF, –78° to rt 2. PhCHO, 15 min, –25° 3. Et_2Zn, CH_2I_2, –25° 4. H^+	 (65) dr >99:1	179
		n-BuZnBr	1. CuI (10 mol %), THF, –78° to rt 2. PhCHO, 15 min, –25° 3. Et_2Zn, CH_2I_2, –25° 4. H^+	 (57) dr >99:1	179
		PivO—ZnI	1. Cu(OTf)$_2$ (2 mol %), THF, –78° to rt 2. H^+	 (55)	180

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
F. COPPER-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES (*Continued*)

Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	RZnX 1.2 eq	1. CuI (10 mol %), THF, 0°; then reflux, time 2. H^+		172
	R^1ZnX 1.2 eq	1. CuI (10 mol %), THF, 0°; then reflux, time 2. R^2Br (1 eq), 50°, $NiPPh_3Cl_2$ (10 mol %)		172
	RZnX 1.2 eq	1. CuI (12 mol %), THF, 0° to reflux 2. E^+ (1.5 eq), rt		173
C_{12}				
	 2 eq	1. $Cu(acac)_2$ (10 mol %), THF, 0° to rt, 6 h 2. H^+		182

R	X	Time (h)		
Ph	Cl	4	(87)	
4-FC_6H_4	Cl	2	(85)	
Bn	Br	4	(89)	
Bu	Cl	4	(91)	

R^1	X	Time (h)	R^2	
n-Bu	Cl	4	allyl	(59)
n-Bu	Cl	4	4-NCC_6H_4	(46)
4-FC_6H_4	Cl	2	allyl	(72)
Bn	Br	4	4-$OHCC_6H_4$	(48)
Bn	Br	4	allyl	(76)
Bn	Br	4	Bn	(63)

R	E^+	X	
n-Bu	I_2	I	(87)
n-Bu	NCS	Cl	(78)
Ph	I_2	I	(84)
Ph	NBS	Br	(85)
Ph	NCS	Cl	(80)
Bn	I_2	I	(85)
Bn	NBS	Br	(84)

(74) dr >19:1

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
G. PALLADIUM-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES

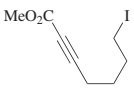
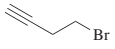
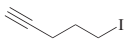
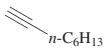
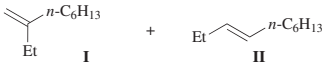
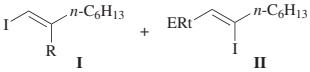
	Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7		Et_2Zn 2 eq	1. $PdCl_2(MeCN)_2$ (1.5 mol %), THF, rt, 4 h 2. H^+	 (73)	30

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

H. ZIRCONIUM-CATALYZED ADDITION OF ARYLZINC DERIVATIVES

Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	EtZnCl **I**	1. BuLi, –78° 2. **I** 3. Et_2Zn, I_2ZrCp_2 4. I_2	 (70)	58
C_5 	EtZnCl **I**	1. BuLi, –78° 2. **I**, CH_2Cl_2 3. Et_2Zn, I_2ZrCp_2 4. Evaporation 5. THF 6. I_2	 (58)	84
C_8 	Et_2Zn	1. I_2ZrCp_2, 20–22°, 3 h 2. H_2O	 **I** + **II** **I + II** (100), **I/II** = 76:24	71
	R_2Zn	1. X_2ZrCp_2, temp, time 2. I_2	 **I** + **II**	71

X	R	Temp (°)	Time (h)	**I + II**	**I/II**
I	Me	rt	3	(100)	95:5
I	Et	20–22	3	(100)	75:25
Cl	Et	50	48	(35)	96:4

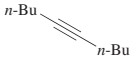
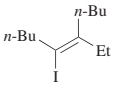
C_{10} 	Et_2Zn	1. I_2ZrCp_2, rt, 6 h 2. I_2	 (88)	71

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
I. TITANIUM-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES

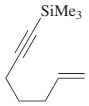
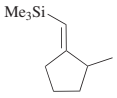
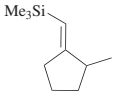
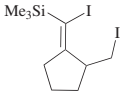
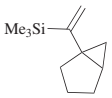
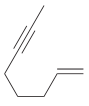
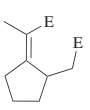
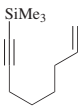
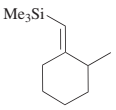
Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 3 h 2. H_3O^+	 (85)	183
	1. Et_2Zn (2.5 eq), $Ti(Oi\text{-}Pr)_4$ (10 mol %), *i*-PrMgCl (20 mol %), Et_2O, hexanes, rt, 42 h 2. H_3O^+	 (84)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 3 h 2. I_2	 (53)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 3 h 2. $MeOCH_2Br$	 (99)	183
C_8			
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 3 h 2. E^+	 E: H (60), I (50)	183
	1. Et_2Zn (2.5 eq), $YTi(Oi\text{-}Pr)_3$ (10 mol %), RMgX (20 mol %), Et_2O, hexanes, rt, time 2. H_3O^+	 Y / RMgX / Time (h): Cl / *i*-PrMgCl / 18 (80); Cl / EtMgBr / 18 (75); *i*-PrO / *i*-PrMgCl / 48 (89)	183

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
I. TITANIUM-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

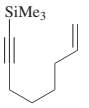
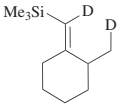
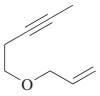
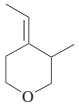
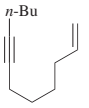
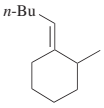
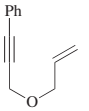
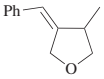
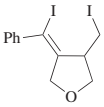
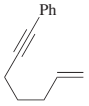
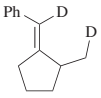
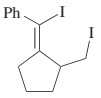
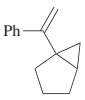
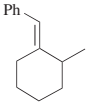
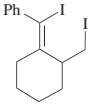
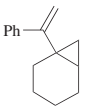
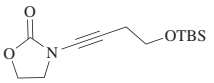
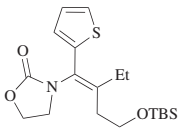
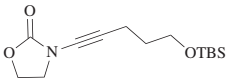
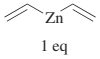
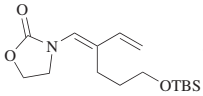
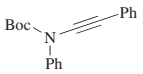
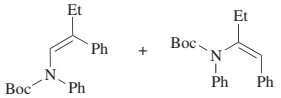
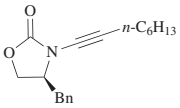
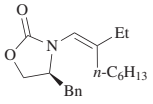
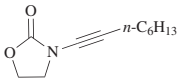
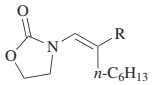
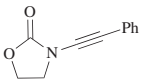
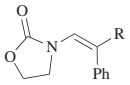
Alkyne	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	1. Et_2Zn (2.5 eq), $Ti(Oi\text{-}Pr)_4$ (10 mol %), *i*-PrMgCl (20 mol %), Et_2O, hexanes, rt, 48 h 2. D_3O^+	 (79)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 18 h 2. H_3O^+	 (65)	183
C_{12} 	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 24 h 2. H_3O^+	 (86)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (20 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 48 h 2. H_3O^+	 (95)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 48 h 2. I_2	 (95)	183
C_{13} 	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 3 h 2. H_3O^+	 (90)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 3 h 2. D_3O^+	 (90)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 3 h 2. I_2	 (59)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 3 h 2. $MeOCH_2Br$	 (61)	183
C_{14} 	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 24 h 2. H_3O^+	 (83)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 24 h 2. I_2	 (56)	183
	1. Et_2Zn (2.5 eq), $ClTi(Oi\text{-}Pr)_3$ (10 mol %), EtMgBr (20 mol %), Et_2O, hexanes, rt, 24 h 2. $MeOCH_2Br$	 (62)	183

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)

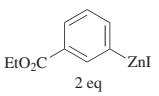
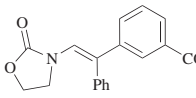
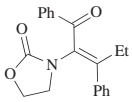
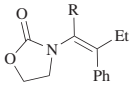
J. RHODIUM-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES

	Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4		Et_2Zn 0.55 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 15 min 2. 2-Iodothiophene, $Pd_2(dba)_3$ (2.5 mol %), $(2\text{-Fur})_3P$ (10 mol %), THF, 65°	 (45)	182
C_5		 1 eq	1. Rh(cod)(acac) (5 mol %), THF, –78° to rt, 14 h 2. H^+	 (59) dr >95:5	182
C_8		Et_2Zn 2 eq	1. Rh(cod)(acac) (5 mol %), THF, –78°, 5 min 2. H^+	 **I** + **II** (80), **I/II** = 1:2.3	182
		Et_2Zn 2 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 15 min 2. H^+	 (70) dr >95:5	182
		R_2Zn 2 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 15 min 2. H^+		182

R		dr[a]
Me	(63)	9:1
Et	(78)	>19:1
n-Bu	(81)	10:1

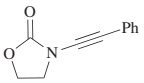
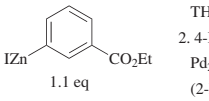
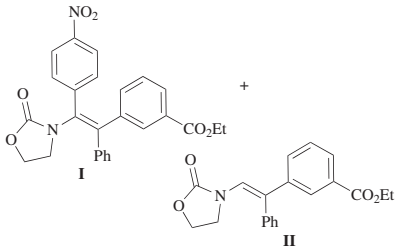
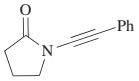
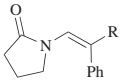
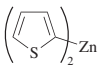
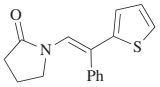
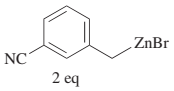
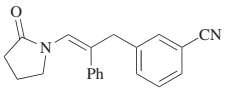
	R_2Zn *x* eq	1. Rh(cod)(acac) (*y* mol %), THF, temp to rt, time 2. H^+			182

R	*x*	*y*	Temp (°)	Time (h)		dr[a]
Me	2	5	0	0.25	(54)	7:1
Et	2	5	0	0.25	(85)	>19:1
Et	0.55	2	0	4	(69)	>19:1
n-Bu	2	5	0	0.25	(91)	>19:1
CH_2=CH	1	5	–78	14	(66)	7:1

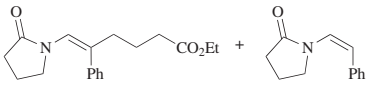
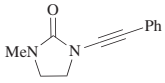
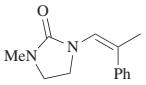
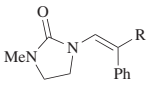
 2 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 5 h 2. H^+		(58)	>19:1	182
Et_2Zn 0.55 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 15 min 2. PhCOCl (1.6 eq), 65°, 36 h		(56)		182
Et_2Zn 0.55 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 15 min 2. RI (1.6 eq), $Pd_2(dba)_3$ (2.5 mol %), $(2\text{-Fur})_3P$ (10 mol %), THF, 65°, 22 h				182

R	
$4\text{-}O_2NC_6H_4$	(54)
MeO_2CCH=CH	(61)

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
J. RHODIUM-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES (*Continued*)

Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 1.1 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt 2. 4-$IC_6H_4NO_2$, $Pd_2(dba)_3$ (2.5 mol %), $(2\text{-Fur})_3P$ (10 mol %), THF, 65°, 48 h	 **I** + **II** (38), **I/II** = 47:53	182
	R_2Zn *x* eq	1. Rh(cod)(acac) (5 mol %), THF, temp to rt, time 2. H^+		182
	 1 eq	1. Rh(cod)(acac) (5 mol %), THF, –78° to rt, 14 h 2. H^+	 (79) dr[a] 5:1	182
	 2 eq	1. $[Rh(cod)Cl]_2$ (5 mol %), *rac*-BINAP (10 mol %), THF, 0–60°, 6 h 2. H^+	 (35) dr —	182

R	*x*	Temp (°)	Time (h)		dr[a]
n-Bu	2	0	0.25	(75)	>19:1
c-C_3H_5	1	–78	14	(77)	1.7:1

	2 eq	1. $[Rh(cod)Cl]_2$ (5 mol %), THF, 0° to rt, 6 h 2. H^+	 **I** + **II** (40), **I/II** = 62.5:37.5	182
	Me_2Zn 2 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 0.25 h 2. H^+	 (61) dr[a] >95:5	182
	R_2Zn	1. RMgX (2.0 eq), $ZnCl_2$ (1.0 eq) 2. Rh(cod)(acac) (*x* mol %), THF, 0° to rt, 0.25 h 3. H^+		182

R	X	*x*	Temp (°)	Temp (h)		dr[a]
Bn	Cl	5	–78	0.25	(71)	>95:5
Ph—≡—	Br	40	0	1.5	(60)	90:10

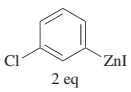
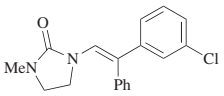
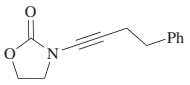
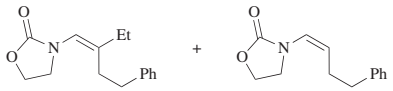
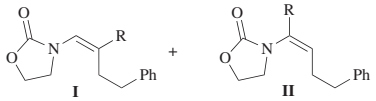
	 2 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 5 h 2. H^+	 (82) dr >95:5	182

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
J. RHODIUM-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES (*Continued*)

Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	Et_2Zn 2 eq	1. Rh salt (5 mol % of Rh), ligand (10 mol %), 0° to rt 2. H^+	 **I** + **II** 100% conv.	182

Rh salt	Ligand	**I/II**
$[Rh(cod)Cl]_2$	—	>95:5
$Rh(cod)(MeCN)_2BF_4$	—	>95:5
$RhCl(PPh_3)_3$	—	1:5
$[Rh(cod)Cl]_2$	Ph_3P	10:90
$[Rh(cod)Cl]_2$	Bu_3P	>95:5
$[Rh(cod)Cl]_2$	*rac*-BINAP	>95:5

	R_2Zn 2 eq	1. Precatalyst (5 mol %), THF, 0° to rt, time 2. H^+	 **I** + **II** + **III**	182

R	Precatalyst	Time (h)	Conv. (%)	**I**	**I/II/III**
Me	Rh(cod)(acac)	0.25	—	(61)	75:25:0
Et	$Ni(acac)_2$	—	100[b]	—	73:9:18[a]
Et	Rh(cod)(acac)	0.25	100[b]	(73)	93:7:0[a]
Et	CuI	20	100	(65)	>95:5:0[a]
Et	(*n*)	18	—	(4)	—
n-Bu	Rh(cod)(acac)	0.25	—	(85)	>95:5:0

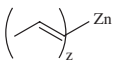
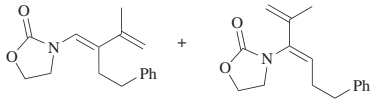
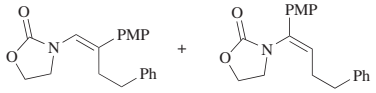
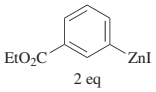
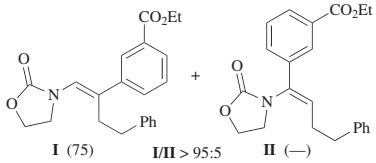
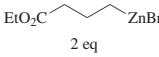
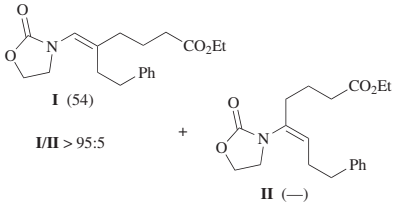
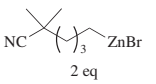
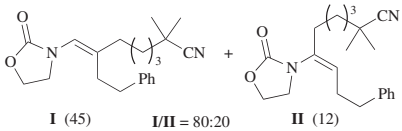
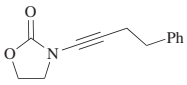
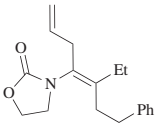
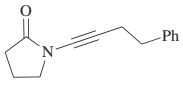
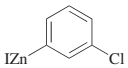
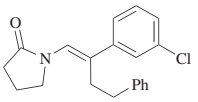
 2 eq		1. Rh(cod)(acac) (5 mol %), THF, 0° to rt 2. H^+	 **I** (47) **I/II** > 95:5 **II** (—)	182
PMP_2Zn 2 eq		1. Rh(cod)(acac) (5 mol %), THF, 0° to rt 2. H^+	 **I** (58) **I/II** > 95:5 **II** (—)	182
 2 eq		1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 1.5 h 2. H^+	 **I** (75) **I/II** > 95:5 **II** (—)	182
 2 eq		1. Rh(cod)(acac) (5 mol %), THF, 0° to rt 2. H^+	 **I** (54) **I/II** > 95:5 **II** (—)	182
 2 eq		1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 4 h 2. H^+	 **I** (45) **I/II** = 80:20 **II** (12)	182

TABLE 1. CARBOZINCATION OF ALKYNES (*Continued*)
J. RHODIUM-CATALYZED ADDITION OF ORGANOZINC DERIVATIVES (*Continued*)

Alkyne	Alkylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
	Et_2Zn 0.55 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 15 min 2. Allyl-Br (5 eq), BINAP (10 mol %), rt, 4.5 h	 (56)	182
	 2 eq	1. Rh(cod)(acac) (5 mol %), THF, 0° to rt, 5 h 2. H^+	 (77) dr >95:5	182

[a] The diastereomeric ratio was determined by ^{1}H-NMR analysis of the crude product.

[b] The reactions proceeded to complete conversion.

TABLE 2. CARBOZINCATION OF ALKENES
A. UNCATALYZED ADDITION OF ALKYL- AND ARYLZINC DERIVATIVES

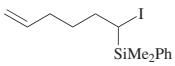
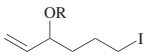
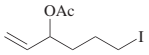
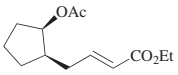
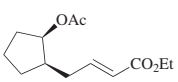
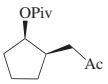
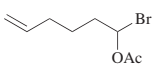
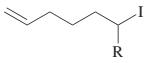
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6			
	1. Zn, DMF, 45° 2. I_2	 (80)	25
	1. Zn*, Et_2O, rt, overnight 2. H^+	 (66) *cis*/*trans* = 66:34	107
	1. Zn*, Et_2O, 20°, time 2. H^+		
		R — Time (h) — *cis*/*trans* Ac — 1.3 — (90) — 1.4:1 — 25 Ac — 12 — (92) — 1.4:1 — 25, 51 Et_2NCO — 1.3 — (80) — 1.5:1 — 25 Piv — 1.5 — (87) — 1.4:1 — 25	
	1. Zn*, Et_2O, 20°, time 2. I_2 (1.5 eq), 0°, 30 min		
		R — Time (h) — *cis*/*trans* Ac — 1.3 — (71) — — Ac — 12 — (90) — — Piv — 1.3 — (73) — 1.4:1	25 25, 51 107
	1. Et_2Zn (2 eq), Et_2O, 20°, 12 h 2. CuCN•2LiCl (1 eq), THF, 0°, 30 min 3. ≡—CO_2Et (2 eq), –40° to rt, overnight 4. H^+	 (72) *cis*/*trans* = 1.4:1, (*E*)/(*Z*) > 99:1	25, 51
	1. Zn*, Et_2O, rt 2. CuCN•2LiCl (1 eq), THF, 0° 3. ≡—CO_2Et (2 eq), –40° to rt, overnight 4. H^+	 (66) *cis*/*trans* = 1.4:1, (*E*)/(*Z*) > 99:1	51
	1. Zn*, Et_2O, 20°, 1.3 h 2. CuCN•2LiCl (1.1 eq), THF, 0° 3. AcCl (1.5 eq), –30°, 2 h 4. H^+	 (60) *cis*/*trans* = 1.2:1	25

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)

A. UNCATALYZED ADDITION OF ALKYL- AND ARYLZINC DERIVATIVES (*Continued*)

Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	1. Zn*, Et_2O 2. H^+	 (50) *cis*/*trans* = 86:14	51
C_{7-10} 	1. Zn*, Et_2O, temp, time 2. I_2 (*x* eq), 0°, 30 min		107

R	*x*	Temp (°)	Time		*cis*/*trans*	
Me	1.1	20	20 min	(73)	81:19	107
i-Pr	1.5	20	2 h	(78)	73:27	51
n-Bu	1.5	20	20 min	(68)	73:27	51
t-Bu	1.5	rt	3 h	(60)	62:38	51

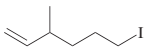
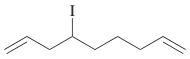
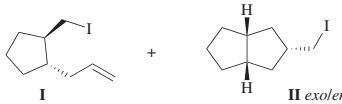
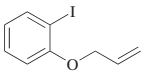
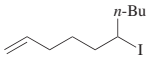
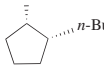
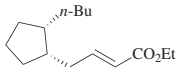
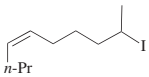
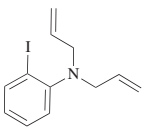
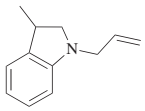
C_7 	1. Zn*, Et_2O 2. I_2 (1.1 eq), 0°, 30 min	 (80) *trans*/*cis* = 93:7	107
C_9 	1. Zn*, Et_2O, 20°, 20 min 2. I_2 (1.5 eq), 0°, 30 min	 **I** + **II** (72), **I**/**II** = 15:85	51
	1. Me_4ZnLi_2, THF, 0°, 2 h 2. rt, 48 h 3. H^+	 (42)	184
C_{10} 	1. Zn*, Et_2O, 20°, 20 min 2. H^+	 (60) *cis*/*trans* = 73:27	51
	1. Zn, Et_2O, 20°, 20 min 2. CuCN•2LiCl (1.5 eq), THF, 0° 3. ≡—CO_2Et (1.5 eq), –30°, 2 h 4. H^+	 (—) *cis*/*trans* = 73:27, (*E*)/(*Z*) > 99:1	107
	1. Zn*, Et_2O, rt, overnight 2. H^+	 (80) *cis*/*trans* = 68:32	51
C_{12} 	1. Me_4ZnLi_2, THF, 0°, 2 h 2. rt, 48 h 3. H^+	 (73)	184

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
B. UNCATALYZED ADDITION OF PROPARGYL/ALLENYLZINC DERIVATIVES

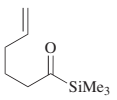
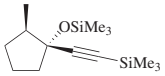
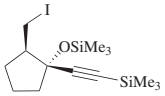
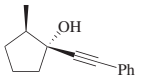
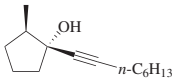
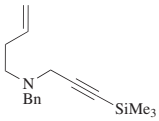
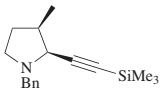
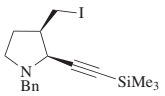
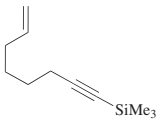
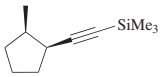
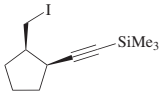
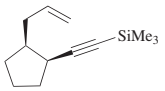
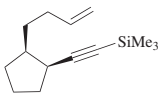
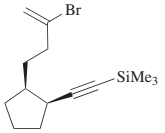
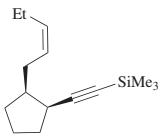
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	1. Me_3Si—≡—MgBr, THF, –80°; reflux, 45 min 2. $ZnBr_2$, –60° to rt 3. H^+		(89) single isomer	33
	1. Me_3Si—≡—MgBr, THF, –80°; reflux, 45 min 2. $ZnBr_2$, –60° to rt 3. I_2		(60) single isomer	33
	1. Ph—≡—MgBr, THF, –80°; reflux, 45 min 2. $ZnBr_2$, –60° to rt 3. H^+		(70) single isomer	33
	1. n-C_6H_{13}—≡—MgBr, THF, –80°; reflux, 45 min 2. $ZnBr_2$, –60° to rt 3. I_2		(50) single isomer	33
C_7 	1. t-BuLi (1.1 eq), Et_2O, –80 to –50° 2. $ZnBr_2$ (1.5 eq), Et_2O, –40° to rt 3. H^+		(60)	118
	1. t-BuLi (1.1 eq), Et_2O, –80 to –50° 2. $ZnBr_2$ (1.5 eq), Et_2O, –40° to rt 3. I_2 (1.5 eq), 0°, 30 min		(70)	118
C_8 	1. s-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –20°, 5–10 min 3. –20° to rt 4. H^+		(80) single isomer	113
	1. s-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –20°, 5–10 min 3. –20° to rt 4. I_2 (1.5 eq), –10°, 30 min		(75) single isomer	113
	1. s-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –20°, 5–10 min 3. –20° to rt 4. Iodoethene (1.5 eq), $Pd(PPh_3)_4$ (5 mol %), 27–35°, 30 min 5. H^+		(63) single isomer	113
	1. s-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –20°, 5–10 min 3. –20° to rt 4. CuCN (1.5 eq), –20°, 1 h 5. Allyl-Br (1.5 eq), –30 to 0°, 2 h 6. H^+		(72) single isomer	113
	1. s-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –20°, 5–10 min 3. –20° to rt 4. CuCN (1.5 eq), –20°, 1 h 5. (1.5 eq), –30 to 0°, 2 h 6. H^+		(72) single isomer	113
	1. s-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –20°, 5–10 min 3. –20° to rt 4. *cis*-1-Iodo-1-butene (1.5 eq), $Pd(PPh_3)_4$ (5 mol %), 27–35°, 30 min 5. H^+		(73) single isomer	113

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
B. UNCATALYZED ADDITION OF PROPARGYL/ALLENYLZINC DERIVATIVES (*Continued*)

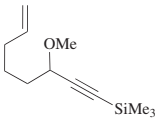
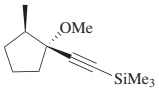
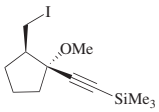
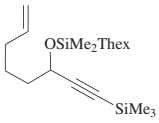
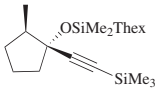
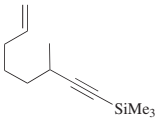
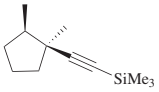
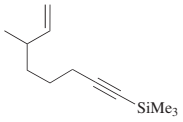
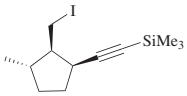
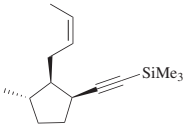
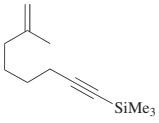
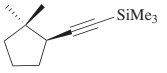
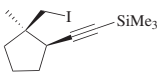
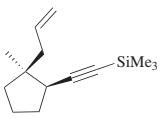
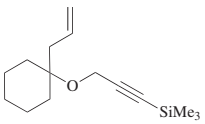
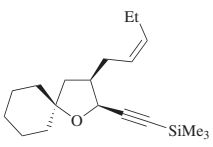
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	1. *n*-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –40° to rt 3. H^+	 (80) single isomer	185
	1. *n*-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –40° to rt 3. I_2 (1.5 eq), 0°, 30 min	 (73) single isomer	185
	1. *n*-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –50° 3. –50° to rt 4. H^+	 (80) single isomer	185
C_9			
	1. *s*-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –20°, 5–10 min 3. –20° to rt 4. H^+	 (65) single isomer	113
	1. *s*-BuLi (1.1 eq), THF, –40°, 5–10 min 2. $ZnBr_2$ (1.5 eq), –40°, 5 min 3. –40 to 20° 4. I_2 (1.5 eq), 0°, 30 min	 (88) single isomer	113
	1. *s*-BuLi (1.1 eq), THF, –40°, 5–10 min 2. $ZnBr_2$ (1.5 eq), –40°, 5 min 3. –40 to 20° 4. *cis*-1-Iodo-1-propene (1.5 eq), $Pd(PPh_3)_4$ (5 mol %), 35°, 1 h 5. H^+	 (67) single isomer	113
	1. *s*-BuLi (1.1 eq), THF, –50° 2. $ZnBr_2$ (1.5 eq) 3. H^+	 (57) single isomer	113
	1. *s*-BuLi (1.1 eq), THF, –50° 2. $ZnBr_2$ (1.5 eq) 3. I_2 (1.5 eq), 0°, 30 min	 (78) single isomer	113
	1. *s*-BuLi (1.1 eq), THF, –50° 2. $ZnBr_2$ (1.5 eq) 3. Iodoethene (1.5 eq), $Pd(PPh_3)_4$ (5 mol %), 35°, 1 h 4. H^+	 (61)	113
C_{12}			
	1. *s*-BuLi (1.1 eq), Et_2O, –70° 2. $ZnBr_2$ (1.5 eq), –50°, 5 min 3. –50° to rt 4. *cis*-1-Iodo-1-butene (1.5 eq), $Pd(PPh_3)_4$ (5 mol %), 35°, 1 h 5. H^+	 (50) single isomer	117, 64

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
B. UNCATALYZED ADDITION OF PROPARGYL/ALLENYLZINC DERIVATIVES (*Continued*)

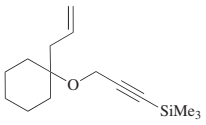
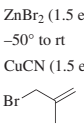
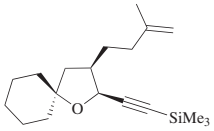
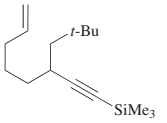
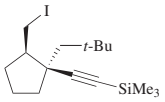
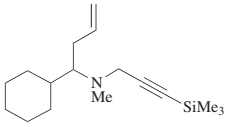
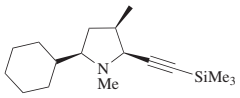
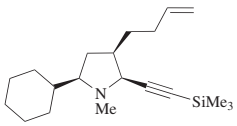
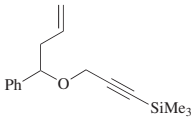
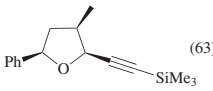
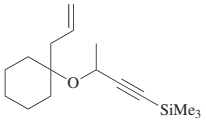
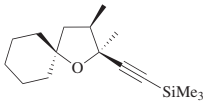
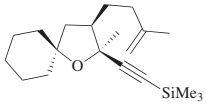
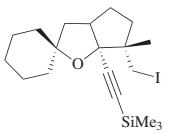
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12} 	1. *s*-BuLi (1.1 eq), Et_2O, –70° 2. $ZnBr_2$ (1.5 eq), –50°, 5 min 3. –50° to rt 4. CuCN (1.5 eq), THF, –20 to 0°, 1 h 5.  (1.5 eq), –20°, 2 h 6. H^+	 (74) single isomer	117, 64
C_{13} 	1. *s*-BuLi (1.1 eq), THF, –40° 2. $ZnBr_2$ (1.5 eq), –20°, 5–10 min 3. –20° to rt 4. I_2 (1.5 eq), 0°, 30 min	 (63) single isomer	113
	1. *s*-BuLi (1.1 eq), Et_2O, –80 to –50° 2. $ZnBr_2$ (1.5 eq), –50° 3. –50° to rt 4. H^+	 (90) *cis*/*trans* = 85:15	118
	1. *s*-BuLi (1.1 eq), Et_2O, –80 to –50° 2. $ZnBr_2$ (1.5 eq), –50° 3. –50° to rt 4. CuCN (1.5 eq), –20 to 0°, 1 h 5. Allyl-Br (1.5 eq), –20 to 0°, 2 h 6. H^+	 (70) *cis*/*trans* = 85:15	118
	1. *s*-BuLi (1.1 eq), Et_2O, –70° 2. $ZnBr_2$ (1.5 eq), –50°, 5 min 3. –50° to rt 4. H^+	 (63) *cis*/*trans* = 80:20	117, 64
	1. *s*-BuLi (1.1 eq), Et_2O, –70° 2. $ZnBr_2$ (1.5 eq), –50°, 5 min 3. –50° to rt 4. H^+	 (71) single isomer	117, 64
C_{17} 	1. *s*-BuLi (1.1 eq), THF, –20° 2. $ZnBr_2$ (1.5 eq), –50° 3. –50° to rt 4. I_2 (1.5 eq), 0°, 30 min	 (60) single isomer	117, 64

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES

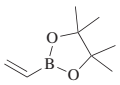
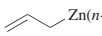
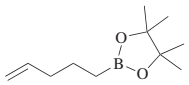
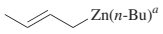
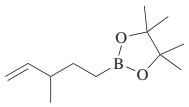
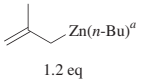
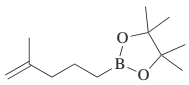
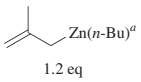
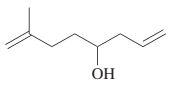
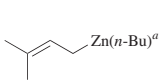
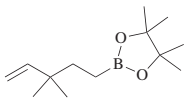
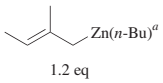
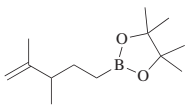
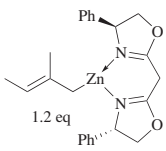
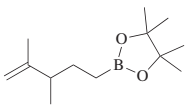
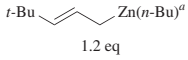
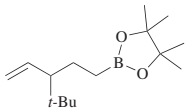
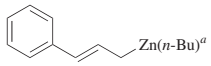
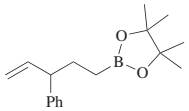
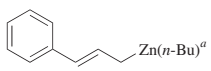
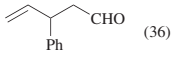
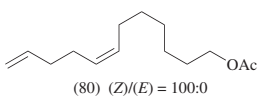
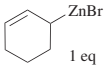
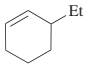
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
	 1.2 eq	1. THF, 0° 2. 0° to rt, 36–48 h 3. H^+	 (82)	186
	 1.2 eq	1. THF, 0° 2. 0° to rt, 36–48 h 3. H^+	 (96)	186
	 1.2 eq	1. THF, 0° 2. 0° to rt, 36–48 h 3. H^+	 (87)	186
	 1.2 eq	1. THF, 0° 2. 0° to rt, 36–48 h 3. $ZnBr_2$ (1.2 eq), 0°, 1 h 4. CuCN•2LiCl (2 eq), –45°, 1 h 5. Allyl-Br (4 eq), –45 to 0°, 20 min 6. H_2O_2 (30%), aq 3 N NaOH, 0°, 10 min 7. H^+	 (83)	186
	 1.2 eq	1. THF, 0° 2. 0° to rt, 36–48 h 3. H^+	 (90)	186
	 1.2 eq	1. THF, 0° 2. 0° to rt, 36–48 h 3. H^+	 (89)	186
	 1.2 eq	1. THF, 0° 2. 0° to rt, 36–48 h 3. H^+	 (21) er 70.5:29.5	186
	 1.2 eq	1. THF, 0° 2. 0° to rt, 36–48 h 3. H^+	 (90)	186
		1. THF, 0° 2. 0° to rt, 36–48 h 3. H^+	 (69)	186
		1. THF, 0° 2. 0° to rt, 36–48 h 3. $ZnBr_2$ (1.2 eq), 0°, 1 h 4. O_2 (bubbled), 1 atm 5. H^+	 (36)	186
		1. THF, 0°, 1 h 2. (0.9 eq), THF, –20°, 30 min 3. H^+	 (80) (*Z*)/(*E*) = 100:0	142
	 1 eq	1. THF, 35°, 1 h 2. H^+	 (21)	78

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TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

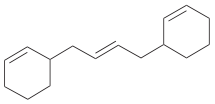
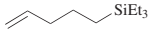
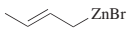
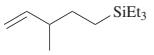
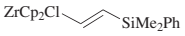
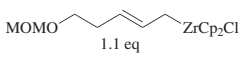
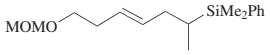
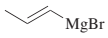
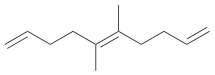
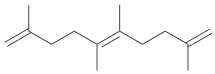
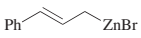
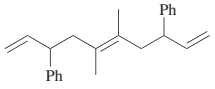
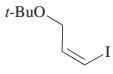
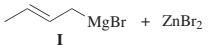
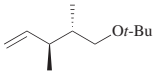
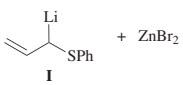
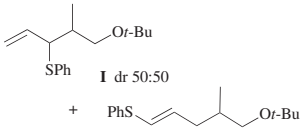
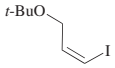
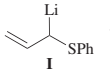
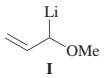
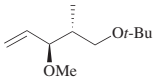
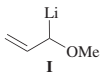
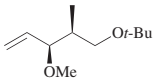
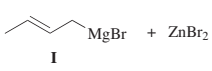
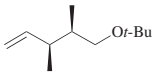
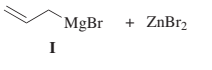
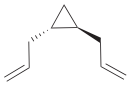
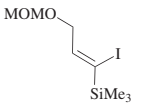
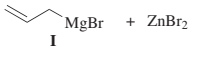
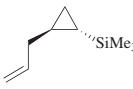
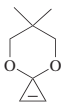
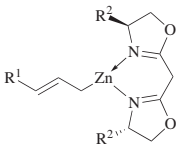
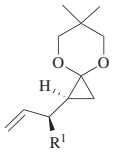
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2				
	 1 eq	1. THF, 65°, 3 h 2. H^+	 (35)	78
	 1.5 eq	1. THF, 35°, 1.75 h 2. H^+	 (90)	141
	 1.5 eq	1. THF, 35°, 3 h 2. H^+	 (83)	141
	 1.1 eq + $ZnCl_2$ (2 eq)	1. Et_2O, 0° 2. 0° to rt, 2 h 3. H^+	 (83) (*E*)/(*Z*) = 1:2.7	187
C_3				
	 1 eq	1. THF, 35°, 45 min 2. H^+	 (24)	76
	 1 eq	1. THF, 35°, 45 min 2. H^+	 (26)	76
	 1 eq	1. THF, 66°, 1 h 2. H^+	 (51) (*E*)/(*Z*) = 50:50	77
	 1 eq	1. THF, 66°, 1 h 2. H^+	 (56) (*E*)/(*Z*) = 50:50	77
	 1 eq	1. THF, 66°, 1 h 2. H^+	 (30) (*E*)/(*Z*) = 50:50	77
	 **I**	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), –50° 3. $ZnBr_2$ (1.5 eq), Et_2O, –50°, 5 h 4. H^+	 (86) *anti*/*syn* = 93:7	188
	 **I**	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), Et_2O, –50° 3. $ZnBr_2$ (2 eq), Et_2O, 10°, 24 h 4. H^+	 **I** dr 50:50 + **II** (*E*)/(*Z*) = 60:40 **I + II** (80), **I/II =** 37.5:62.5	145

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), Et_2O, –50° 3. $ZnBr_2$ (2 eq), Et_2O, rt, 24 h 4. H^+	 (95)	145
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), THF, –20° 3. $ZnBr_2$ (2 eq), Et_2O, –20°, 5 h 4. H^+	 (77) *anti*/*syn* = 95:5	145
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), THF, –20° 3. $ZnBr_2$ (2 eq), Et_2O, –20°, 5 h 4. H^+	 (81) *syn*/*anti* = 95:5	145
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), –50° 3. $ZnBr_2$ (1.5 eq), Et_2O, –50°, 5 h 4. H^+	 (81) *syn*/*anti* = 92:8	188
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq) 3. –20° to rt, 2 h 4. $Me_2CuCNLi_2$ (1.5 eq), THF, 0°, 1 h 5. Allyl-I (1.5 eq), –30°, 1 h 6. H^+	 (55) *anti*/*syn* = 100:0	150
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –30° 3. –20°, 4 h 4. –20° to rt, 2 h 5. H^+	 (70) single isomer	150
	 1.1 eq	1. rt, THF, hexane, 12 h 2. H^+		

R^1	R^2		dr	er	
H	Ph	(85)	—	>98:2	105
H	*i*-Pr	(89)	—	>99:1	105
Me	*i*-Pr	(81)	73:27	>98:2	189
c-C_6H_{11}	*i*-Pr	(94)	83:17	82:18	189
Ph	*i*-Pr	(86)	73:27	78:22	105
c-C_6H_{11}	*t*-Bu	(58)	81:19	98.5:1.5	189

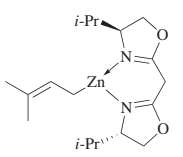
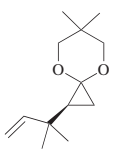
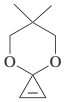
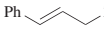
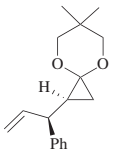
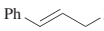
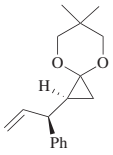
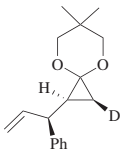
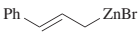
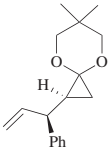
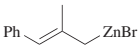
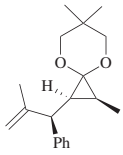
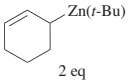
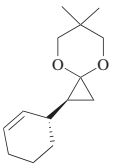
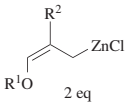
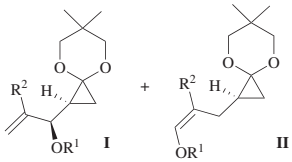
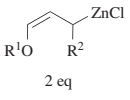
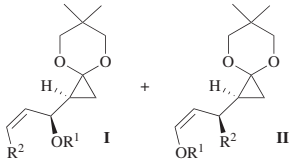
		1. rt, THF 2. H^+	 (90) er 96.5:3.5	105

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)

C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
		1. THF, temp 2. H^+	 Y Temp (°) dr Br 0 (81) 82.0:18.0 *n*-Bu –23 (87) 90.5:9.5 Mes –23 (97) 94.5:5.5	104
	 2 eq	1. THF, HMPA, –23° 2. H^+	 Y dr *n*-Bu (66) 97.5:2.5 Mes (70) 98.0:2.0	104
	 2 eq	1. THF, HMPA, –23° 2. D_2O	 (93) dr 96.0:4.0	104
		1. CH_2Cl_2, 0° 2. H^+	 (64) dr 62.0:38.0	104
	 2 eq	1. THF, HMPA, –23° 2. H^+	 (79) dr 98.0:2.0	104
	 2 eq	1. THF, –23° 2. H^+	 (85) dr 99.3:0.8	104
	 2 eq	1. THF, 0°, time 2. H^+	 **I** + **II**	103

R^1	R^2	Time (h)	**I + II**	**I/II**	dr
PMP	H	5	(79)	97:3	>98.5:1.5
PMP	Me	12	(89)	97:3	>98.5:1.5
MOM	Me	19	(82)	94:6	>98.5:1.5

	 2 eq	1. THF, 0°, time 2. H^+	 **I** + **II**		103

R^1	R^2	Time (h)	**I + II**	**I/II**	dr
MME	H	9	(48)	97:3	>98.5:1.5
MOM	Ph	19	(84)	80:20	>98.5:1.5
PMP	Ph	5	(90)	92:18	>98.5:1.5

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

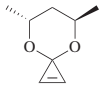
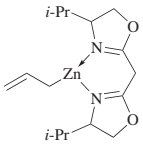
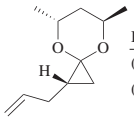
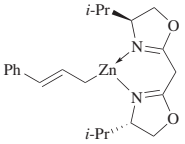
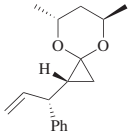
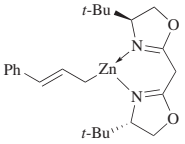
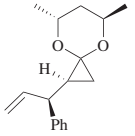
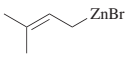
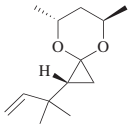
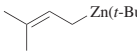
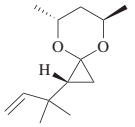
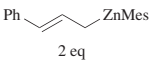
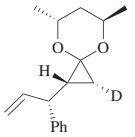
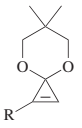
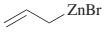
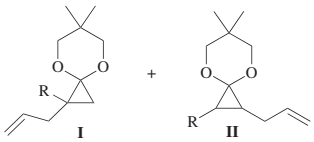
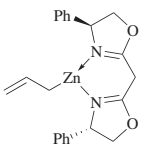
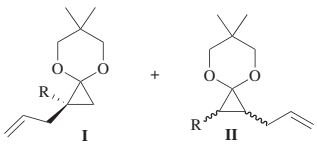
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
		1. THF, rt 2. H^+	 BOX Ligand: (*S,S*) (73) er 0.8:99.2; (*R,R*) (76) er 49:51	105
		1. THF, rt 2. H^+	 (94) er 1:99, dr 86:14	105
		1. THF, rt 2. H^+	 (70) er 54:46, dr 80:20	105
		1. THF, 0° 2. H^+	 (94) dr 90.5:9.5	104
		1. THF, HMPA (*x* eq), –23° 2. H^+	 *x*: 0 (98) dr 98.5:1.5; 5 (58) dr 96.5:3.5	104
	 2 eq	1. THF, HMPA, –23° 2. D_2O	 (80)	104
		1. THF, 0°, 1 h 2. H^+	 **I** + **II**	190
			R: Me_3Si (97) I/II 20:80; Me_3Ge (94) 15:85; Me_3Sn (94) 5:95	
		1. THF, 0°, 24 h 2. H^+	 **I** + **II**	190
			R: Me_3Si (83) I + II, 98:2 I/II, er 98.9:1.1; Me_3Ge (96) 98:2, 99.8:0.2; Me_3Sn (83) 94:6, 99.9:0.1	

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

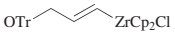
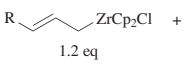
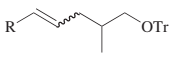
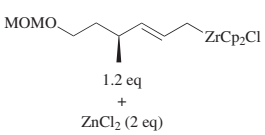
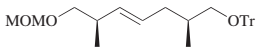
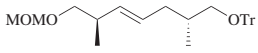
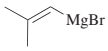
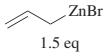
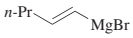
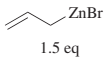
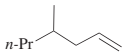
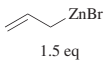
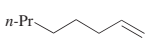
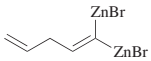
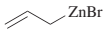
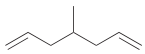
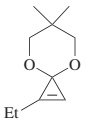
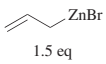
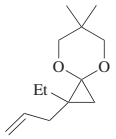
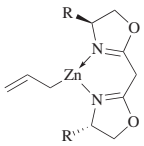
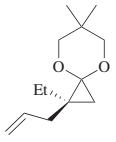
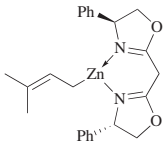
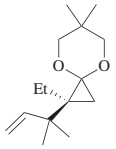
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3				
	 1.2 eq + $ZnCl_2$ (2 eq)	1. "Allylzinc", 0° 2. 0° to rt, 2 h 3. H^+		187
			R — (*E*)/(*Z*) $MOMO(CH_2)_2$ (83) 1:2.7 $TBDPSO(CH_2)_2$ (85) 1.3:1 *c*-C_6H_{11} (76) 1:1 Ph (60) 49:1 $(EtO)_2CHCH_2$ (76) 1:2.6	
	 1.2 eq + $ZnCl_2$ (2 eq)	1. "Allylzinc", 0° 2. 0° to rt, 2 h 3. H^+	 **I** (*E*)/(*Z*) = 42:1 +  **II** (*E*)/(*Z*) = 1:2.4 **I** + **II** (—), **I/II** = 93:7	187
C_4				
	 1.5 eq	1. THF, 35°, 2 h 2. Me_3SnCl (1.5 eq), –20 to 5°, 45 min 3. H^+	 (69)	141
C_5				
	 1.5 eq	1. THF, 35°, 1 h 2. H^+	 (58)	76
	 1.5 eq	1. THF, 35°, 1 h 2. H^+	 (36)	76
	 1.5 eq	1. THF, 35°, 30 min 2. H^+	 (30)	77
	 1.5 eq	1. THF, rt, 36 h 2. H^+	 (45)	190
		1. THF, pressure, rt, time 2. H^+		190, 191
		R — Pressure — Time (h) — er *i*-Pr — — 72 (48) 87.0:13.0 — 190 *t*-Bu — — 72 (<5) 93.5:6.5 — 190 Ph — — 200 (64) 99.5:0.5 — 190 Ph — 1 GPa 12 (95) 99.0:1.0 — 190, 191		
		1. THF, pressure, rt, time 2. H^+		190
		Pressure — Time (h) — er — 72 (19) >99.8:0.2 1 GPa 12 (93) >99.8:0.2		

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

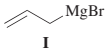
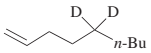
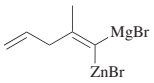
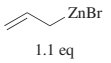
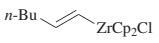
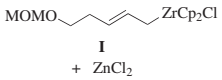
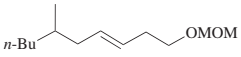
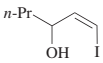
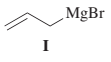
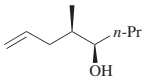
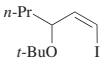
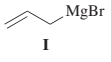
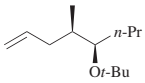
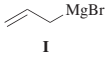
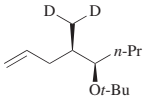
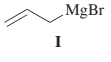
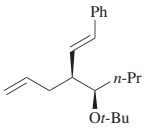
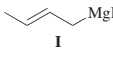
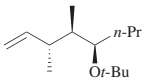
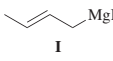
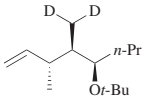
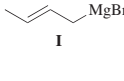
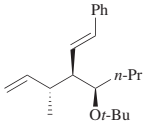
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –20°, 3 h 3. D^+	 (91)	156
	 1.1 eq	1. THF, 66°, 3 h 2. H^+	 (45)	77
	 + $ZnCl_2$	1. $ZnCl_2$ (2 eq), 0° to rt, 2 h 2. **I** (1.5 eq), 0° 3. rt, 2 h 4. H^+	 (82) (*E*)/(*Z*) = 1:4.9	187
	 + $ZnBr_2$	1. MeLi, Et_2O, –40°, 10 min 2. *t*-BuLi (2 eq), –80° 3. –80 to –60°, 30 min 4. **I** (2 eq) 5. $ZnBr_2$ (2 eq), –20° 6. –20 to 0°, 5 h 7. H^+	 (72) *syn*/*anti* = 80:20	147, 148
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.1 eq), Et_2O, –40° 3. $ZnBr_2$ (1.1 eq), Et_2O, –40°, 3 h 4. H^+	 (81) dr 95:5	148
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.1 eq), Et_2O, –40° 3. $ZnBr_2$ (1.1 eq), Et_2O, –40°, 3 h 4. D^+	 (87) dr 95:5 >98% D	148
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.1 eq), Et_2O, –40° 3. $ZnBr_2$ (1.1 eq), Et_2O, –40°, 3 h 4. PhCHO (2 eq), –40° 5. –40° to rt, 2 h 6. H^+	 (78) dr 95:5 (*E*)/(*Z*) > 99:1	148
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), Et_2O, –30° 3. $ZnBr_2$ (2 eq), Et_2O, –20°, 4 h 4. H^+	 (75) dr >95:5	192
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), Et_2O, –30° 3. $ZnBr_2$ (2 eq), Et_2O, –20°, 4 h 4. D^+	 (75) dr >95:5	192
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), Et_2O, –30° 3. $ZnBr_2$ (2 eq), Et_2O, –20°, 4 h 4. PhCHO (2 eq), –20° 5. –20° to rt, 2 h 6. H^+	 (68) dr >95:5 (*E*)/(*Z*) > 99:1	192

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

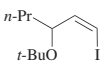
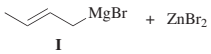
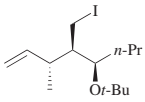
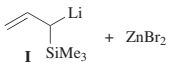
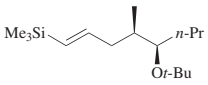
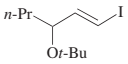
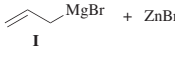
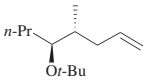
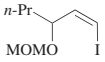
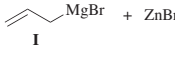
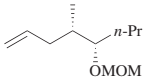
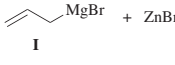
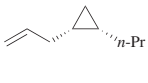
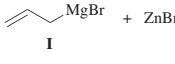
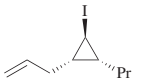
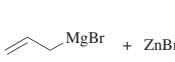
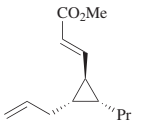
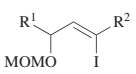
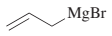
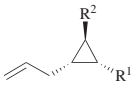
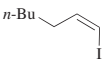
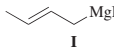
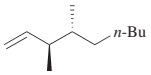
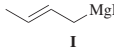
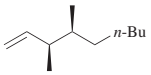
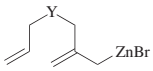
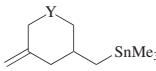
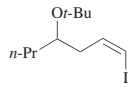
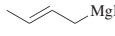
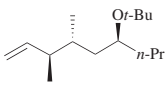
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), Et_2O, –30° 3. $ZnBr_2$ (2 eq), Et_2O, –20°, 4 h 4. *i*-PrOH (1 eq), –20° to rt, 30 min 5. I_2 (1.1 eq), –20° 6. –20° to rt, 30 min 7. H^+	 (56) dr >95:5	192
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), Et_2O, –30° 3. $ZnBr_2$ (1.5 eq), Et_2O, –20°, 3 h 4. H^+	 (78) dr 73:27, (*E*)/(*Z*) = 98:2	148
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –20°, 5 h 3. H^+	 (60) dr 76:24	182
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –30° 3. –20°, 4 h 4. H^+	 (78) *syn*/*anti* = 95:5	150
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –30° 3. –20°, 4 h 4. –20° to rt, 2 h 5. H^+	 (70) *syn*/*anti* = 95:5	150
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –30° 3. –20°, 4 h 4. –20° to rt, 2 h 5. I_2 (1.5 eq), –20 to 20°, 1 h	 (65) *cis*/*trans* > 95:5	150
		1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –30° 3. –20°, 4 h 4. –20° to rt, 2 h 5. $Me_2CuCNLi_2$ (2 eq), THF, 0°, 1 h 6. ≡—CO_2Me (2 eq), –40°, 1 h 7. H^+	 (68) *cis*/*trans* > 95:5 (*E*)/(*Z*) > 99:1	150

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-9}				
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq) 3. –20°, 4 h 4. –20° to rt, 2 h 5. Step 5 6. Step 6		150

R^1	R^2	Step 5	Step 6		dr
n-Pr	Me_3Si	H^+	—	(68)	—
Ph	H	I_2 (1.5 eq), –20°	–20 to 20°, 1 h	(60)	>95:5

C_7					
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), –50° 3. $ZnBr_2$ (1.5 eq), Et_2O, –50°, 5 h 4. H^+		(87) *anti*/*syn* = 92:8	188
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), –50° 3. $ZnBr_2$ (1.5 eq), Et_2O, –50°, 5 h 4. H^+		(81) *syn*/*anti* = 95:5	188
	Intramolecular	1. THF, 80°, time 2. $ClSnMe_3$ 3. H^+		Y Time (h) MeN 24 (64) O 23 (57)	8, 111
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), –20° 3. $ZnBr_2$, Et_2O, –20°, 4 h 4. H^+		(80) dr >95:5	188

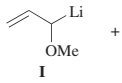
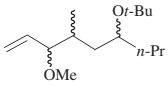
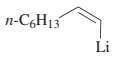
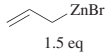
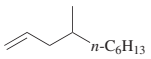
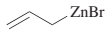
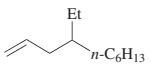
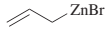
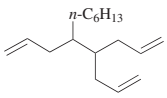
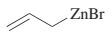
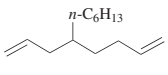
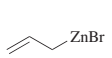
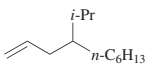
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (2 eq), –30° 3. $ZnBr_2$ (2 eq), Et_2O, 20°, 48 hr 4. H^+		(80) dr 70:20:10	188
C_8					
	 1.5 eq	1. THF, 5°, 15 h 2. H^+		(90)	141
	 1.1 eq	1. THF, 5°, 14 h 2. MeI (5 eq), rt, 12 h 3. H^+		(58)	193
	 1.1 eq	1. THF, 5°, 14 h 2. CuCN (1 eq), –40° 3. –40 to –35°, 15 min 4. Allyl-Br (2.5 eq), –40 to 0° 5. H^+		(88)	143
	 1.1 eq	1. THF, 5°, 14 h 2. *s*-BuOH (1 eq), THF, –40°, 15 min 3. Allyl-Br (5 eq), –40 to 0°, 10 min 4. H^+		(79)	143
	 1.1 eq	1. THF, 5°, 14 h 2. CuCN (1 eq), –40°, 15 min 3. MeI (5 eq), 0°, 8 h 4. H^+		(64)	143

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

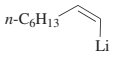
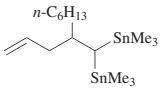
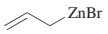
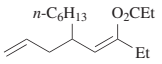
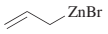
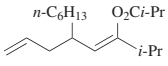
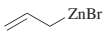
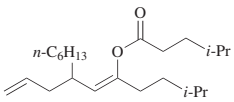
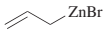
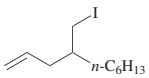
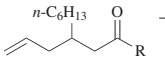
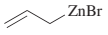
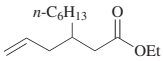
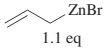
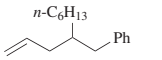
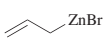
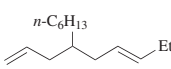
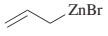
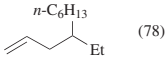
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 1.1 eq	1. THF, 5°, 14 h 2. CuCN (1 eq), –40°, 15 min 3. Me_3SnCl (2 eq), THF, –20°, 30 min 4. H^+	 (85)	143
	 1.1 eq	1. THF, 5°, 14 h 2. CuCN (1 eq), –40° 3. –40 to –35°, 15 min 4. EtCOCl (3 eq), –10°, 2 h 5. H^+	 (74) (*Z*)/(*E*) = 20:80	143
	 1.1 eq	1. THF, 5°, 14 h 2. CuCN (1 eq), –40° 3. –40 to –35°, 15 min 4. *i*-PrCOCl (3 eq), –10°, 2 h 5. H^+	 (54) (*Z*)/(*E*) = 20:80	143
	 1.1 eq	1. THF, 5°, 14 h 2. CuCN (1 eq), –40° 3. –40 to –35°, 15 min 4. *i*-Pr$(CH_2)_2$COCl (3 eq), –10°, 2 h 5. H^+	 (67) (*Z*)/(*E*) = 23:77	143
	 1.1 eq	1. THF, 5°, 14 h 2. MeOH (1 eq), –70° 3. –70 to –30° 4. I_2 (1 eq), –78° 5. –78 to –40° 6. H^+	 (73)	194
	 1.1 eq	1. THF, 5°, 14 h 2. *i*-BuOH (1 eq), –70° 3. –70 to –30°, 30 min 4. RCOCl (2.5 eq), $Pd(PPh_3)_4$ (5 mol %), 0.5–2 h 5. H^+		R | (88) 194 Et | (88) 194 *i*-Pr | (84) $(Me)_2C{=}CH$ | (89)
	 1.1 eq	1. THF, 5°, 14 h 2. *i*-BuOH (1 eq), –70° 3. –70 to –30°, 30 min 4. EtOCOCl (2.5 eq), $Pd(PPh_3)_4$ (5 mol %), rt, 8 h 5. H^+	 (66)	194
	 1.1 eq	1. THF, 5°, 14 h 2. *i*-BuOH (1 eq), –70° 3. –70 to –30°, 30 min 4. PhI, $Pd(PPh_3)_4$ (5 mol %), rt, 4 h 5. H^+	 (73)	194
	 1.1 eq	1. THF, 5°, 14 h 2. *i*-BuOH (1 eq), –70° 3. –70 to –30°, 30 min 4. EtCH=CHI (1.2 eq), $Pd(PPh_3)_4$ (5 mol %), rt 5. H^+	 (64)	194
	 1.1 eq	1. THF, 5°, 14 h 2. *t*-BuSH (1 eq), –70° 3. –70 to –30° 4. CuI (1 eq), –15°, 45 min 5. MeI (5 eq), rt, 4 h 6. H^+	 (78)	194

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

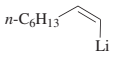
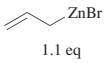
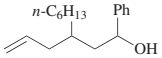
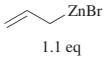
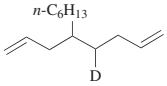
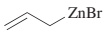
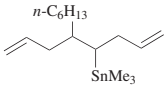
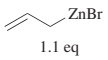
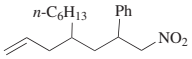
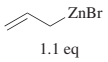
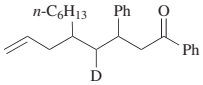
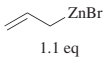
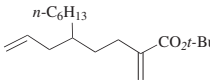
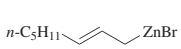
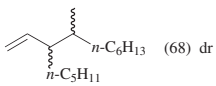
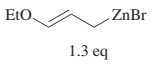
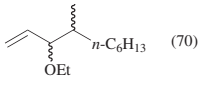
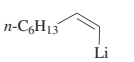
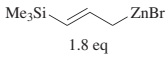
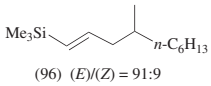
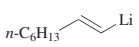
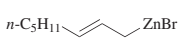
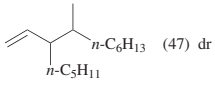
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 1.1 eq	1. THF, 5°, 14 h 2. *i*-BuOH (1 eq), –70° 3. –70 to –30°, 30 min 4. $ClTi(Oi\text{-}Pr)_3$ (2 eq), –60°, 30 min 5. PhCHO (1.5 eq), rt, 22 h 6. H^+	 (56) dr —	194
	 1.1 eq	1. THF, 5°, 14 h 2. MeOD (1 eq), –70° 3. –70 to –20°, 30 min 4. CuCN (1 eq), –40°, 25 min 5. Allyl-Br (excess), –40° 6. –40° to rt, 30 min 7. H^+	 (76)	194
	 1.1 eq	1. THF, 5°, 14 h 2. Me_3SnCl (1 eq), –40° 3. –40 to –30°, 1 h 4. CuCN (1 eq), –30°, 30 min 5. Allyl-Br (3 eq), –30° 6. –30 to –10°, 30 min 7. H^+	 (79) dr — diastereoselectivity not specified	194
	 1.1 eq	1. THF, 5°, 14 h 2. CuCN (1 eq), –30°, 30 min 3.  (1 eq), –50°, 2 h 4. H^+	 (65)	194
	 1.1 eq	1. THF, 5°, 14 h 2. CuCN (1 eq), –30°, 30 min 3. (1 eq), –78° 4. –78 to 0°, 1 h 5. D^+	 (63) dr —	194
	 1.1 eq	1. THF, 5°, 14 h 2. MeOH (1 eq), –78 to –30° 3. CuCN (1 eq), –40°, 30 min 4. –40 to –30°, 30 min 5. (1.1 eq), –50 to –20°, 1 h 6. H^+	 (77)	194
	 1.1 eq	1. THF, 5°, 19 h 2. H^+	 (68) dr 88:12	195
	 1.3 eq	1. THF, rt, 30 h 2. H^+	 (70) dr 86:14	195
 (*Z*)/(*E*) = 88:12	 1.8 eq	1. THF, 35°, 4 h 2. rt, 8 h 3. H^+	 (96) (*E*)/(*Z*) = 91:9	195
	 1.1 eq	1. THF, 5°, 19 h 2. H^+	 (47) dr 22:78	195

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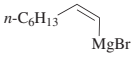
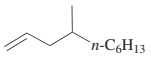
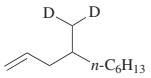
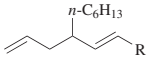
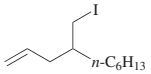
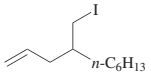
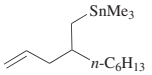
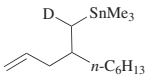
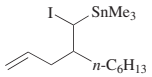
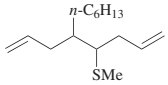
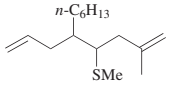
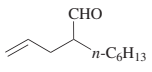
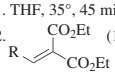
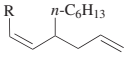
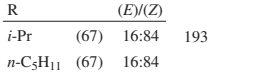
TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	 1.5 eq	1. THF, 35°, 45 min 2. H^+	 (93)	141
	 1.5 eq	1. THF, 35°, 45 min 2. D^+	 (93)	141
	 1.1 eq	1. THF, 35°, 45 min 2. RCHO (x eq), THF, –50° 3. BF_3•OEt_2 (y eq), –90° 4. Temp, 15 min 5. –50°, 45 min 6. H^+		141

R	x	y	Temp		(E)/(Z)
Et	1.1	1	–90 to –50°	(61)	95:5
i-Pr	2	1	–90 to –50°	(75)	99:1
t-Bu	2	1	–90 to –20°	(49)	99:1
n-C_5H_{11}	2	1.1	–90 to –50°	(75)	94:6
i-$PrCH_2CH_2$	2	1	–90 to –50°	(85)	88:12
Ph	1.1	1	–90 to –50°	(78)	99:1
PhCH=CH	2	1.1	–90 to –50°	(58)	92:8

 1.1 eq	1. THF, 35°, 45 min 2. I_2 (1 eq), –78°, 10 min 3. H^+		(61)	193
 1.1 eq	1. THF, 35°, 45 min 2. AcOH (1 eq), –80° 3. –80 to –40°, 15 min 4. I_2 (1 eq), –40 to 0°, 30 min 5. H^+		(60)	193
 1.1 eq	1. THF, 35°, 45 min 2. Me_3SnCl (1 eq), –25° 3. –25 to –5°, 45 min 4. H^+		(88)	193
 1.1 eq	1. THF, 35°, 45 min 2. Me_3SnCl (1 eq), –25° 3. –25 to –5°, 45 min 4. D^+		(94)	193
 1.1 eq	1. THF, 35°, 45 min 2. Me_3SnCl (1 eq), –78°, 10 min 3. I_2 (1 eq), –78 to 0°, 1 h		(75)	193
 1.1 eq	1. THF, 35°, 45 min 2. Allyl-Br (5 eq), rt, 2 h 3. MeSSMe (2.3 eq), rt, 20 h 4. H^+		(76) dr —	193
 1.1 eq	1. THF, 35°, 45 min 2.  (5 eq), rt, 2 h 3. MeSSMe (2.3 eq), rt, 20 h 4. H^+		(77) dr —	193
 1.1 eq	1. THF, 35°, 45 min 2. MeSSMe (2.5 eq), rt, 20 h 3. 0.01N HCl		(53)	193
 1.1 eq	1. THF, 35°, 45 min 2.  (1.5 eq), –78°, 30 min 3. H^+			193

R		(E)/(Z)
i-Pr	(67)	16:84
n-C_5H_{11}	(67)	16:84
Ph	(74)	75:25

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

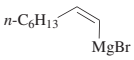
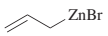
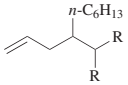
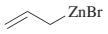
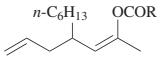
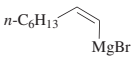
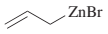
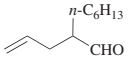
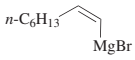
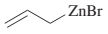
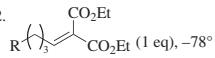
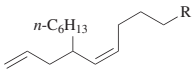
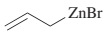
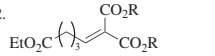
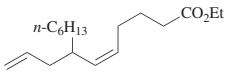
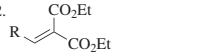
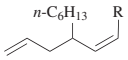
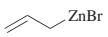
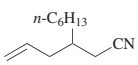
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 1.1 eq	1. THF, 35°, 45 min 2. CuCN (1 eq), –40° 3. –40 to –35°, 15 min 4. RX (*x* eq), temp 5. H^+		143
			RX — *x* — Temp (°):  5 –40 to 0 (93);  5 –40 to rt (76);  2.5 –40 to 0 (52);  2.5 –40 to 0 (73)	
	 1.1 eq	1. THF, 35°, 45 min 2. CuCN (1 eq), –40° 3. –40 to –35°, 15 min 4. RCOCl (3 eq), –10°, 2 h 5. H^+	 R — (*E*)/(*Z*): Me (78) 17:83; Et (63) 18:82	143
 (*Z*)/(*E*) = 88:12	 1.1 eq	1. THF, 35°, 45 min 2. Me_3SnCl (1 eq), 0°, 15 min 3. O_2, TMSCl (1 eq), –10°, 10 h 4. H^+	 (81)	152
	 1.1 eq	1. THF, 35°, 45 min 2.  (1 eq), –78° 3. –78 to –20°, 10 min 4. NH_4Cl	 R — (*Z*)/(*E*): EtO_2C (83) 82:18; NC– (88) 83:17; $ClCH_2$ (75) 88:12; AcO (79) 79:21; PhS (91) 70:30	142
	 1.1 eq	1. THF, 35°, 45 min 2.  (1 eq), –78° 3. –78 to –20°, 10 min 4. NH_4Cl	 R — (*Z*)/(*E*): *i*-Pr (60) 84:16; *c*-C_6H_{11} (82) 91:9	142
	 1.1 eq	1. THF, 35°, 45 min 2.  (1 eq), –78° 3. –78 to –20°, 10 min 4. NH_4Cl	 R — (*Z*)/(*E*): $PhMe_2Si$ (83) 14:86; *c*-C_6H_{11} (79) 78:22; $OHCC_6H_4$ (72) 80:20	142
	 1.1 eq	1. THF, 35°, 1 h 2. TosCN (2 eq), –30 to 0°, 2 h 3. H^+	 (93)	88

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TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

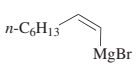
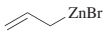
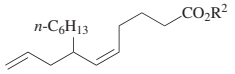
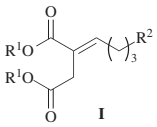
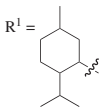
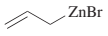
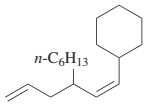
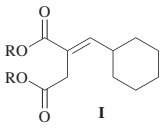
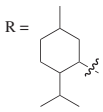
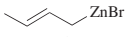
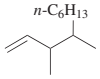
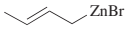
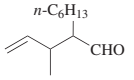
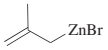
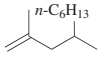
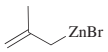
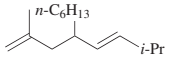
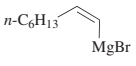
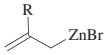
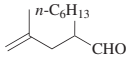
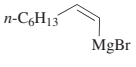
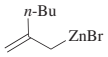
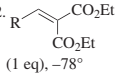
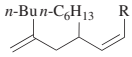
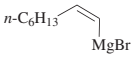
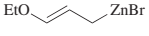
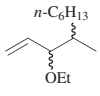
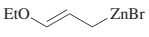
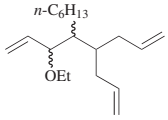
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 1.1 eq	1. THF, 35°, 45 min 2. **I** (1.1 eq), –78 to –20°, 10 min 3. H^+		196
		 **I** 	R^2 (Z)/(E) EtO_2C (76) 100:0 NC– (79) 97:3 AcO (86) 100:0	
	 1.1 eq	1. THF, 35°, 45 min 2. **I** (1.1 eq), –78 to –20°, 10 min 3. H^+	 (91) (Z)/(E) = 92:8	196
		 **I** 		
	 1.5 eq	1. THF, 35°, 2.5 h 2. H^+	 (82) dr 70:30	141
	 1.1 eq	1. THF, 35°, 45 min 2. Me_3SnCl (1 eq), 0°, 15 min 3. O_2, TMSCl (2 eq), –10°, 4 h 4. H^+	 (78) dr —	152
	 1.5 eq	1. THF, 35°, 45 min 2. H^+	 (92)	141
	 1.1 eq	1. THF, 35°, 45 min 2. *i*-PrCHO (1.1 eq), –50° 3. BF_3•OEt_2, –90 to –50°, 15 min 4. –50°, 45 min	 (79) (E)/(Z) = 98:2	141
 (Z)/(E) = 88:12	 *x* eq	1. THF, 35°, 45 min 2. Me_3SnCl (1 eq), 0°, 15 min 3. O_2, TMSCl (1 eq), –10°, time 4. H^+		152
			R x Time (h) Me 1.1 5 (87) *n*-Bu 1.3 4 (66)	
	 1.1 eq	1. THF, 35°, 45 min 2.  (1 eq), –78° 3. –78 to –20°, 10 min 4. NH_4Cl		142
			R (Z)/(E) $Cl(CH_2)_4$ (86) 100:0 $EtO_2C(CH_2)_3$ (81) 45:55 $NC(CH_2)_3$ (79) 7:93 c-C_6H_{11} (76) 77:23	
 (Z)/(E) = 88:12	 1.3 eq	1. THF, 40°, 3 h 2. 30°, 14 h 3. H^+	 (65) dr 86:14	195
	 1.3 eq	1. THF, 40°, 3 h 2. 30°, 14 h 3. CuCN (1 eq), –30°, 25 min 4. Allyl-Br (excess), –30° 5. –30° to rt, 1 h 6. H^+	 (54) dr = 86:14	195

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

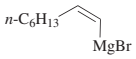
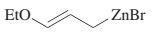
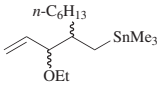
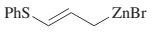
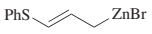
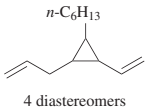
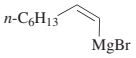
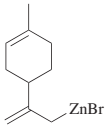
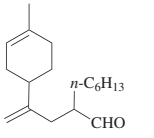
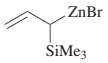
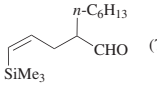
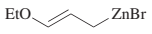
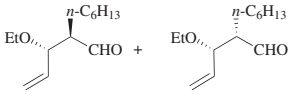
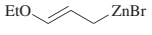
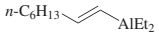
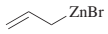
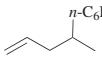
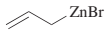
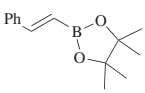
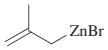
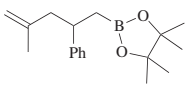
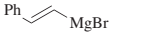
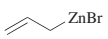
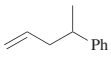
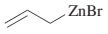
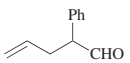
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
 (*Z*)/(*E*) = 88:12	 1.3 eq	1. THF, 40°, 3 h 2. 30°, 14 h 3. Me_3SnCl (1 eq), –30 to –10°, 1 h 4. –30 to –10°, 1 h 5. H^+	 (40) dr = 86:14	195
	 1.3 eq	1. THF, 40°, 3 h 2. 30°, 14 h 3. H^+	 (72) dr = 70:30	195
	 1.3 eq	1. THF, 40°, 3 h 2. 30°, 14 h 3. CuCN (1 eq), –30° 4. Allyl-Br (excess), –30° 5. –30° to rt, 1 h 6. H^+	 4 diastereomers (72)	195
	 1.3 eq	1. THF, 35°, 45 min 2. Me_3SnCl, 0°, 15 min 3. O_2, TMSCl (1 eq), –10°, 4 h 4. H^+	 (60)	152
	 1.8 eq	1. THF, 35°, 45 min 2. Me_3SnCl, 0°, 15 min 3. O_2, TMSCl (4 eq), –10°, 5 h 4. H^+	 (77) (*Z*)/(*E*) = 88:12	152
	 1.3 eq	1. THF, 35°, 45 min 2. Me_3SnCl (1 eq), 0°, 15 min 3. O_2, TMSCl (1 eq), –10°, 6 h 4. H^+	 **I** **II** **I + II** (56), **I/II** = 88:12	152
	 1.8 eq	1. THF, 45° 2. H^+	 (48) *cis*/*trans* = 5:95	152
	 1.5 eq	1. THF, 35°, 1 h 2. H^+	 (71)	141
	 1.1 eq	1. THF, 0°, 3 h 2. H^+	 (72)	157
	 1.2 eq	1. THF, 0° 2. 0° to rt, 36–48 h 3. H^+	 (95)	186
	 1.5 eq	1. THF, 35°, 1 h 2. H^+	 (58)	141
	 1.1 eq	1. THF, 35°, 45 min 2. Me_3SnCl (1 eq), 0°, 15 min 3. Dry air (bubbled), TMSCl (1 eq), –10°, 30 min 4. H^+	 (89)	152

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

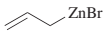
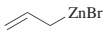
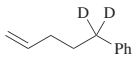
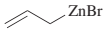
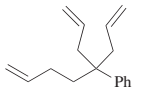
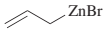
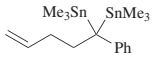
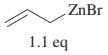
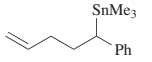
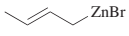
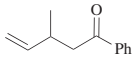
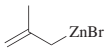
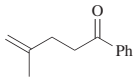
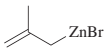
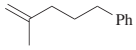
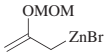
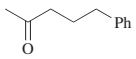
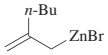
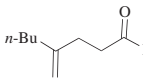
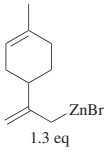
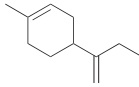
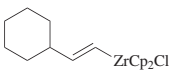
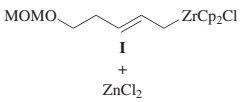
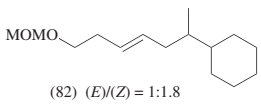
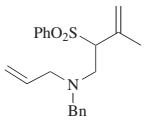
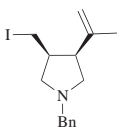
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 1.1 eq	1. THF, 0–35°, 0.5–2 h 2. H^+	 (91)	157
	 1.1 eq	1. THF, 0° to rt, 2 h 2. D_2O/MeCOCl, –10° to rt	 (91)	157
	 1.1 eq	1. THF, 0° to rt, 2 h 2. CuCN (1 eq), –20°, 30 min 3. Allyl-Br (excess), –30° to rt, 1 h 4. H^+	 (61)	157
	 1.1 eq	1. THF, 0° to rt, 2 h 2. CuCN (1 eq), –20°, 30 min 3. Me_3SnCl (2 eq), –40 to 0° 4. H^+	 (98)	157
	 1.1 eq	1. THF, 0° to rt, 2 h 2. Me_3SnCl (2 eq), –40 to 0° 3. AcOH, –10 to 20° 4. H^+	 (82)	157
	 1.3 eq	1. THF, 35°, 45 min 2. Me_3SnCl, 0°, 15 min 3. O_2, TMSCl (1 eq), –10°, 4 h 4. H^+	 (57)	152
	 1.3 eq	1. THF, 35°, 45 min 2. Me_3SnCl (1 eq), 0°, 15 min 3. Dry air (bubbled), TMSCl (1 eq), –10°, 1 h 4. H^+	 (85)	152
	 1.1 eq	1. THF, 0° to rt, 0.5–2 h 2. H^+	 (87)	157
	 1.3 eq	1. THF, 0° to rt, 2 h 2. Et_2O, H^+	 (89)	157
	 1.3 eq	1. THF, 35°, 45 min 2. Me_3SnCl, 0°, 15 min 3. O_2, TMSCl (1 eq), –10°, 2 h 4. H^+	 (91)	152
	 1.3 eq	1. THF, 35°, 45 min 2. Me_3SnCl, 0°, 15 min 3. O_2, TMSCl (1 eq), –10°, 3 h 4. H^+	 (65)	152
		1. **I** (1.5 eq) + $ZnCl_2$ (2 eq), 0° 2. 0° to rt, 2 h 3. H^+	 (82) (*E*)/(*Z*) = 1:1.8	187
	Intramolecular	1. $Pd(PPh_3)_4$, Et_2O 2. Et_2Zn, reflux, 2.25 h 3. I_2 (1 M in THF)	 (60) dr >40:1	39

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

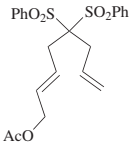
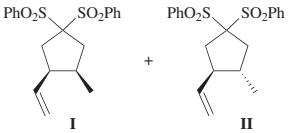
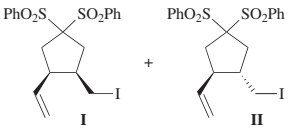
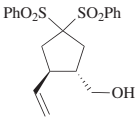
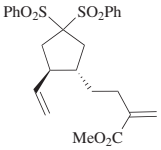
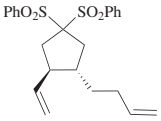
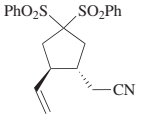
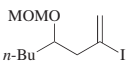
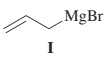
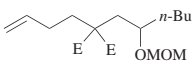
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %) 2. EtZnR (5 eq), Et_2O, rt, time 3. H^+	 **I** + **II** R / Time (h) / **I + II** / **I/II** Et / 1.5 / (79) / 84:16 $AdCO_2$ / 3.5 / (90) / 89:11 $PhCO_2$ / 4 / (72) / 89:11	137
	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %) 2. EtZnR (*x* eq), solvent, temp, time 3. I_2 (*y* eq)	 **I** + **II** R / *x* / *y* / Solvent / Temp (°) / Time (h) / **I + II** / **I/II** Et / 5 / 7 / Et_2O / rt / 1.5 / (66) / 83:17 CF_3O_2SO / 2.5 / 1.5 / CH_2Cl_2 / 40 / 2 / (70) / 2:98 $CF_3CF(OMe)CO_2$ / 2.5 / 1.5 / CH_2Cl_2 / 35 / 1.5 / (74) / 3:97	137
	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %) 2. $EtZnOSO_2CF_3$ (2.5 eq), CH_2Cl_2, 35°, 1 h 3. $ZnBr_2$, THF, O_2 4. Zn/HCl or $P(OMe)_3$ 5. H^+	 (51) dr 96:4	137
	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %) 2. $EtZnOSO_2CF_3$ (2.5 eq), CH_2Cl_2, 35°, 1 h 3. CuCN•2LiCl, THF 4. Methyl 2-(bromomethyl)acrylate 5. H^+	 (56) dr 99:1	137
	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %) 2. $EtZnOSO_2CF_3$ (2.5 eq), CH_2Cl_2, 35°, 1 h 3. CuCN•2LiCl, THF 4. Allyl-Br 5. H^+	 (80) dr 98:2	137
	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %) 2. $EtZnOSO_2CF_3$ (2.5 eq), CH_2Cl_2, 35°, 1 h 3. CuCN•2LiCl, THF 4. TosCN 5. H^+	 (68) dr 97:3	137
	 **I** + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –20°, 3 h 3. E^+, –20°	 E / (%) H / (75) D / (78)	156

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

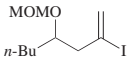
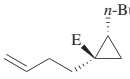
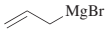
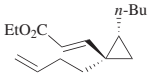
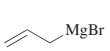
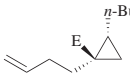
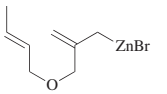
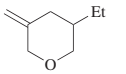
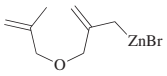
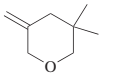
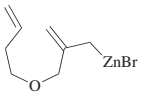
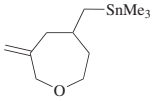
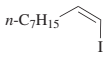
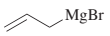
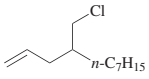
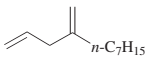
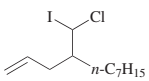
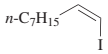
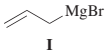
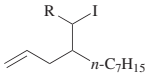
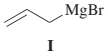
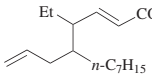
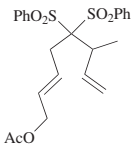
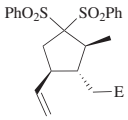
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –20°, 3 h 3. –20° to rt, 12 h 3. E^+, –20°, 1 h	 E H (80) D (80) I (70) Br (80)	156
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –20°, 3 h 3. –20° to rt, 12 h 4. $Me_2CuCNLi_2$ (1.5 eq), THF, 0°, 1 h 5. (1.5 eq), –70°, 2 h 6. H^+	 (64)	156
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.5 eq), $ZnBr_2$ (1.5 eq), Et_2O, –20°, 3 h 3. –20° to rt, 12 h 4. $Me_2CuCNLi_2$ (1.5 eq), THF, 0°, 1 h 5. E–R (1.5 eq), –30°, 2 h 6. H^+	 E–R allyl–I (65) Et_2NCH_2–O*n*-Bu (60)	156
	Intramolecular	1. THF, 80°, 45 h 2. H^+	 (80)	8, 111
	Intramolecular	1. THF, 130°, 22 h 2. H^+	 (50)	8, 111
	Intramolecular	1. THF, 80°, 24 h 2. Me_3SnCl 3. H^+	 (62)	111
C_9				
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.2 eq), $ZnBr_2$ (1.2 eq), Et_2O, –40° 3. $PhSO_2Cl$ (3 eq), –80°, 1 h 4. MeOH, –80°	 (90)	87
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.2 eq), $ZnBr_2$ (1.2 eq), Et_2O, –40° 3. $PhSO_2Cl$ (3 eq), –80°, 1 h 4. –80 to 20° 5. H^+	 (70)	87
	+ $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.2 eq), $ZnBr_2$ (1.2 eq), Et_2O, –40° 3. $PhSO_2Cl$ (3 eq), –80°, 1 h 4. *n*-BuLi (2 eq), –80°, 30 min 5. I_2 (2 eq), –50 to 0° 6. H^+	 (70) dr —	87

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

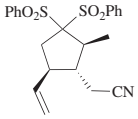
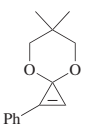
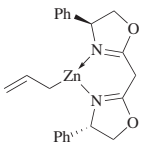
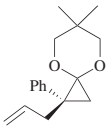
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.2 eq), $ZnBr_2$ (1.2 eq), Et_2O, –40° 3. $PhSO_2Cl$ (3 eq), –80°, 1 h 4. Nuc^- (2 eq), –80° 5. –60 to –30°, 2 h 6. I_2 (2 eq), 20°, 8 h 7. H^+	 dr —	87

Nuc^-	R	
MeMgCl	Me	(<20)
EtMgBr	Et	(60)
i-PrMgCl	*i*-Pr	(51)
allylMgBr	allyl	(49)
n-BuLi	*n*-Bu	(60)
s-BuLi	*s*-Bu	(66)
t-BuMgCl	*t*-Bu	(47)

	 + $ZnBr_2$	1. *t*-BuLi (2 eq), Et_2O, –80 to –60°, 30 min 2. **I** (1.2 eq), $ZnBr_2$ (1.2 eq), Et_2O, –40° 3. $PhSO_2Cl$ (3 eq), –80°, 1 h 4. EtMgCl (2 eq), –60° 5. –60° to –30°, 2 h 6. CuCN (2 eq), THF, 0°, 1 h 7. ≡—CO_2Et (2 eq), –40°, 2h	 (55) dr — (E)/(Z) > 99:1	87

	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %) 2. EtZnR (*n* eq), CH_2Cl_2, 40°, 1 h 3. E^+ (*y* eq)		137

R	*x*	E	*y*		dr
Et	5	H	—	(69)[b]	—
CF_3O_2SO	2.5	H	—	(86)[c]	—
$CF_3CF(OMe)CO_2$	2.5	I_2 / 2	4	(74)	99:1

	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %) 2. $EtZnOSO_2CF_3$ (2.5 eq), CH_2Cl_2, 40°, 1 h 3. CuCN•2LiCl (1 eq), THF 4. TosCN (5 eq) 5. H^+	 (66) dr 97:3	137
		1. rt, pressure, time, THF 2. H^+		

h	Pressure	Time (h)		er	
	1 GPa	12	(98)	>99.0:1.0	191, 190
	1 atm	70	(51)	>99.8:0.2	190

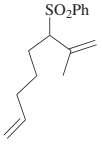
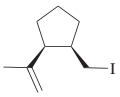
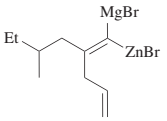
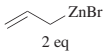
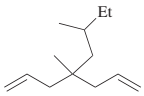
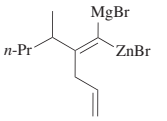
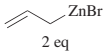
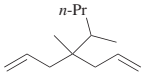
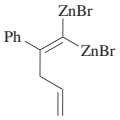
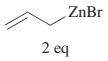
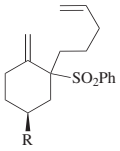
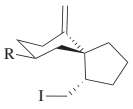
	Intramolecular	1. $Pd(PPh_3)_4$ (cat.), Et_2O 2. Et_2Zn, rt, 30 h 3. I_2 (1 M in THF)	 (98)	39

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)

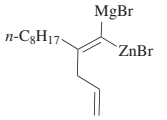
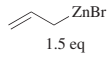
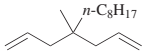
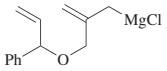
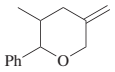
C. UNCATALYZED ADDITION OF ALLYLZINC DERIVATIVES (*Continued*)

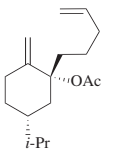
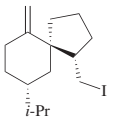
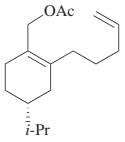
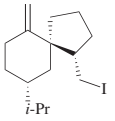
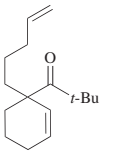
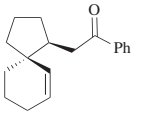
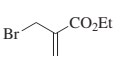
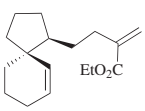
Alkene	Allylzinc Derivative	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	 2 eq	1. THF, 66°, 3 h 2. H^+	 (75)	77
	 2 eq	1. THF, 66°, 3 h 2. H^+	 (40)	77
C_{11} 	 2 eq	1. THF, temp 2. H^+		76, 77

Temp (°C)	Time		
35	0.5	(65)	
35	3	(75)	
66	3	(75)	

$C_{12–15}$ 	Intramolecular	1. $Pd(PPh_3)_4$, Et_2O 2. Et_2Zn, rt, time 3. I_2 (1 M in THF)		39

R	Time (h)		dr
H	18	(96)	100:0
i-Pr	27	(94)	95:5

C_{13} 	 1.5 eq	1. THF, 66°, 3 h 2. H^+	 (77)	77
	Intramolecular	1. $ZnBr_2$, THF 2. 80°, 48 h 3. H^+	 (76) *trans*/*cis* = 2:1	111, 8

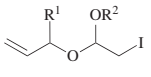
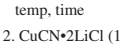
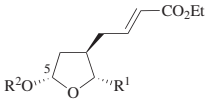
C_{15} 	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %), Et_2O 2. Et_2Zn (20 eq) 3. 37°, 14 h 4. I_2 (1 M in THF, 40 eq)	 (90) dr 95:5	197, 198
	Intramolecular	1. $Pd(PPh_3)_4$ (5 mol %), Et_2O 2. Et_2Zn (20 eq) 3. 37°, 14 h 4. I_2 (1 M in THF, 40 eq)	 (90) dr 95:5	197, 198
C_{16} 	Intramolecular	1. BuLi, 0°, THF 2. $ZnCl_2$, –78° 3. –78° to rt, 5 h 4. THF, rt, 4 h 5. CuCN•2LiCl, THF, 0° 6. PhCOCl	 (60) *syn*/*anti* > 98:2	34
	Intramolecular	1. BuLi, 0°, THF 2. $ZnCl_2$, –78° 3. –78° to rt, 5 h 4. THF, rt, 4 h 5. CuCN•2LiCl, THF, 0° 6.  7. H^+	 (72) *syn*/*anti* > 98:2	34

[a] The allkylzinc derivative was prepared from the corresponding alkylzinc bromide and*n*-BuLi.

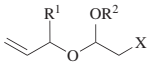
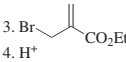
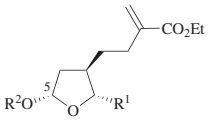
[b] The product was a mixture of two diastereomers.

[c] Two additional diastereomers were detected. The overall yield was 90%.

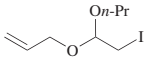
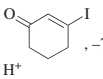
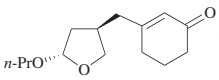
TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
D. NICKEL-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES

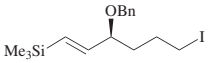
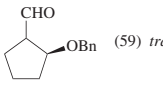
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-11}			
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (*x* mol %), LiI (*y* mol %), THF, temp, time 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78 to –20°, 12 h 4. H^+		

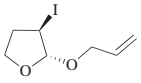
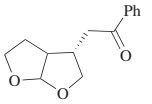
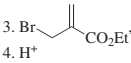
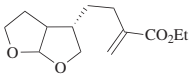
R^1	R^2	*x*	*y*	Temp	Time (h)		*trans*/*cis*	(*E*)/(*Z*)	
H	Et	2	0	rt	—	(63)	85:15	—	199
H	*n*-Bu	2	0	rt	—	(61)	88:12	>99:1	133
n-C_6H_{13}	Et	5	25	40°	12	(60)	98:2	—	133

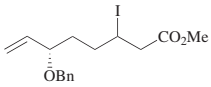
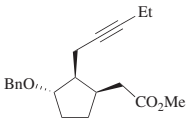
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (*x* mol %), LiI (*y* mol %), THF, rt 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , temp, 2 h 4. H^+		

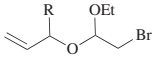
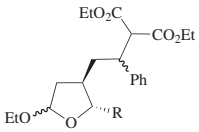
R^1	R^2	X	*x*	*y*	Temp		*trans*/*cis*	
H	Et	I	2	0	–78° to rt	(69)	85:15	199
H	*n*-Bu	I	2	0	–78 to –20°	(70)	88:12	133
n-C_6H_{13}	Et	I	2	0	–78° to rt	(61)	98:2	133
Ph	Et	Br	3	25	–78° to rt	(64)	98:2	199
Ph	*n*-Bu	I	2	0	–78° to rt	(69)	99:1	133

C_5			
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (2 mol %), THF, rt 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78° to rt, 1 h 4. H^+	 (62) *trans*/*cis* = 88:12	133

C_6			
	1. Et_2Zn (2.2 eq), $Ni(acac)_2$ (2.5 mol %), –78 to –10° , 1 h 2. O_2 (bubbled), THF, –10°, 12 h 3. H^+	 (59) *trans*/*cis* = 83:17	200

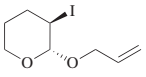
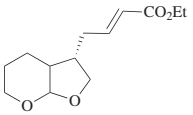
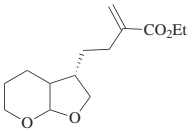
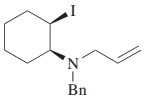
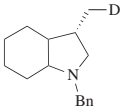
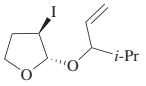
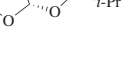
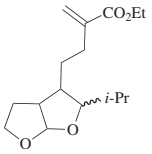
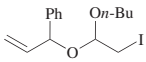
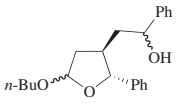
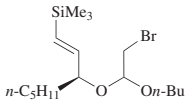
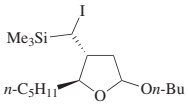
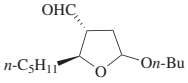
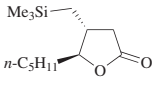
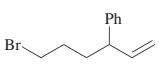
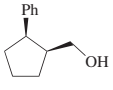
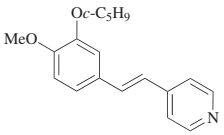
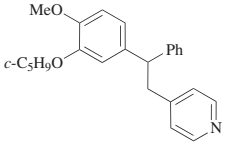
C_7			
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (2 mol %), THF, 0°, 30 min 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. PhCOCl (1 eq), –10°, 2 h 4. H^+	 (62) *endo*/*exo* > 98:2	133
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (2 mol %), THF, rt 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. Br  , –78° to rt, 2 h 4. H^+	 (83) *trans*/*cis* = 98:2	199

C_8			
	1. Et_2Zn (2.1 eq), $Ni(acac)_2$ (2.5 mol %), THF, rt, 4 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. Et—≡—Br (1 eq), –55° , 48 h 4. H^+	 (86) *cis*/*trans* = 95:5	28, 135

C_{8-11}			
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (*x* mol %), LiI (25 mol %), THF, 40°, time 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. Ph  , –78 to –20°, 5 h 4. H^+		

R	*x*	Time (h)		*trans*/*cis*	
i-Pr	5	12	(60)	>99:1	133
n-C_6H_{11}	3	—	(60)	98:2	199
Ph	3	—	(61)	98:2	199

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
D. NICKEL-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (2 mol %), THF, rt 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. , –78 to –20°, 12 h 4. H^+	 (65) *trans*/*cis* = 96:4	199
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (2 mol %), THF, 0°, 30 min 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. , –78° to rt, 2 h 4. H^+	 (66) *endo*/*exo* = 96:4	133
C_9			
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (2 mol %) 2. AcOD (3 eq), –50° to rt, 1 h 3. H^+	 (73) *endo*/*exo* > 96:4	133
C_{10}			
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (2 mol %), THF, rt 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  –78° to rt, 2 h 4. H^+	 (67) *endo*/*exo* = 98:2 2 diastereomers	199
C_{11}			
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (2 mol %), THF, rt 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. PhCHO, –78° to rt, 3 h 4. H^+	 (60) *trans*/*cis* = 98:2	199
	1. Et_2Zn, $Ni(acac)_2$ (5 mol %), LiI (25 mol %), THF, 40°, 12 h 2. I_2 (1 eq), –10°, 1 h 3. H^+	 (76)	161
	1. Et_2Zn, $Ni(acac)_2$ (5 mol %), LiI (25 mol %), THF, 40°, 12 h 2. O_2 (bubbled), TMSCl (2 eq), THF, –5°, 4 h 3. H^+	 (55)	161
	1. Et_2Zn, $Ni(acac)_2$ (5 mol %), LiI (25 mol %), THF, 40°, 12 h 2. H^+ 3. *m*-CPBA, BF_3 4. H^+	 (63)	161
C_{12}			
	1. Et_2Zn (1.8 eq), $Ni(acac)_2$ (5 mol %), LiI (0.5 eq), –78 to 40°, 2.5 h 2. O_2 (bubbled), THF, 0°, 1 h 3. H^+	 (63) *cis*/*trans* = 100:0	200
C_{13}			
	1. $Ni(acac)_2$ (10 mol %), RZnM (*x* eq), THF, 45° 2. H^+		201

RZnM	*n*	
$Ph_3ZnMgCl$	2	(93)
Ph_3ZnLi	2	(67)
$PhZnMe_2MgCl$	1.2	(65)

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
D. NICKEL-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

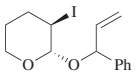
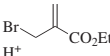
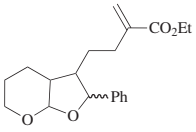
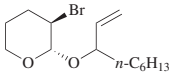
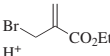
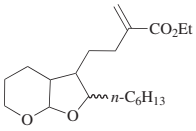
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (2 mol %), THF, rt 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  –78° to rt, 2 h 4. H^+		(75) *trans/cis* = 96:4 2 diastereoisomers 199
	1. Et_2Zn (2 eq), $Ni(acac)_2$ (3 mol %), LiI (25 mol %), THF, 40° 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  –78° to rt, 2 h 4. H^+		(65) *endo*/*exo* = 96:4 199

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)

E. PALLADIUM-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES

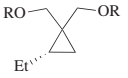
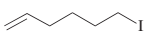
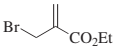
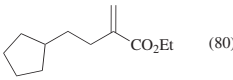
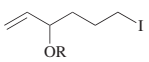
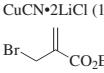
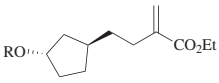
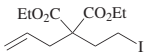
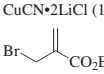
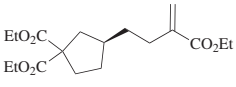
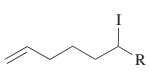
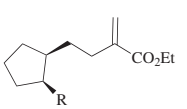
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	1. $Pd(MeCN)_2Cl_2$ (5 mol %), *p*-Tol-BINAP (6 mol %), $Zn(OTf)_2$ (10 mol %), CH_2Cl_2, rt, 1 h 2. Et_2Zn (1.5 eq), –78° to rt, 12 h 3. H_2O	 R (98) er TBS 84.0:16.0 Bn (48) 70.5:29.5 Bz (59) 87.0:13.0 TBDPS (86) 79.5:20.5	202
C_6			
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 0° to rt, 4 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  (1 eq), –78° to rt, 2 h 4. H^+	 (80)	29
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  (1 eq), –78° to rt, 2 h 4. H^+	 R *trans*/*cis* Bn (73) >99:1 Bz (47) >99:1	30
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  (1 eq), –78° to rt, 2 h 4. H^+	 (73)	29
C_7			
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  (1 eq), –78° to rt, 2 h 4. H^+	 R *cis*/*trans* Me (65) 78:22 Et (87) 75:25	134

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
E. PALLADIUM-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

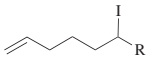
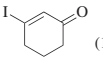
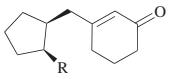
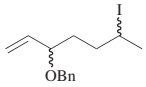
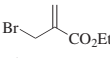
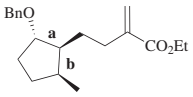
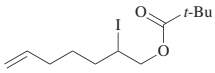
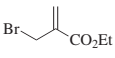
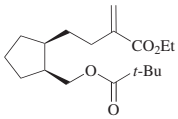
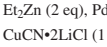
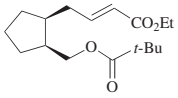
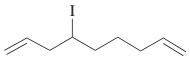
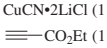
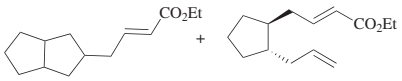
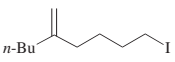
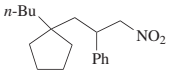
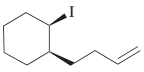
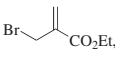
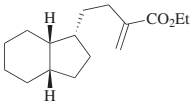
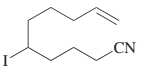
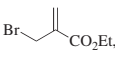
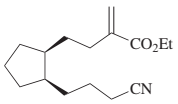
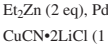
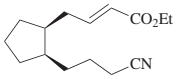
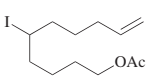
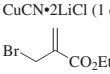
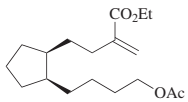
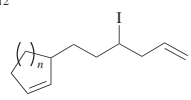
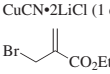
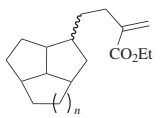
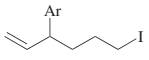
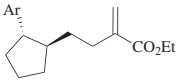
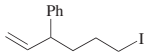
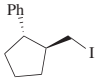
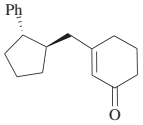
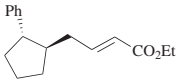
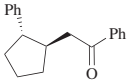
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  (1 eq), –78° to rt, 2 h 4. H^+	 R = Me (62) *cis*/*trans* 78:22; Et (81) 75:25	134
 1:1 mixture	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  (1 eq), –78° to rt, 2 h 4. H^+	 (71) **a** *cis*/*trans* < 1:99; **b** *cis*/*trans* = 95:5	28, 134 30
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  (1 eq), –78° to rt, 2 h 4. H^+	 (87) *cis*/*trans* = 78:22	30
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78° to rt, 2 h 4. H^+	 (80) *cis*/*trans* = 78:22; (*E*)/(*Z*) > 99:1	134
C_9			
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  (1 eq), –78 to –20°, 12 h 4. H^+	 **I** *endo*/*exo* = 43/57; **II** **I** + **II** (82), **I**/**II** = 86:14	134, 30
C_{10}			
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (1.5 mol %), THF, 0° to rt, 2 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. , 60°, 12 h 4. H^+	 (81)	30
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78° to rt, 2 h 4. H^+	 (90) *endo*/*exo* = 80:20	134
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (1.5 mol %), THF, rt, 2 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78° to rt, 2 h 4. H^+	 (88) *cis*/*trans* = 81:19	30
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, rt, 2 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  (1 eq), –78 to –20°, 12 h 4. H^+	 (71) *cis*/*trans* = 81:19	30
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78° to rt, 2 h 4. H^+	 (75) *cis*/*trans* = 77:23	30
C_{11-12}			
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (1.5 mol %), THF, rt, 2 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78° to rt, 2 h 4. H^+	 *n* = 1 (85) *exo*/*endo* 1:2; *n* = 2 (63) 1:2	30

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
E. PALLADIUM-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12-13} 	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (1.5 mol %), THF, 0° to rt, 2 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78° to rt, time 4. H^+	 Ar — Time (h) — *cis*/*trans* Ph — 1 — (73) — >98:2 — 30 *t*-$BuCO_2C_6H_4$ — 2 — (62) — >99:1 — 29 4-NCC_6H_4 — 2 — (83) — — — 29	
C_{12} 	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (1.5 mol %), THF, 0° to rt, 2 h 2. I_2 (1 eq), –78°, 30 min	 (77)	29
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (1.5 mol %), THF, 0° to rt, 2 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78° to rt, 2 h 4. H^+	 (80)	29
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. $\equiv$—CO_2Et (1 eq), –78 to –20°, 12 h 4. H^+	 (64)	29
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3. PhCOCl, –10°, 12 h 4. H^+	 (76)	29

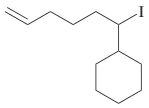
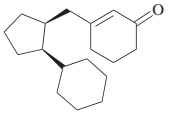
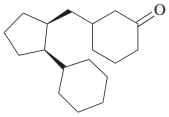
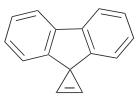
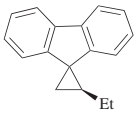
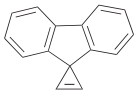
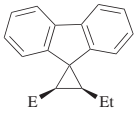
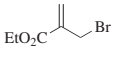
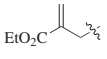
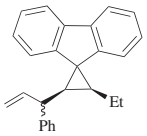
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –78° to rt, 2 h 4. H^+	 (65) *cis*/*trans* = 70:30	134, 30
	1. Et_2Zn (2 eq), $PdCl_2(dppf)$ (2 mol %), THF, 20°, 5–20 h 2. CuCN•2LiCl (1 eq), THF, –40 to 0°, 1 h 3.  , –40 to 0°, 2 h 4. H^+	 (52) *cis*/*trans* = 70:30	134
C_{15} 	1. $Pd(MeCN)_2Cl_2$ (5 mol %), *p*-Tol-BINAP (6 mol %), $Zn(OTf)_2$ (10 mol %), CH_2Cl_2, rt, 1 h 2. Et_2Zn (1.5 eq), –78° to rt, 12 h 3. H_2O	 (20) er —	202
	1. $Pd(MeCN)_2Cl_2$ (5 mol %), *p*-Tol-BINAP (5 mol %), $Zn(OTf)_2$ (10 mol %), CH_2Cl_2, rt, 1 h 2. Et_2Zn (1.5 eq), –78° to rt, 12 h 3. H_2O	 (99) er 95.5:4.5	202

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
E. PALLADIUM-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	1. Pd(MeCN)$_2$Cl$_2$ (5 mol %), *p*-Tol-BINAP (5 mol %), Zn(OTf)$_2$ (10 mol %), CH_2Cl_2, rt, 1 h 2. Et_2Zn (1.5 eq), –78° to rt, 12 h 3. CuCN•2LiCl (3 eq), THF, –78° 4. E-X (4 eq), –78° to rt	 *cis*/*trans* > 95:5	202

E-X	E		er
I_2[a]	I	(89)	95.0:5.0
BzCl	Bz	(75)	96.5:3.5
EtCOCl	EtCO	(66)	96.5:3.5
Ph—≡—Br	Ph—≡—≈	(81)	95.5:4.4
Et—≡—CH_2Br	Et—=•=—≈	(93)	95.0:5.0
allyl-Br	allyl	(100)	95.0:5.0
		(93)	95.5:4.4

1. Pd(MeCN)$_2$Cl$_2$ (5 mol %), *p*-Tol-BINAP (6 mol %), Zn(OTf)$_2$ (10 mol %), CH_2Cl_2, rt, 30 min 2. Et_2Zn (1.5 eq), –78° to rt, 5 h 2. CuCN•2LiCl (3 eq), THF, –78° 3. Ph  Br (4 eq), –78° to rt		(95)[b,c] *cis*/*trans* > 95:5 er 95.5:4.5	202

[a] No transmetalation to copper occurs in this reaction. (*S*)-*p*-Tol-BINAP was used as the ligand.

[b] The ratio of branched to linear product is 86:14.

[c] A mixture of diastereomers in the *exo* position was formed.

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)

F. MANGANESE AND COPPER-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES

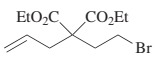
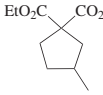
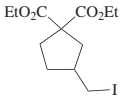
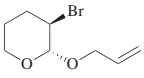
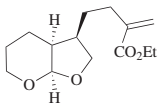
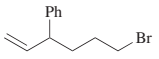
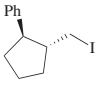
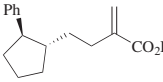
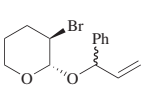
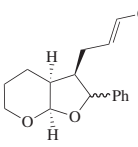
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	1. Et_2Zn (1.1 eq), $MnBr_2$ (5 mol %), CuCl (3 mol %), DMPU, 60°, 7 h 2. H^+	 (71)	203
	1. Et_2Zn (1.1 eq), $MnBr_2$ (5 mol %), CuCl (3 mol %), DMPU, 60°, 7 h 2. I_2	 (75)	203
C_8 	1. Et_2Zn (1.1 eq), $MnBr_2$ (5 mol %), CuCl (3 mol %), DMPU, 60°, 12 h 2. CuCN•2LiCl (1.5 eq), 0°, 1 h 3.  (1.5 eq), –20°, 1 h 4. H^+	 (71) single isomer	203
C_{12} 	1. Et_2Zn (1.1 eq), $MnBr_2$ (5 mol %), CuCl (3 mol %), DMPU, 60°, 7 h 2. I_2 (1.5 eq), 0°, 30 min	 (80) single isomer	203
	1. Et_2Zn (1.1 eq), $MnBr_2$ (5 mol %), CuCl (3 mol %), DMPU, 60°, 7 h 2.  (1.2 eq), –20°, 1 h 3. H^+	 (73)	203
C_{14} 	1. Et_2Zn (1.1 eq), $MnBr_2$ (5 mol %), CuCl (3 mol %), DMPU, 60°, 12 h 2. CuCN•2LiCl (1.5 eq), –20 to 0°, 1 h 3. $\equiv$—CO_2Et (1.5 eq), –30°, 1 h 4. H^+	 (63) 1:1 epimer	203

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
F. MANGANESE AND COPPER-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

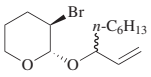
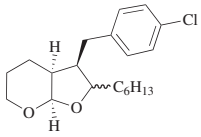
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	1. Et_2Zn (1.1 eq), $MnBr_2$ (5 mol %), CuCl (3 mol %), DMPU, 60°, 12 h 2. $PdCl_2$ (dppf) (5 mol %) 3. 4-ClC_6H_4I (1.5 eq) , 60°, 4 h 4. H^+	 (61)	203

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES

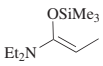
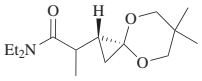
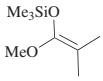
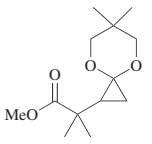
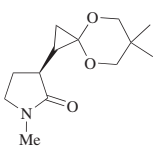
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3			
	1. BuLi (1.2 eq), 0°, 30 min 2. $ZnCl_2$ (1.2 eq), 0°, 30 min 3.  (1 eq), 0°, 19 h 4. H^+	 (64) dr 93.5:6.5	130
C_4			
	1. BuLi (*x* eq), 0°, 30 min 2. $ZnCl_2$ (*x* eq), 0°, 30 min 3. BuLi (1 eq), 0° to rt, 1 h 4.  (1 eq), rt, 17 h 5. H^+		130
		x: 1 (58); 2 (97)	
	1. LDA, –70°, 1.5 h 2. $ZnCl_2$, –70 to 0°, 15 min 3. BuLi, 0°, 30 min 4.  (0.5 eq), 0°, 30 min 5. H^+	 (85) dr 99.0:1.0	130

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

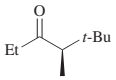
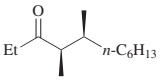
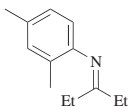
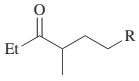
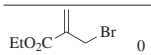
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. 2-methylprop-1-ene, temp, press., time 8. H^+	 R — Temp (°) — Press. (atm) — Time (h) Ph — 65 — 4 — 60 — (8) $Et_2NC_6H_4$ — 65 — 4 — 60 — (19) $2\text{-}MeC_6H_4$ — 65 — 4 — 60 — (54) $3\text{-}MeC_6H_4$ — 65 — 4 — 60 — (10) $4\text{-}MeC_6H_4$ — 65 — 4 — 60 — (12) $2,4\text{-}Me_2C_6H_3$ — 65 — 4 — 60 — (85) $2,4\text{-}Me_2C_6H_3$ — 80 — 5 — 36 — (84) $2\text{-}Me\text{-}4\text{-}Et_2NC_6H_4$ — 65 — 4 — 60 — (84) $2,4,6\text{-}Me_3C_6H_2$ — 65 — 4 — 72 — (69) Me_2N — 65 — 4 — 60 — (6)	204
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. Oct-1-ene (1.2 eq), hexane, 65°, 12 h 8. H^+	 R — dr $MeO(CH_2)_2$ (17) 70:30 Ph (62) 70:30 $2\text{-}MeOC_6H_4$ (7) 70:30 $4\text{-}MeOC_6H_4$ (81) 70:30 $4\text{-}Et_2NC_6H_4$ (89) 70:30 $2,4\text{-}Me_2C_6H_3$ (92) 67:33 Me_2N (28) 70:30	204
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. Ethylene, 50°, 20 h, 1 atm 8. RX (2.2 eq), TMEDA (*x* eq), $PdCl_2(PPh_3)_2$ (*y* mol %), temp, time 9. H^+	 RX — *x* — *y* — Temp — Time (h)  0 0 0° 4 (85) $4\text{-}AcC_6H_4I$ 2 5 rt 8 (86) $4\text{-}O_2NC_6H_4I$ 2 5 rt 8 (80)	204
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. Alkene (*x* eq), solvent, temp, press., time 8. H^+	 Alkene — *x* — R — Solvent — Temp (°) — Press. (atm) — Time (h) ethylene — — Et — hexane — 50 — 1 — 12 (94) propene — — *i*-Pr — hexane — 65 — 1 — 60 (86) methylenecyclohexane — 3 —  — — 65 — 1 — 12 (77)	204

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

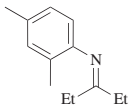
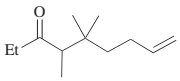
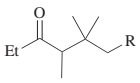
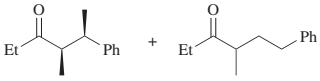
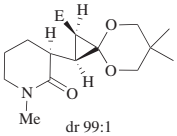
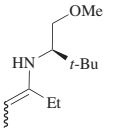
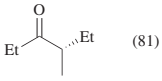
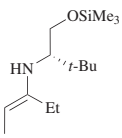
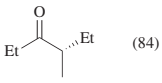
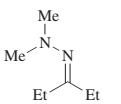
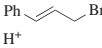
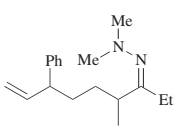
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. 2-Methylprop-1-ene, 65°, 4 atm, 72 h 8. Allyl-Br (2.4 eq), rt, 3 h 9. H^+	 (82)	204
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. 2-Methylprop-1-ene, 65°, 4 atm, 72 h 8. Alkene (2.4 eq), MeI (0.2 eq), TMSCl (*x* eq), TMEDA (2 eq), CuCN (*y* eq), 0°, time 9. H^+	 Alkene *x* *y* R Time (h)  2.4 0.3  6 (71)  0 1  8 (78)	204
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. Styrene (1.2 eq), hexane, 30°, 12 h 8. H^+	 **I** dr 66:34 **II** **I + II** (90), **I/II** = 54:46	204
	1. Mesityllithium (*x* eq), –70 to 0°, 1.5 h 2. $ZnCl_2$ (*x* eq), 0°, 30 min 3. BuLi (*x* eq), –70 to 0°, 30 min 4.  (1 eq), 0°, 30 min 5. E^+	 dr 99:1 *x* E^+ E 1 H^+ H (53) 1 D^+ D (53) 1 I_2 I (55) 2 H^+ H (100)	130
	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. Mesityllithium (1 eq), –78 to 0° 4. Hexane (2 mL), 45°, 30 min 5. Ethylene, 40°, 20 atm, 24 h 6. H^+	 (81) er 79.0:21.0	205
	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. MeLi (1 eq), –78 to 0° 4. Hexane (2 mL), 45°, 30 min 5. Ethylene, 40°, 20 atm, 24 h 6. H^+	 (84) er 59.0:41.0	205
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Ethylene (excess), Et_2O, 35°, 8 atm, 4 days 5. CuCN (1 eq) 6.  (3 eq) 7. H^+	 (74) dr 50:50	131

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

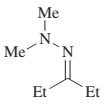
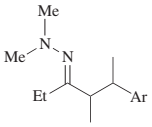
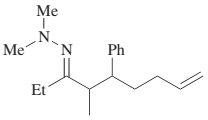
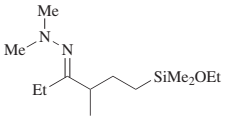
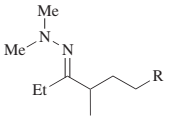
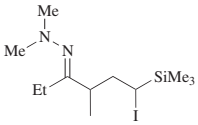
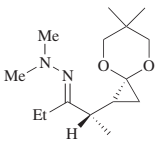
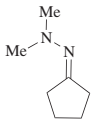
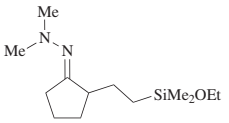
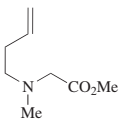
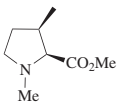
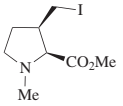
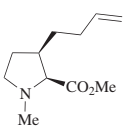
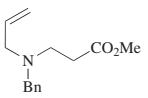
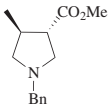
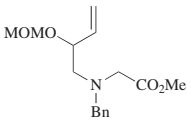
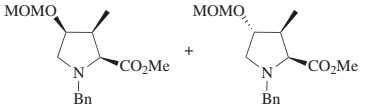
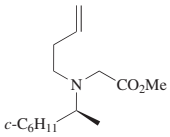
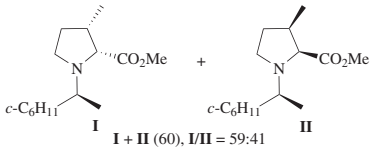
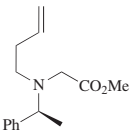
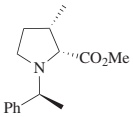
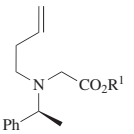
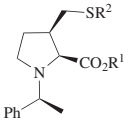
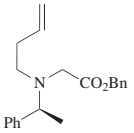
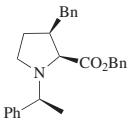
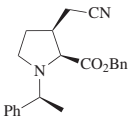
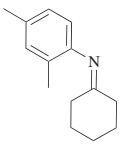
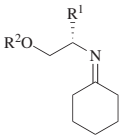
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
	1. *t*-BuLi (1 eq), –70 to 0°, 1 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. $ArCH{=}CH_2$, Et_2O, 35°, 8 atm, 11 days 5. H^+	 Ar (46) dr 50:50: Ph; 4-$MeOC_6H_4$ (33) 50:50; 2-$CF_3C_6H_4$ (69) 50:50	130
	1. *t*-BuLi (1 eq), –70 to 0°, 1 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Styrene, Et_2O, 35°, 8 atm, 11 days 5. CuCN (1 eq) 6. Allyl-Br (3 eq) 7. H^+	 (45) dr 50:50	130
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. $SiMe_2OEt$, solvent, rt, time 5. H^+	 Solvent / Time: Et_2O 2 h (73); DME 4 d (97); THF 4 d (30)	132
	1. *t*-BuLi (1 eq), –70 to 0°, 1 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. R  , rt, time 5. H^+	 R / Time: Me_3Si 2 d (87); (*t*-BuO)Me_2Si 6 h (85); Ph_3Si 9 d (58)	132
	1. *t*-BuLi (1 eq), –70 to 0°, 1 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Me_3Si  (2 eq), Et_2O, 35°, 1 d 5. I_2 (2 eq), 0°, 1 h	 (75) dr 50:50	132
	1. Base (*x* eq), –70°, 1.5 h 2. $ZnBr_2$ (*x* eq), –70 to 0°, 15 min 3. BuLi (*x* eq), 0°, 30 min 4.  (*y* eq), 0°, 30 min 5. H^+	 Base *x* *y* dr: LDA 2 2 (96) 98.0:2.0; *t*-BuLi 2 1 (96) 94.5:5.5; *t*-BuLi 1 1 (58) 91.5:8.5	130
	1. *t*-BuLi (1 eq), –70 to 0°, 1 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. $EtOMe_2Si$  , DME, rt, 4 d 5. H^+	 (45)	132
C_6			
	1. LDA (2 eq), Et_2O, –40 to 0° 2. $ZnBr_2$ (2 eq), –40° to rt 3. rt, 3 h 4. H^+	 (70) single diastereomer	120
	1. LDA (2 eq), Et_2O, –40 to 0° 2. $ZnBr_2$ (2 eq), –40° to rt 3. rt, 3 h 4. I_2 (2 eq), 0°, 30 min	 (64)	120
	1. LDA (2 eq), Et_2O, –40 to 0° 2. $ZnBr_2$ (2 eq), –40° to rt 3. rt, 3 h 4. CuCN (2 eq), –20 to –5°, 15 min 5. Allyl-Br (2.5 eq), –40 to 0°, 1 h 6. H^+	 (55)	120

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	1. LDA (1.1 eq), THF, –78 to 0° 2. $ZnBr_2$ (5 eq), inverse addition 3. H^+	 (51) dr 87:13	125
	1. LDA (1.1 eq), Et_2O, –40 to 0°, 1 h 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to 0°, 3 h 3. H^+	 **I** **II** **I** + **II** (75), **I/II** = 85:15	120, 206
	1. LDA (1 eq), Et_2O, –40 to 0°, 1 h 2. $ZnBr_2$ (2 eq), Et_2O, –40° to rt 3. H^+	 **I** **II** **I** + **II** (60), **I/II** = 59:41	120
	1. LDA (2 eq), Et_2O, –40 to 0° 2. $ZnBr_2$ (2 eq), –40° to rt 3. rt, 3 h 4. H^+	 (93) dr 98:2	120
	1. LDA (1 eq), THF, –78°, 1 h 2. $ZnBr_2$ (x eq), –90° to rt 3. CuCN•2LiCl (1.2 eq), THF, 0°, 10 min 4. $R^2SSO_2R^2$ (2 eq), rt, 12 h 5. H^+	 R^1 R^2 x dr Me Ph 2.5 (74) — Et Me 3 (71) 98:2	123, 207 119
	1. LDA (1 eq), –78°, 30 min 2. $ZnBr_2$ (3 eq), –78° to rt 3. PhI (1.3 eq), $Pd(dba)_2$ (2 mol %), $P(Op\text{-Tol})_3$ (5 mol %), rt, 30 min 4. H^+	 (50)	208
	1. LDA (1 eq), THF, –78°, 1 h 2. $ZnBr_2$ (2.5 eq), –90° to rt 3. CuCN•2LiCl (1.2 eq), THF, 0°, 10 min 4. TosCN (1 eq), rt, 10 h 5. H^+	 (68)	122
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. Alkene (x eq), hexane, temp, press., time 8. H^+		204

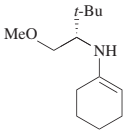
Alkene	x	R	Temp (°)	Press. (atm)	Time (h)	
ethylene	—	Et	65	1	24	(90)
propene	—	*i*-Pr	65	8	24	(88)
2-methylprop-1-ene	—	*t*-Bu	80	5	72	(24)
styrene	2	$Ph(CH_2)_2$	50	—	12	(87)

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

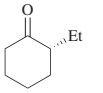
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. R^3Li (1 eq), –78 to 0° 4. Hexane, 45°, 30 min 5. Alkene, temp, press. time 6. H^+		205

R^1	R^2	R^3	Alkene	R^4	Temp (°)	Press. (atm)	Time (h)		er
i-Pr	Me	Me	ethylene	Et	40	20	24	(85)	96.0:4.0
i-Pr	Me	Me	propene	*i*-Pr	60	8	48	(45)	92.0:8.0
i-Pr	TMS	Me	ethylene	Et	40	20	24	(81)	97.0:3.0
n-Bu	TBS	*n*-Bu	ethylene	Et	40	20	24	(14)	77.5:22.5
Ph	TMS	Me	ethylene	Et	40	20	24	(86)	88.3:11.7

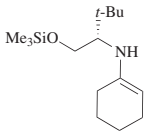
730



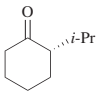
1. Mesityllithium (1 eq), Et_2O, 0°, 12 h
2. $ZnCl_2$ (1 eq), 0°, 50 min
3. RLi (1 eq), –78 to 0°
4. Hexane (2 mL), 45°, 30 min
5. Ethylene, 40°, 20 atm, 24 h
6. H^+



R		er	Refs.
Me	(87)	96.8:3.2	205
t-Bu	(73)	94.0:6.0	

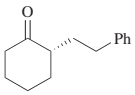


1. Mesityllithium (1 eq), Et_2O, 0°, 12 h
2. $ZnCl_2$ (1 eq), 0°, 50 min
3. MeLi (1 eq), –78 to 0°
4. Hexane (2 mL), 45°, 30 min
5. Propene, 60°, 8 atm, 48 h
6. H^+

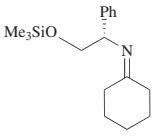


(47) er 96.5:3.5 — 205

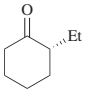
1. Mesityllithium (1 eq), Et_2O, 0°, 12 h
2. $ZnCl_2$ (1 eq), 0°, 50 min
3. MeLi (1 eq), –78 to 0°
4. Hexane (2 mL), 45°, 30 min
5. Styrene (1.5 eq), 70°, 48 h
6. H^+



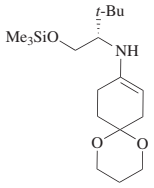
(71) er 88.5:11.5 — 205



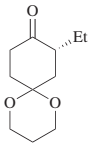
1. Mesityllithium (1 eq), Et_2O, 0°, 12 h
2. $ZnCl_2$ (1 eq), 0°, 50 min
3. MeLi (1 eq), –78 to 0°
4. Hexane (2 mL), 45°, 30 min
5. Ethylene, 40°, 20 atm, 24 h
6. H^+



(86) er 88.5:11.5 — 205

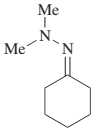


1. Mesityllithium (1 eq), Et_2O, 0°, 12 h
2. $ZnCl_2$ (1 eq), 0°, 50 min
3. MeLi (1 eq), –78 to 0°
4. Hexane (2 mL), 45°, 30 min
5. Ethylene, 40°, 20 atm, 24 h
6. H^+

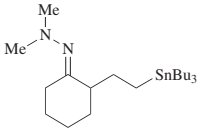


(89) er 95.0:5.0 — 205

731

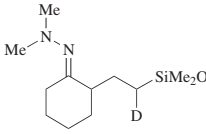


1. *t*-BuLi (1 eq), Et_2O, –78 to 0°, 65 h
2. BuZnI (1 eq), THF, 0°, 1.5 h
3.  ($SnBu_3$ (2 eq), 0°
4. 30°, 44 h
5. H^+



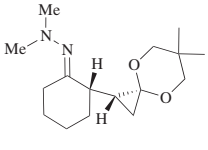
(45) — 129

1. *t*-BuLi (1 eq), –70 to 0°, 4 h
2. $ZnBr_2$ (1 eq), 0°, 1 h
3. BuLi (1 eq), 0° to rt, 1 h
4. $EtOMe_2Si$  , rt, 4 days
5. D^+



(95) dr 50:50 — 132

1. *t*-BuLi (*x* eq), –50°, 4 h
2. $ZnCl_2$ (*x* eq), 0°, 30 min
3. BuLi (*x* eq), –78 to 0°, 30 min
4.  , 0°, 10 min
5. H^+



dr 98.0:2.0

x		Refs.
1	(63)	130
2	(100)	

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

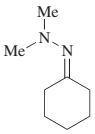
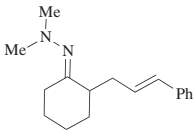
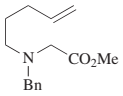
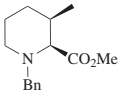
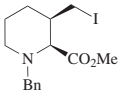
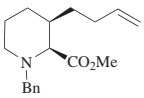
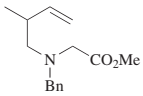
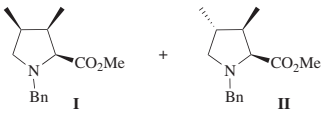
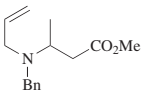
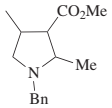
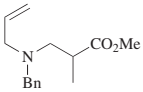
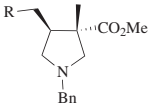
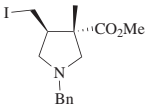
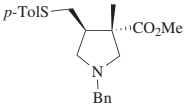
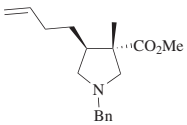
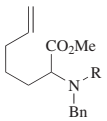
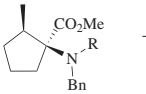
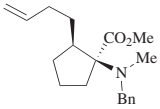
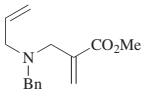
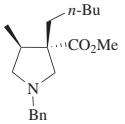
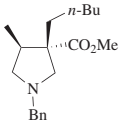
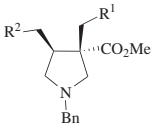
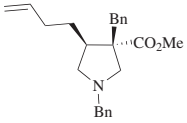
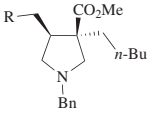
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. PhCHO (11 eq), 0°, 1 h 5. H^+	 (76) (*E*)/(*Z*) = 82:18–67:33	209
C_7 	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to 20°, 5 h 3. H^+	 (66)	128
	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to 20°, 5 h 3. I_2 (1.5 eq), 0°, 30 min	 (81) single isomer	128
	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to 20°, 5 h 3. CuCN (1 eq), –20°, 30 min 4. Allyl-Br (2 eq), –20 to 0°, 1 h 5. H^+	 (65) single isomer	128
	1. LDA (1.1 eq), Et_2O, –40 to 0° 2. $ZnBr_2$ (1.1 eq), –40° to rt 3. rt, 3 h 4. H^+	 **I** + **II** (65), **I**/**II** = 20:80	120, 206
	1. LDA (1.1 eq), THF, –78 to 0° 2. $ZnBr_2$ (5 eq), inverse addition 3. H^+	 (91) 3 diastereomers 52:35:10	125
	1. LDA (1.1 eq), THF, –78 to 0° 2. $ZnBr_2$ (1.2 eq), 0° to rt, 3 h 3. R^+	 single isomer R: H (75), D (70)	125
	1. LDA (1.1 eq), THF, –78 to 0° 2. $ZnBr_2$ (1.2 eq), 0° to rt, 3 h 3. I_2 (1.2 eq), 0°, 30 min	 (68) single isomer	125
	1. LDA (1.1 eq), THF, –78 to 0° 2. $ZnBr_2$ (1.2 eq), 0° to rt, 3 h 3. CuCN (1.2 eq), THF, 0°, 1 h 4. *p*-TolSSO$_2$Tol-*p* (2 eq), rt, 12 h 5. H^+	 (67) single isomer	125
	1. LDA (1.1 eq), THF, –78 to 0° 2. $ZnBr_2$ (1.2 eq), 0° to rt, 3 h 3. CuCN (1.2 eq), THF, 0°, 1 h 4. Allyl-Br (2 eq), –20 to 0°, 3 h 5. H^+	 (56) single isomer	125
	1. LDA (5 eq), THF, –40 to 10°, 10 min 2. $ZnBr_2$ (4 eq), –40° to rt, time 3. H^+	 R: Me, 20 min (80), 80:20; Bn, 3 h (19), 80:20	206
	1. LDA (5 eq), THF, –40 to 10°, 10 min 2. $ZnBr_2$ (4 eq), –40° to rt, 4 h 3. CuCN (4 eq), –40° to rt, 1 h 4. Allyl-Br (4 eq), rt, 12 h 5. H^+	 (58) dr 80:20	206

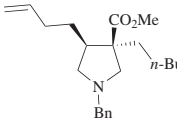
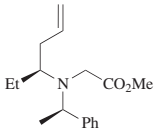
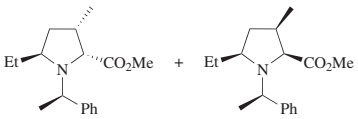
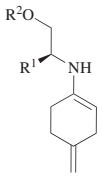
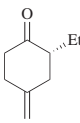
TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. Bu_3ZnLi (1.3 eq), Et_2O, –78°, 1 h 2. $ZnBr_2$ (3 eq), 0° 3. rt, 30 min 4. H^+	 (54) single isomer	126
	1. $Bu_2Cu(CN)Li_2$ (1.5 eq), Et_2O, –40°, 2 h 2. $ZnBr_2$ (3 eq), Et_2O, rt 3. H^+	 (52) single isomer	126
	1. $R^1Cu(CN)ZnBr•xLiBr$ (2 eq), Et_2O, rt, 2 h 2. $(R^2)^+$		126

R^1	x	R^2		dr
n-Bu	1	H	(60)	84:16
Ph	3	H	(55)	>95:5
Ph	3	D	(53)	—
2-propenyl	3	H	(60)	>95:5
1-cyclohexenyl	3	H	(52)	>95:5

	1. PhCu(CN)ZnBr•3LiBr (2 eq), Et_2O, rt, 2 h 2. Allyl-Br (2 eq), rt, 24 h 3. H^+	 (57)	126
	1. Bu_2Zn (2 eq), Et_2O, rt 2. See table.		210, 211

Step 2	R		*cis*/*trans*
H^+	H	(50)	75:25
MeOD	D	(83)	76:24
I_2 (2 eq)	I	(48)	76:24

	1. Bu_2Zn (2 eq), Et_2O, rt 2. CuCN (0.25 eq) 3. Allyl-Br (excess) 4. H^+	 (68) *cis*/*trans* = 76:24	210, 211
	1. LDA (1 eq), Et_2O, –40 to 0°, 1 h 2. $ZnBr_2$ (2 eq), Et_2O, –40° to rt 3. H^+	 **I** + **II** (69), **I**/**II** = 40:60	120
	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. MeLi (1 eq), –78 to 0° 4. Hexane (2 mL), 45°, 30 min 5. Ethylene, 40°, 20 atm, 24 h 6. H^+		205

R^1	R^2		er
i-Pr	Me	(93)	95.5:4.5
t-Bu	TMS	(92)	99.0:1.0

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

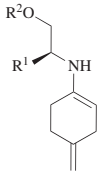
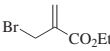
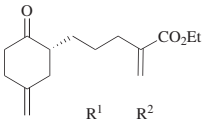
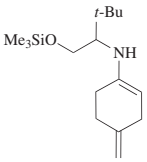
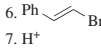
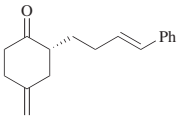
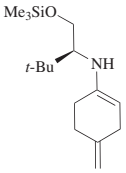
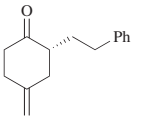
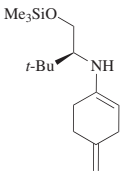
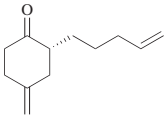
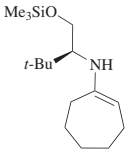
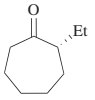
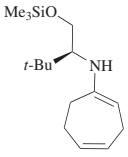
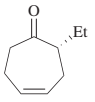
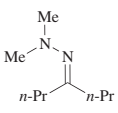
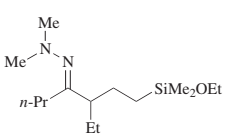
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. MeLi (1 eq), –78 to 0° 4. Hexane (2 mL), 45°, 30 min 5. Ethylene, 40°, 20 atm, 24 h 6.  (2 eq), THF, $CuBr•Me_2S$ (1 eq), –78°, 50 min 7. 0°, 3 h 8. H^+	 R^1 R^2 er *i*-Pr Me (86) 95.0:5.0 *t*-Bu TMS (84) 98.5:1.5	205
	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. MeLi (1 eq), –78 to 0° 4. Hexane (2 mL), 45°, 30 min 5. Ethylene, 40°, 20 atm, 24 h 6.  (2 eq), THF, $Pd(PPh_3)_4$ (5 mol %), rt, 12 h 7. H^+	 (90) (*E*)/(*Z*) > 99:1 er 98.5:1.5	205
	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. MeLi (1 eq), –78 to 0° 4. Hexane (2 mL), 45°, 30 min 5. Ethylene, 40°, 20 atm, 24 h 6. PhI (2 eq), THF, $Pd(PPh_3)_4$ (5 mol %), 50°, 12 h 7. H^+	 (83) er 98.5:1.5	205
	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. MeLi (1 eq), –78 to 0° 4. Hexane (2 mL), 45°, 30 min 5. Ethylene, 40°, 20 atm, 24 h 6. $CuBr•Me_2S$ (20 mol %), –78° 7. Allyl-Br (2 eq), –78° 8. 0°, 3 h 9. H^+	 (89) er 98.5:1.5	205
	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. MeLi (1 eq), –78 to 0° 4. Hexane (2 mL), 45°, 30 min 5. Ethylene, 40°, 20 atm, 24 h 6. H^+	 (82) er 98:2	205
	1. Mesityllithium (1 eq), Et_2O, 0°, 12 h 2. $ZnCl_2$ (1 eq), 0°, 50 min 3. MeLi (1 eq), –78 to 0° 4. Hexane (2 mL), 45°, 30 min 5. Ethylene, 40°, 20 atm, 24 h 6. H^+	 (93) er 98:2	205
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4.  , DME, rt, 4 d 5. H^+	 (77)	132

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

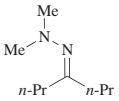
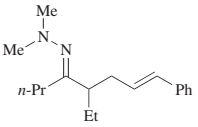
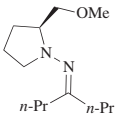
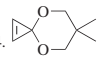
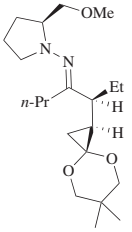
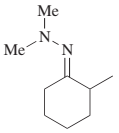
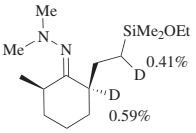
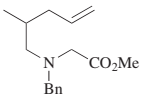
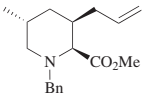
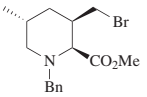
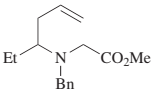
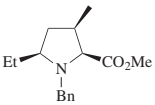
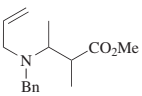
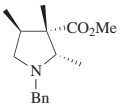
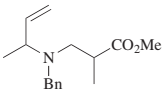
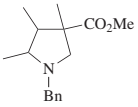
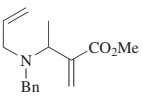
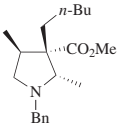
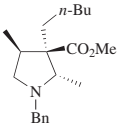
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. PhCHO (11 eq), 0°, 1 h 5. H^+	 (83) (*E*)/(*Z*) = 84:16	209
	1. *t*-BuLi (2 eq), –70°, 1.5 h 2. $ZnCl_2$ (2 eq), –70 to 0°, 15 min 3. BuLi (2 eq), 0°, 3 min 4.  (1 eq), 0°, 2 h 5. H^+	 (92) dr 89.0:11.0	130
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4.  $SiMe_2OEt$, DME, rt, 4 d 5. D^+	 (73) dr 68:32	132
C_8			
	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to 20°, 5 h 3. CuCN (1 eq), –20°, 30 min 4. Allyl-Br (2 eq), –20 to 0°, 1 h 5. H^+	 (62) single isomer	128
	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to 20°, 5 h 3. NBS (2 eq), –30 to 0°, 2 h 4. H^+	 (56) single isomer	128
	1. LDA (1.1 eq), Et_2O, –40 to 0°, 1 h 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to rt, 3 h 3. H^+	 (60) single isomer	120, 206
	1. LDA (1.1 eq), Et_2O, –78 to 0° 2. ZnI_2 (5 eq), inverse addition 3. H^+	 (—)	206
	1. LDA (1.1 eq), Et_2O, –78 to 0° 2. ZnI_2 (5 eq), inverse addition 3. H^+	 (—) dr 83:12:5	206
	1. Bu_3ZnLi (1 eq), Et_2O, –78°, 1 h 2. $ZnBr_2$ (3 eq), 0° 3. rt, 30 min 4. H^+	 (43) dr 85:15	126
	1. Bu_2Zn (2 eq) 2. H^+	 (56) *cis*/*trans* = 87:13	211

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

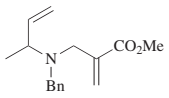
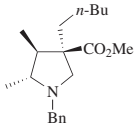
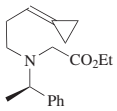
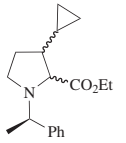
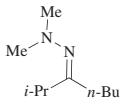
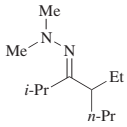
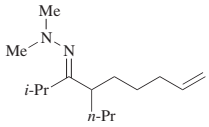
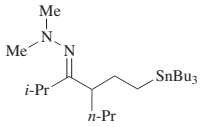
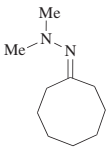
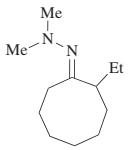
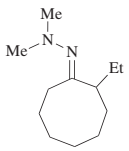
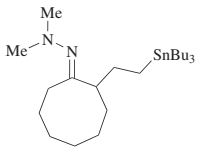
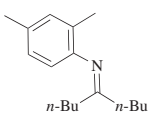
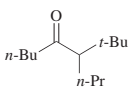
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	1. Bu_2Zn (2 eq), Et_2O, rt 2. H^+	 (64) *cis*/*trans* = 85:15	210, 211
	1. LDA (1.1 eq), Et_2O, –78°, 30 min 2. $ZnBr_2$ (3 eq), –40° to rt 3. H^+	 (68) single isomer	207
	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. H^+	 (74)	209
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Ethylene (excess), Et_2O, 35°, 8 atm, 4 d 5. CuCN (1 eq) 6. Allyl-Br (3 eq) 7. H^+	 (71)	131
	1. *t*-BuLi (1 eq), Et_2O, –78 to 0°, 65 h 2. BuZnI (1 eq), THF, 0°, 1.5 h 3. $SnBu_3$ (2 eq), 0° 4. 30°, 44 h 5. H^+	 (66)	129
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Ethylene (excess), Et_2O, 35°, 8 atm, 4 d 5. H^+	 (83)	131
	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. H^+	 (85)	209
	1. *t*-BuLi (1 eq), Et_2O, –78 to 0°, 65 h 2. BuZnI (1 eq), THF, 0°, 1.5 h 3. $SnBu_3$ (2 eq), 0° 4. 30°, 44 h 5. H^+	 (52)	129
C_9			
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. 2-methylprop-1-ene, neat, 80°, 5 atm, 72 h 8. H^+	 (76)	204

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

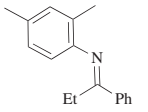
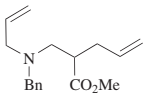
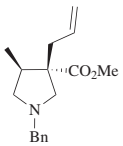
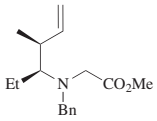
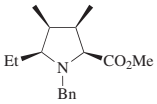
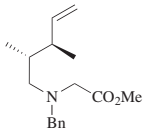
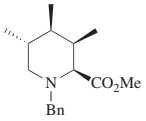
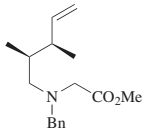
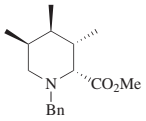
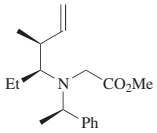
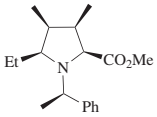
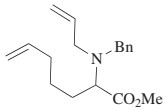
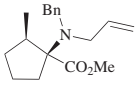
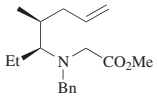
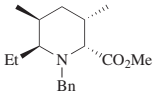
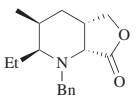
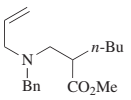
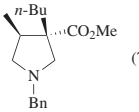
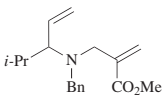
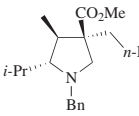
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	1. LDA (1.1 eq), THF, 0°, 6 h 2. Solvents are removed, 0°, 0.1 mmHg, 30 min 3. Et_2O (0.5 mL/mmol) 4. $ZnCl_2$ (1 eq), 0°, 30 min 5. BuLi (1 eq), 0° to rt 6. Solvents are removed, rt, 0.1 mmHg, 10 min 7. Propene, neat, 80°, 10 atm, 72 h 8. H^+	 (74)	204
	1. LDA (1.1 eq), THF, –78 to 0° 2. $ZnBr_2$ (1.2 eq), 0° to rt, 3 h 3. H^+	 (78) single isomer	125
	1. LDA (1.1 eq), Et_2O, –40 to 0°, 1 h 2. $ZnBr_2$ (1.1 eq), –40° to rt, 3 h 3. H^+	 (62) dr 95:5	120, 206
	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), –40 to 20°, 5 h 3. H^+	 (70) single isomer	128, 206
	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), –40 to 20°, 5 h 3. H^+	 (68) dr 90:10	128, 206
	1. LDA (1 eq), Et_2O, –40 to 0°, 1 h 2. $ZnBr_2$ (2 eq), Et_2O, –40° to rt 3. H^+	 (65) dr >95:5	120
C_{10}			
	1. LDA (5 eq), THF, –40 to 10°, 10 min 2. $ZnBr_2$ (4 eq), –40° to rt, 3 h 3. H^+	 (36) dr 80:20	206
	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to –20°, 5 h 3. H^+	 (60)	128, 206
	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to –20°, 5 h 3. O_2 (bubbled), 1 h 4. H^+	 (60)	128
	1. LDA (1.1 eq), THF, –78 to 0° 2. $ZnBr_2$ (5 eq), inverse addition 3. H^+	 (70) single isomer	125
	1. Bu_2Zn (2 eq) 2. H^+	 (56) *cis*/*trans* = 96:4	211

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

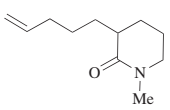
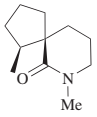
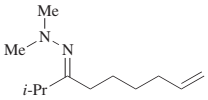
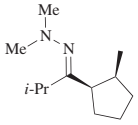
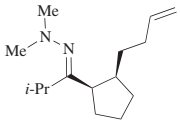
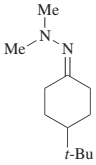
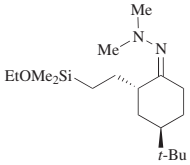
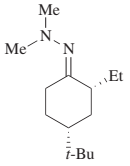
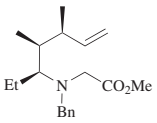
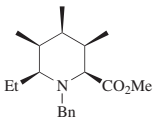
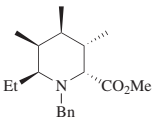
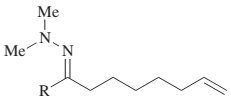
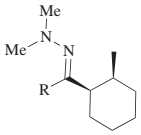
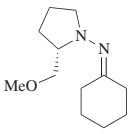
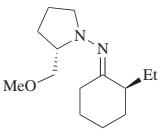
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. BuLi (1 eq), 0°, 1 h 4. rt, 4 d 5. H^+	 (70) dr 100:0	127
	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. BuLi (1 eq), 0°, 1 h 4. rt, 24 h 5. H^+	 (90) dr 94.0:6.0	127
	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. BuLi (1 eq), 0°, 1 h 4. rt, 24 h 5. CuCN (1 eq), HMPA (3 eq) 6. Allyl-Br (3 eq), 0°, 3 h 7. H^+	 (78) dr 94.0:6.0	127
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. $EtOMe_2Si$  , DME, rt, 4 d 5. H^+	 (64) dr 72:28	132
	1. BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnCl_2$ (1 eq), Et_2O, 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. H^+	 (74) dr 62:38	209
C_{11} 	1. LDA (1.1 eq), Et_2O, –40 to –10°, 30 min 2. $ZnBr_2$ (1.1 eq), Et_2O, –40 to 20°, 5 h 3. H^+	 +  **I** **II** **I + II** (45), **I/II** = 38:62	128, 206
C_{11-12} 	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. BuLi (1 eq), 0° 4. rt, time 5. H^+	 R Time dr *i*-Pr 24 h (83) 95.5:4.5 *t*-Bu 4 d (42) 100:0	127
C_{11} 	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Ethylene, Et_2O, rt to 35°, 8 atm, 4 d 5. H^+	 (42) dr 82:18	131

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

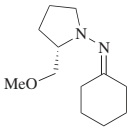
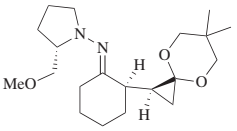
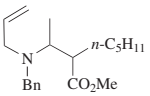
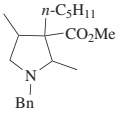
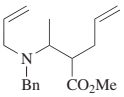
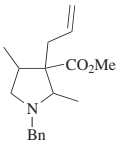
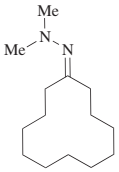
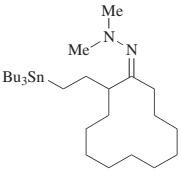
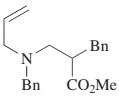
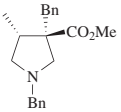
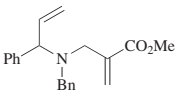
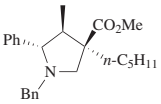
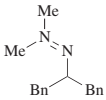
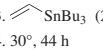
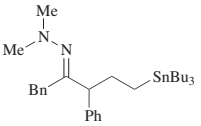
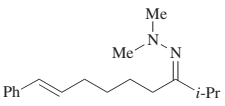
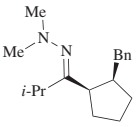
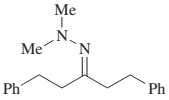
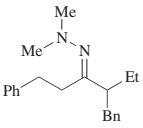
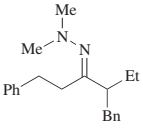
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	1. BuLi (2 eq), –70°, 1.5 h 2. $ZnCl_2$ (2 eq), –70 to 0°, 15 min 3. BuLi (2 eq), 0°, 30 min 4.  (1 eq), 0°, 2 h 5. H^+	 (87) dr 99.0:1.0	130
C_{12} 	1. LDA (1.1 eq), Et_2O, –78 to 0° 2. ZnI_2 (5 eq), inverse addition 3. H^+	 (—) dr 69:22:9	206
	1. LDA (1.1 eq), Et_2O, –78 to 0° 2. ZnI_2 (5 eq), inverse addition 3. H^+	 (—) dr 52:36:8:4	206
	1. *t*-BuLi (1 eq), Et_2O, –78 to 0°, 6.5 h 2. BuZnI (1 eq), THF, 0°, 1.5 h 3. Bu_3Sn  (2 eq), 0° 4. 30°, 44 h 5. H^+	 (55)	129
C_{13} 	1. LDA (1.1 eq), THF, –78 to 0° 2. $ZnBr_2$ (5 eq), inverse addition 3. H^+	 (82) single isomer	125
	1. Bu_2Zn (2 eq), Et_2O, rt 2. H^+	 (64) *cis*/*trans* = 92:8	210, 211
C_{15} 	1. *t*-BuLi (1 eq), Et_2O, –78 to 0°, 6.5 h 2. BuZnI (1 eq), THF, 0°, 1.5 h 3.  $SnBu_3$ (2 eq), 0° 4. 30°, 44 h 5. H^+	 (69)	129
C_{16} 	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. BuLi (1 eq), 0° 4. rt, 24 h 5. H^+	 (40) dr 97.5:2.5	127
C_{17} 	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Ethylene (excess), Et_2O, 35°, 8 atm, 4 d 5. H^+	 (90)	131
	1. *t*-BuLi (1 eq), Et_2O, 0°, 4 h 2. $ZnBr_2$ (1 eq), Et_2O, 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. H^+	 (93)	209

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

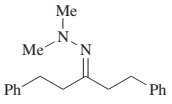
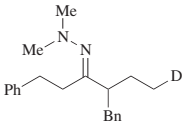
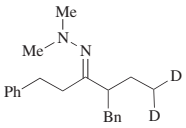
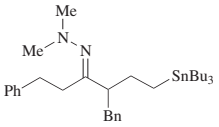
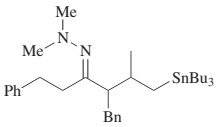
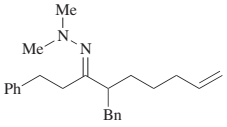
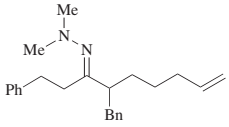
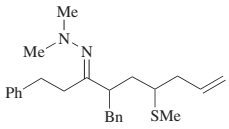
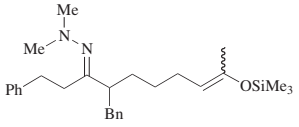
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17}			
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Ethylene (excess), Et_2O, 35°, 8 atm, 4 d 5. D^+	 (90)	131
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. D^+	 (93)	209
	1. *t*-BuLi (1 eq), Et_2O, –78 to 0°, 6.5 h 2. BuZnI (1 eq), THF, 0°, 1.5 h 3.  $SnBu_3$ (2 eq), 0° 4. 30°, 44 h 5. H^+	 (82)	129
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4.  $SnBu_3$ (6 eq), 35°, 5 atm, 11 d 5. H^+	 (35) dr 50:50	131
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Ethylene (excess), Et_2O, 35°, 8 atm, 4 d 5. CuCN (1 eq), 0° 6. Allyl-Br (3 eq), rt 7. H^+	 (81)	131
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. *t*-BuOH (1 eq), –70 to –40°, 1 h 5. CuCN (1 eq), LiCl (1 eq), –23°, 1 h 6. Allyl-Br (2 eq), –70°, 15 min 7. –23°, 1 h 8. 0°, 1 h 9. H^+	 (82)	209
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. MeSSMe (1.1 eq), 0° to rt, 1.5 h 5. Allyl-Br (5 eq), rt, 15 h 6. H^+	 (84) dr 44:29:27	209
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. *t*-BuOH (1 eq), –70 to –40°, 1 h 5. CuCN (1 eq), LiCl (1 eq), –23°, 1 h 6. TMSCl (3 eq), CH_2=CHAc (2 eq), HMPA (3 eq), –70°, 15 min 7. –23°, 1 h 8. 0°, 1 h 9. H^+	 (33)	209

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
G. ADDITION OF ZINC ENOLATE DERIVATIVES (*Continued*)

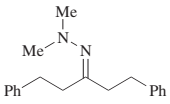
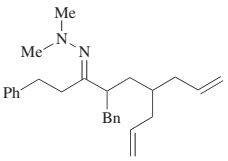
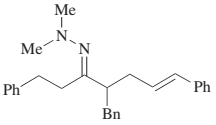
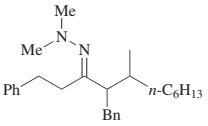
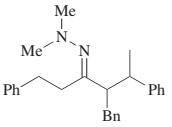
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17} 	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. CuCN (1 eq), HMPA (3 eq), THF (1 eq), –40°, 20 min 5. Allyl-Br (3 eq), –70°, 15 min 6. –23°, 1 h 7. 0°, 1 h 8. H^+	 (78)	209
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. Vinyl-MgBr, 0°, 1 h 4. PhCHO (1.1 eq), 0°, 1 h 5. H^+	 (67) (*E*)/(*Z*) = 78:22	209
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Oct-1-ene (6 eq), 35°, 8 atm, 11 d 5. H^+	 (30) dr 50:50	131
	1. *t*-BuLi (1 eq), –70 to 0°, 4 h 2. $ZnBr_2$ (1 eq), 0°, 1 h 3. BuLi (1 eq), 0° to rt, 1 h 4. Styrene (excess), Et_2O, 35°, 8 atm, 4 d 5. H^+	 (39) dr 50:50	131

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
H. IRON-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES

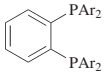
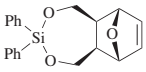
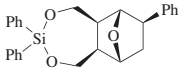
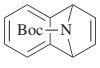
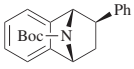
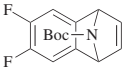
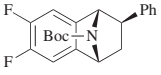
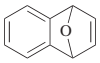
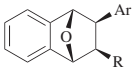
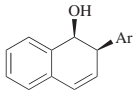
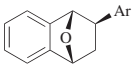
Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
*The **bold** ligand numbers used in Table 2H refer to these structures:*  Ar **L1** 4-$MeOC_6H_4$ **L2** 4-FC_6H_4 **L3** 3,4-$F_2C_6H_4$			
C_8 	1. $FeCl_3$ (3 mol %), **L3** (6 mol %), Ph_2Zn (1.5 eq), THF/toluene (1:1), 40°, 24 h 2. AcOH/MeOH (5% solution)	 (65)[a]	212
C_9 	1. $FeCl_3$ (3 mol %), **L3** (6 mol %), Ph_2Zn (1.5 eq), THF/toluene (1:1), 40°, 24 h 2. AcOH/MeOH (5% solution)	 (75)	212
C_{10} 	1. $FeCl_3$ (1 mol %), **L3** (2 mol %), Ph_2Zn (1.5 eq), THF/toluene (1:1), rt, 2 h 2. AcOH/MeOH (5% solution)	 (94)	212
	1. $FeCl_3$ (1 mol %), **L3** (2 mol %), Ph_2Zn (1.5 eq), THF/toluene (1:1), rt, 2 h 2. AcOH/MeOH (5% solution)	 (96)	212

TABLE 2. CARBOZINCATION OF ALKENES (*Continued*)
H. IRON-CATALYZED ADDITION OF ALKYLZINC DERIVATIVES (*Continued*)

Alkene	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	1. $FeCl_3$ (1 mol %), ligand (2 mol %), $ArZnY$ (1.5 eq), THF/toluene (1:1), time, 0° 2. E^+	 +  **I** **II**	212

Ligand	Ar	Y	Time (h)	E^+	R	**I** + **II**	**I/II**	*cis*/*trans*
dppe	Ph	Ph	5	H_3O^+	H	(95)[a]	92:8	—
dppp	Ph	Ph	5	H_3O^+	H	(92)[a]	76:24	—
dppb	Ph	Ph	5	H_3O^+	H	(98)[a]	3:97	—
dppbz	Ph	Ph	5	H_3O^+	H	(100)[a]	88:12	—
L1	Ph	Ph	4	H_3O^+	H	(100)[a]	83:17	—
L2	Ph	Ph	2	H_3O^+	H	(100)[a]	95:5	—
L3	Ph	Ph	5	H_3O^+	H	(100)[a]	89:11	—
L2	Ph	Ph	2	CD_3CO_2D	D	(92) >96% D	—	>99:1
L2	Ph	Ph	2	I_2	I	(91)	—	83:17
L3	Ph	Ph	2	allyl-Br	allyl	(93)	—	>99:1
L3	Ph	$TMSCH_2$	2	AcCl	Ac	(77)[a]	—	>99:1
L3	Ph	Ph	2	H_3O^+	H	(94)	—	—
L3	4-MeC_6H_4	4-MeC_6H_4	2	H_3O^+	H	(95)	—	—
L3	2-MeC_6H_4	2-MeC_6H_4	8	H_3O^+	H	(86)	—	—
L3	4-$MeOC_6H_4$	4-$MeOC_6H_4$	2	H_3O^+	H	(95)	—	—
L3	4-FC_6H_4	4-FC_6H_4	2	H_3O^+	H	(94)	—	—

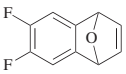
1. $FeCl_3$ (*x* mol %), **L3** (*y* mol %), Ar_2Zn THF/toluene (1:1), 0°, time
2. AcOH/MeOH (5% solution)



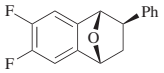
212

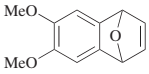
x	*y*	Ar	Time (h)	
10	20	4-$MeO_2CC_6H_4$	4	(66)
10	20	4-NCC_6H_4	6	(63)
1	2	2-thienyl	24	(81)

752

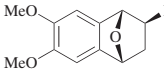


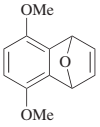
1. $FeCl_3$ (1 mol %), **L3** (2 mol %), Ph_2Zn (1.5 eq), THF/toluene (1:1), 0°, 1 h,
2. AcOH/MeOH (5% solution)

 (96) 212

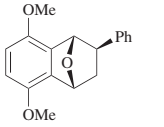


1. $FeCl_3$ (1 mol %), **L3** (2 mol %), Ph_2Zn (1.5 eq), THF/toluene (1:1), 0°, 2 h
2. AcOH/MeOH (5% solution)

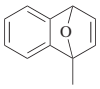
 (94) 212



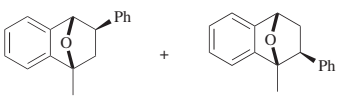
1. $FeCl_3$ (1 mol %), **L3** (2 mol %), Ph_2Zn (1.5 eq), THF/toluene (1:1), 0°, 2 h
2. AcOH/MeOH (5% solution)

 (90) 212

753



1. $FeCl_3$ (10 mol %), **L3** (20 mol %), Ph_2Zn (1.5 eq), THF/toluene (1:1), 0°, 9 h
2. AcOH/MeOH (5% solution)

 212

I **II**

I + **II** (62), **I/II** = 4:1

[a] The yield was determined using ^{1}H-NMR spectroscopy.

TABLE 3. CARBOZINCATION OF METALATED ALLENES

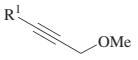
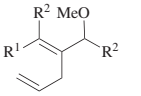
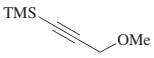
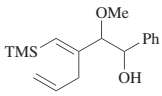
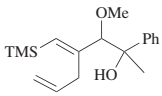
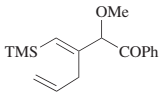
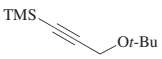
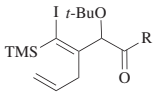
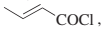
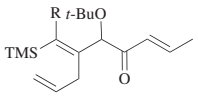
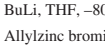
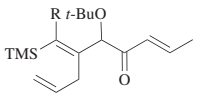
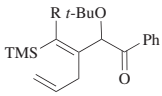
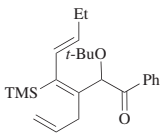
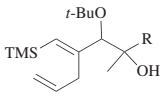
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3			
	1. BuLi, THF, temp 1, 0.5 h 2. Allylzinc bromide, –70° 3. 65°, time 4. $MeOR^2$, temp 4	 R^1 R^2 Temp 1 (°) Time (h) Temp 4 (°) TMS H –80 0.5 0 (90) $PhMe_2Si$ D –70 1 — (—)	159 158
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. 65°, 0.5 h 4. PhCHO, –80°, ether 5. H_2O	 (55)	158
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. 65°, 0.5 h 4. PhCOMe, –80°, ether 5. H_2O	 (55) dr 50:50	158
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. 65°, 12 h 4. $PhCO_2Et$, –80°, ether 5. H_2O	 (55)	158
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4. RCOCl, –80°, ether 5. I_2, rt	 R Me (66) Et (78)	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4.  5. See table.	 (67) R Step 5 H H_3O^+ (64) I I_2, rt (67)	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4.  5. RI, $Pd(PPh_3)_4$ (5 mol %), CuBr, DMA, time, rt 6. H_3O^+	 R Time (h) (*E*)-EtCH=CH 2.5 (70) (*Z*)-*t*-BuO_2CCH=CH 1 (51) 4-$MeOC_6H_4$ 4 (63)	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4. PhCOCl, –80°, ether 5. See table.	 Step 5 R H_3O^+ H (78) I_2, rt I (78)	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4. PhCOCl, –80°, ether 5. (*E*)-EtCH=CHI, $Pd(PPh_3)_4$ (5 mol %), CuBr, DMA, 2.5 h, rt 6. H_3O^+	 (74)	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4. RCOMe, –80°, ether 5. H_3O^+	 R (78) dr Me (78) — CH_2=CH (60) 90:10 Ph (88) 50:50	159

TABLE 3. CARBOZINCATION OF METALATED ALLENES (*Continued*)

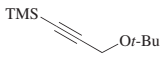
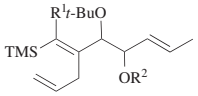
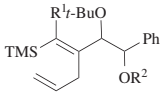
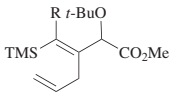
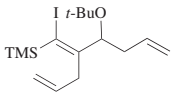
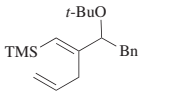
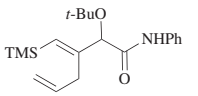
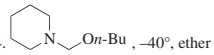
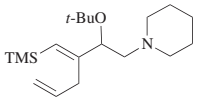
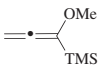
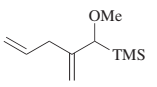
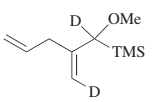
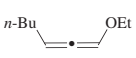
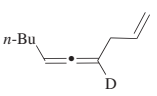
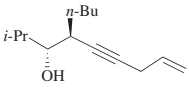
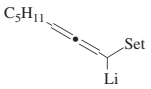
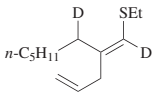
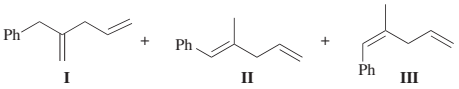
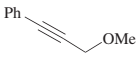
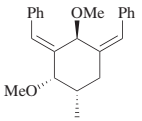
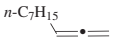
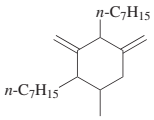
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3			
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4.  , TMSCl (*x* eq), –80°, ether 5. See table.	 *x* Step 5 R^1 R^2 dr 0 H_3O^+ H H (63) 75:25 1.4 I_2, rt I TMS (66) 97:3	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4. PhCHO, TMSCl (*x* eq), –80°, ether 5. See table.	 *x* Step 5 R^1 R^2 dr 0 H_3O^+ H H (60) 50:50 0 DCl D H (—) — 1.4 H_3O^+ H TMS (60) 50:50 1.4 I_2, rt I TMS (63) 50:50	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4. $ClCO_2Me$, –80°, ether 5. See table.	 Step 5 R H_3O^+ H (68) I_2, rt I (67)	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4. Allyl-Br, –80°, ether 5. I_2, rt	 (50)	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4. BnBr, –40°, ether 5. H_3O^+	 (70)	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4. PhNCO, –80°, ether 5. H_3O^+	 (69)	159
	1. BuLi, THF, –80°, 0.5 h 2. Allylzinc bromide 3. 65°, 0.5 h 4.  , –40°, ether 5. H_3O^+	 (33)	159
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. 65°, 12 h 4. NH_4Cl	 (60)	158
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. 65°, 12 h 4. MeOD	 (—) single isomer	158
C_7			
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. MeOD	 (75)	213
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. *i*-PrCHO, –80°, ether 4. H_2O	 (75)	213

TABLE 3. CARBOZINCATION OF METALATED ALLENES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. 65°, 1 h 4. D_2O	 (56)	158
C_9			
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. 60°, 2 h 4. H_2O	 **I** **II** **III** **I** + **II** + **III** (74), **I/II/III** = 78:16:6	160
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. 65°, 3 h 4. H_2O	 (60)	160
	1. BuLi, THF, –70°, 0.5 h 2. Allylzinc bromide, –70° 3. 50°, 0.5 h 4. H_2O	 (70)	160

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