CHAPTER 1

THE SCHMIDT REACTION

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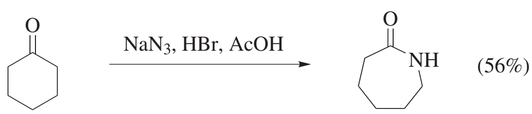
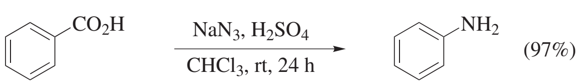
INTRODUCTION

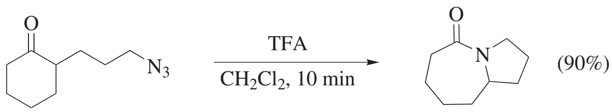
The term “Schmidt reaction” describes a family of related reactions that use hydrazoic acid or an alkyl azide to react with an electrophile. A few representative examples are depicted in Eqs. 1–3.[1–3] Depending on the reactants employed, the product of the reaction can contain an amide or a number of related functional groups (Fig. 1). Despite this diversity, all Schmidt reactions have the characteristic of incorporating nitrogen into the product and it is this feature that has placed this chemistry among the most useful means for the synthesis of nitrogenous compounds.



(Eq. 1)



(Eq. 2)



(Eq. 3)

The Schmidt reaction was first reported in 1924 by K. F. Schmidt,[4] but came into its own in the 1940's and 1950's, largely through the efforts of P. A. S. Smith[1,5–8] and L. H. Briggs.[9,10] The classical Schmidt reactions, defined as those that specifically employ hydrazoic acid as the azide component, are the subject of an earlier *Organic Reactions* chapter.[11] In addition, extensive review literature exists on the subject.[12–20]

The most commonly used variant of the Schmidt reaction is the reaction of a ketone or aldehyde with hydrazoic acid to afford an amide. These reactions usually employ a stronger protic acid to enhance the reactivity of the carbonyl group. Cyclic ketones afford lactams that contain one additional ring atom relative to the starting material. The utility of this reaction is heightened by the availability

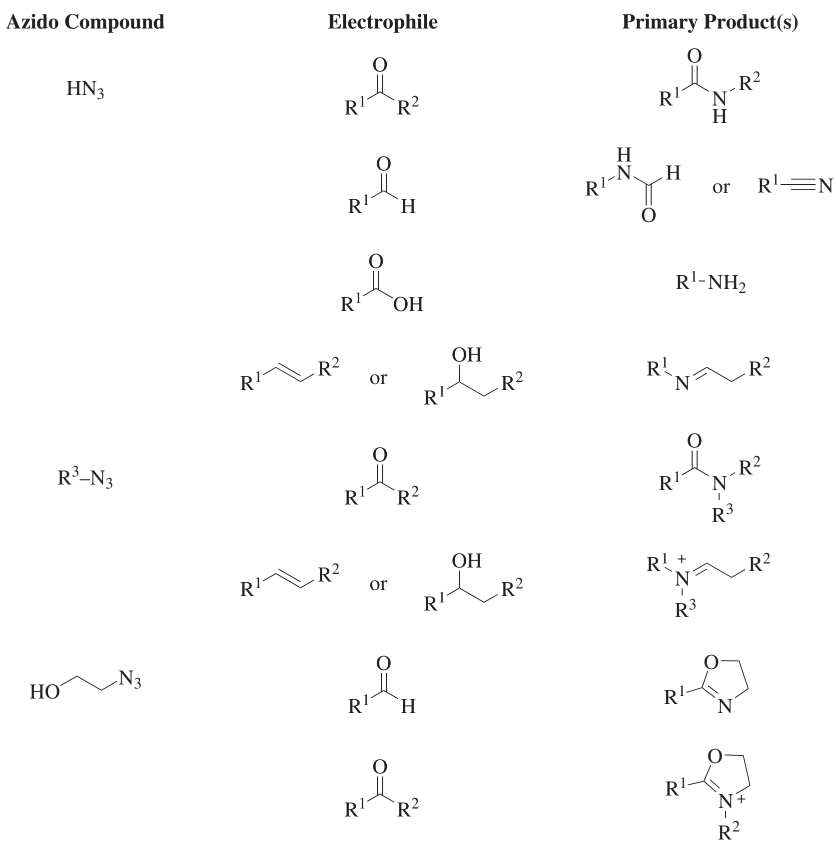


Figure 1. The family of Schmidt reactions.

of an essentially limitless number of ketones and by the ready reduction of the amide carbonyl group to afford the corresponding amino compound. In addition, most Schmidt reactions of this type occur with predictable (if not fully selective) site selectivity and stereoselectivity.

Hydrazoic acid also reacts with related species such as carboxylic acids and carbocations derived from alcohols or alkenes. The identification of all of these processes as variants of the Schmidt reaction is due to their common mechanistic features, involving first, the nucleophilic addition of hydrazoic acid to the reactive electrophile and, second, the rearrangement of this unstable adduct to afford the product. The loss of molecular nitrogen during the second stage of these reactions provides a powerful driving force for conversion into product. The mechanistic variations among classes are discussed in the appropriate sections.

The superficial similarity of alkyl azides to hydrazoic acid, entailing only the replacement of the proton in HN_3 with an alkyl group, immediately suggests that azides should undergo their own Schmidt reactions when encountering an electrophilic species. In the 1950's, Boyer reported a limited series of successful reactions of alkyl azides with aromatic aldehydes to afford amides.[21] In the 1990's, it was reported that Lewis acids could effect the addition of azides to ketones and also that azides were facile partners in Schmidt reactions of carbocations, thus opening the door to the direct synthesis of *N*-alkylated amides from ketones[3,22] or tertiary amines from cations derived from alcohols or alkenes.[23,24] Simultaneously, it was recognized that intramolecular variants of these reactions can provide routes to multicyclic nitrogen heterocycles.[3,23]

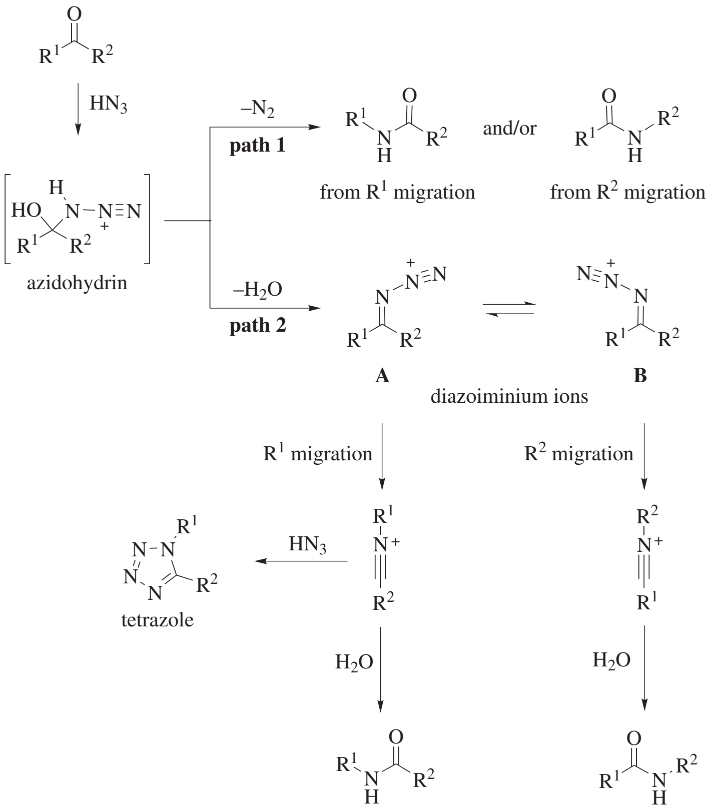
This chapter will discuss progress in all of the above classes of reactions, with the main restriction that only examples not included in the 1946 edition of *Organic Reactions*[11] will appear in the tables, ending with references published through the end of 2009.

MECHANISM AND STEREOCHEMISTRY

All Schmidt reactions involve the initial nucleophilic attack of hydrazoic acid or a related azide species onto an electrophile. Although the latter is most commonly a carbonyl group activated by a protic or Lewis acid, the electrophile can also be either a stabilized or unstabilized carbocation. The greatest mechanistic diversity through the class arises from the ultimate fate of the intermediate formed in this initial step. Every one of these reactions is driven by the loss of molecular nitrogen en route to its nitrogen-containing product. Each of the different classes of Schmidt reactions will be considered separately.

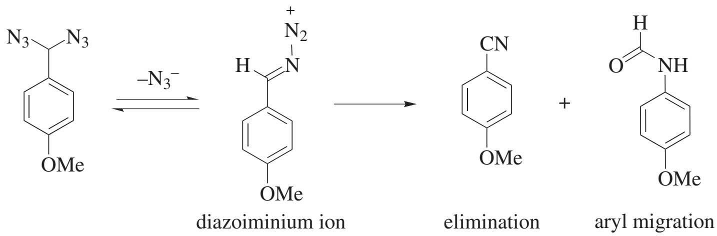
Reactions of Hydrazoic Acid with Ketones

The most heavily studied variant of the Schmidt reaction is that of a ketone with hydrazoic acid (Scheme 1). This reaction begins with the addition of HN_3 to the protonated carbonyl group to afford an azidohydrin intermediate. At this stage, the reaction can proceed via one of two principal routes. In path 1, rearrangement of the azidohydrin intermediate directly affords an amide via a mechanism related to that of the Baeyer–Villiger reaction.[25] Alternatively, path 2 involves elimination of water to afford a diazoiminium species, which can subsequently rearrange to form an iminium ion that must be hydrated to give the final product (analogous to the commonly accepted mechanism of the Beckmann rearrangement).



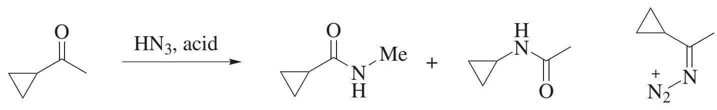
Scheme 1

The Beckmann mechanism was originally proposed by Smith[1] and, although the subject of considerable spirited discussion over the years, this mechanism is still favored by most authors. The main reasons are (1) the correlation of the migrating group with size, which is consistent with formation of the least sterically encumbered diazoiminium ion and antiperiplanar migration (also seen in the Beckmann rearrangement); and (2) the fact that tetrazoles are common byproducts of the Schmidt reaction, and form in increasing amounts when high concentrations of hydrazoic acid are present. The diazoiminium ion generated in the absence of water from the diazidoalkyl species shown in Eq. 4 gives the Schmidt reaction product; in this case, both elimination to nitrile (typical of Schmidt reactions of aldehydes) and aryl migration are noted.[26,27] Parenthetically, a protonated gem-diazide has been suggested as a possible intermediate in some Schmidt reactions.[28] Although this work proves that diazoiminium ions are possible intermediates in the reaction, it is difficult to establish the *required* involvement of such species.



(Eq. 4)

The demonstration of successful Schmidt reactions of alkyl azides clearly removes any objection to a mechanism involving direct azidohydrin rearrangement.[3,22,29] Thus, despite the general acceptance of the Beckmann mechanism, it has been suggested that the Baeyer–Villiger mechanism can operate under certain conditions. For example, Shechter has suggested that the mechanism of the Schmidt reaction of cyclopropyl ketones depends in part on the acid strength of the reaction medium (Eq. 5).[30,31] However, alternative explanations, such as the preferential formation of stereoisomeric intermediate **III** in 50% sulfuric acid, cannot be totally ruled out.

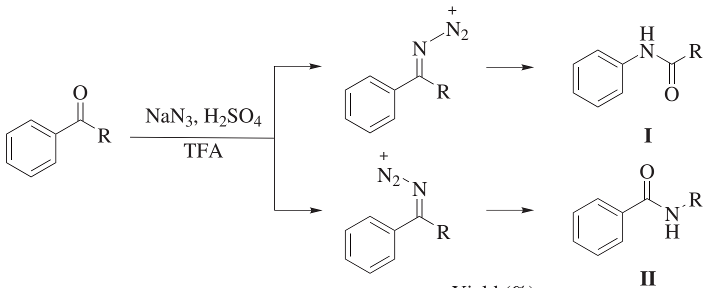


I **II** **III**

(Eq. 5)

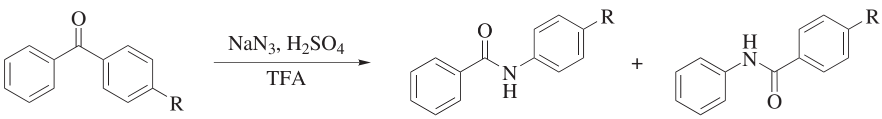
89% H_2SO_4, **I** + **II** (88–100%) **I**:**II** = 27:73
50% H_2SO_4, **I** + **II** (88–100%) **I**:**II** = 90:10

Under the Beckmann mechanism, stereoelectronic effects determine which group undergoes migration. In a systematic examination of a series of phenyl ketones containing increasingly larger alkyl substituents, the product ratio correspondingly favors alkyl group migration (Scheme 2).[6] These results are consistent with the hypothesis that the ratio of the intermediate diazoiminium ions, coupled with the synchronous and antiperiplanar migration of the carbon to the electron-deficient nitrogen, determines the site selectivity. An important proviso is that theoretical calculations suggest a high barrier for direct interconversion of the diazoiminium ions.[32] However, intermediates leading to **A** or **B** (Scheme 1) can interconvert via reversible addition of water under the reaction conditions (i.e., by reversion to the azidohydrin and subsequent dehydration); it is also possible that their ratio is kinetically controlled. An analogous study of substituted benzophenones does not belie any clear dependence of migrating group selectivity on the electronic nature of the aromatic rings, suggesting that "migratory aptitude" does not play a strong role in determining the site selectivity in these particular reactions (Eq. 6).[7]



R	Yield (%) I + II	I:II
Me	81	95:5
Et	80	85:15
i-Pr	57	51:49
t-Bu	—	0:100

Scheme 2

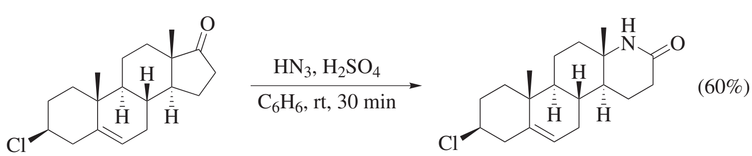


I **I + II** (—) **II**

R	I:II
O_2N	51:49
Cl	59:41
Me	54:46
Ph	52:48
MeO	61:39

(Eq. 6)

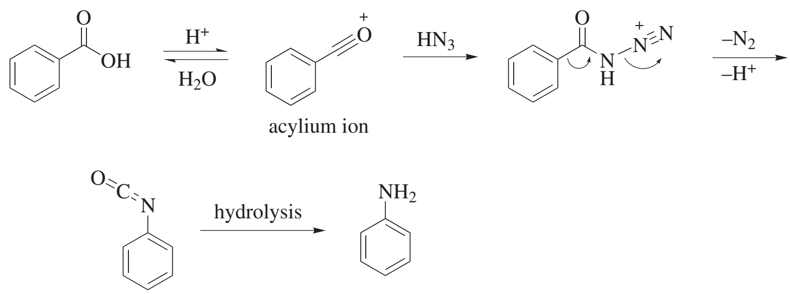
An important feature of the Schmidt reaction is that a stereogenic carbon migrates with retention of configuration. This behavior is consistent with related processes such as the Beckmann[33] and Baeyer–Villiger[25] reactions and extends throughout the entire family of Schmidt reactions. The reaction of the steroidal ketone shown in Eq. 7 is typical; for an acyclic example, see Eq. 60 in the "Applications to Synthesis" section.[34]



(Eq. 7)

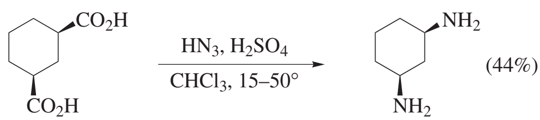
Reactions of Hydrazoic Acid with Carboxylic Acids and Aldehydes

These variants of the Schmidt reaction are mechanistically less ambigious. The reactions of carboxylic acids with hydrazoic acid uniformly afford amines as there is only the possibility of migration of a single group in an acyl azide intermediate. In these cases, the primary product formed following alkyl or aryl group migration is an isocyanate. Addition of water followed by loss of carbon dioxide leads to the final product, an amine (Scheme 3).

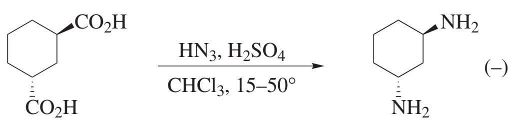


Scheme 3

The reactions of carboxylic acids with hydrazoic acid permit the stereospecific synthesis of amines via migration of a stereogenic carbon with retention of configuration (Eqs. 8 and 9).[35]

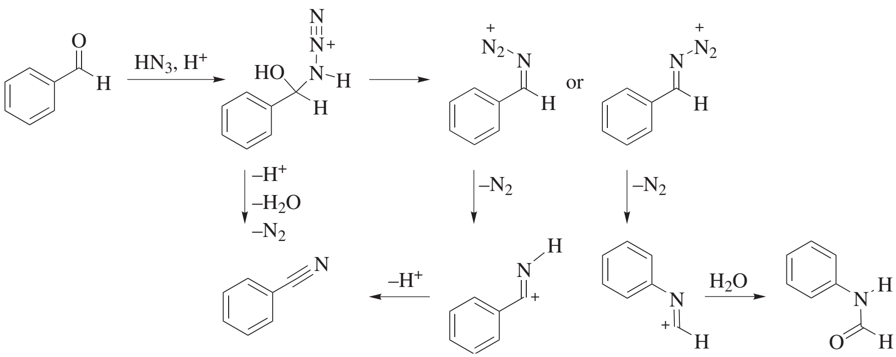


(Eq. 8)



(Eq. 9)

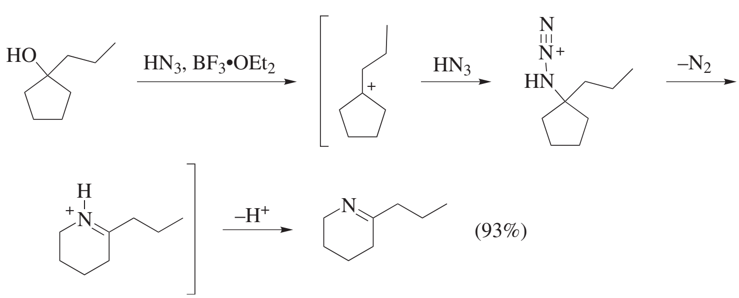
The mechanism of the reaction of hydrazoic acid with an aldehyde has not been fully established, partly because this variant of the Schmidt reaction is not as useful as others and therefore little work has been devoted to understanding it. These reactions are believed to occur via the Beckmann mechanism, affording first a diazoiminium ion that can rearrange via migration of an aryl or alkyl group to ultimately afford a formamide derivative upon hydration and tautomerization. However, the predominant product of this reaction is usually a nitrile (Scheme 4). One mechanism for the formation of a nitrile requires the intermediacy of the sterically unfavorable diazoiminium ion; however, this isomer may be kinetically favored.[36] Formation of the nitrile from this intermediate occurs by either hydride migration followed by proton elimination or concerted elimination. An alternative proposed mechanism is that the unprotonated version of the azidohydrin intermediate is converted into the nitrile (by an unspecified series of steps), whereas the formamide product arises from the diazoiminium ion as shown (Scheme 4).[37,38] This proposed mechanism is based in part on the observation of overall second-order kinetics and on the dependence of product ratio on acid strength.[37,38]



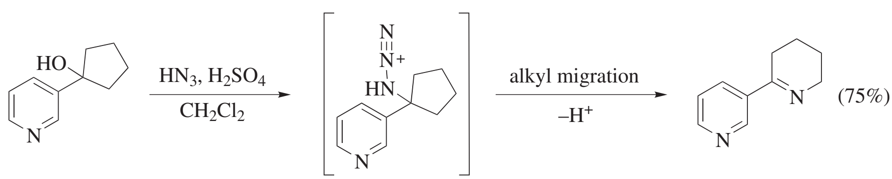
Scheme 4

Reactions of Hydrazoic Acid with Carbocations Derived from Alkenes or Alcohols

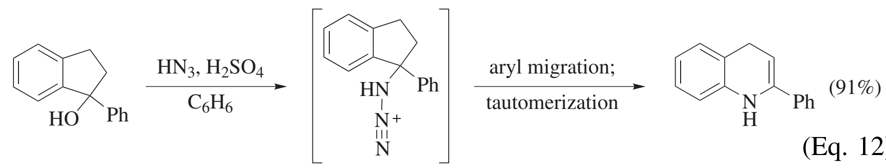
The reactions of hydrazoic acid with carbocationic species generated from alcohols or alkenes afford imines that result from nucleophilic addition of hydrazoic acid to the cation followed by alkyl or aryl group migration (Eqs. 10[39] and 11[40]). For cyclic compounds, imines are the usual reaction products, but tautomerization to the corresponding enamine is possible (Eq. 12).[41]



(Eq. 10)

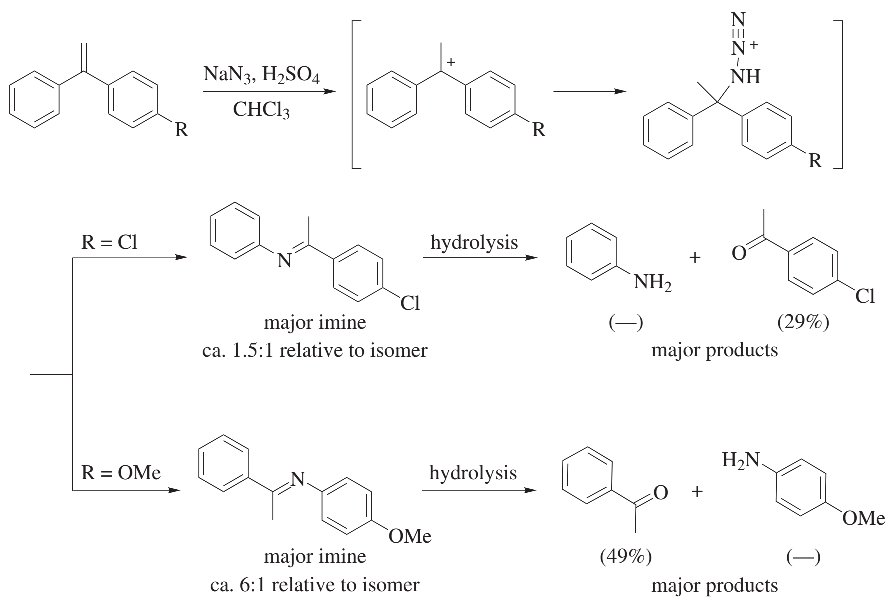


(Eq. 11)



(Eq. 12)

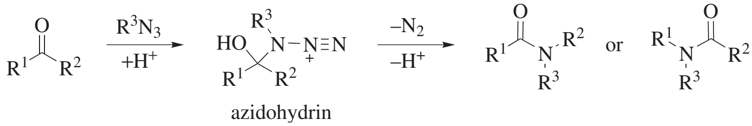
Also possible, and often observed in acyclic substrates, is hydrolysis of the imine to an amine and a carbonyl compound. Migratory aptitude likely plays a role in determining the site selectivity of the migration step due to the lack of a stereochemically defined diazoiminium intermediate in the reaction (Scheme 5).[42]



Scheme 5

Reactions of Alkyl Azides and Hydroxyalkyl Azides with Electrophiles

The discovery that alkyl azides react with various electrophiles[3,21,23] expands the scope of the Schmidt reaction and adds to the understanding of its mechanism. Specifically, because the adduct of an alkyl azide and a ketone is very unlikely to undergo loss of water to afford a diazoiminium ion containing adjacent positive charges, the competency of the initially formed azidohydrin species to directly afford an amide is generally viewed as unambiguously established. This reaction proceeds in both the intermolecular sense (Eq. 13)[22] and also when the azide is covalently attached to the ketone (Eq. 14).[3]

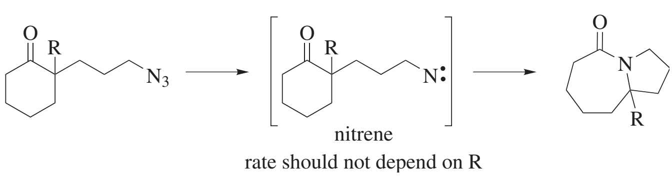


(Eq. 13)

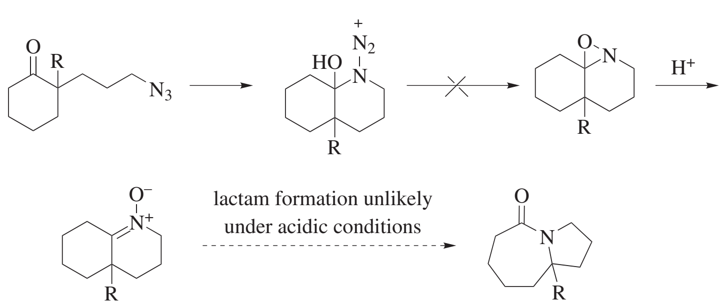
(Eq. 14)

R = H, 10 min (83%)
R = CO_2Me, 10 min, >90% recovered starting material
R = CO_2Me, 16 h (66%)

The possible involvement of nitrene intermediates is ruled out by comparing the rates of reactions of electronically disparate ketones. Whereas 2-(3-azidopropyl)cyclopentanone undergoes complete reaction in trifluoroacetic acid within 10 minutes at room temperature, similar treatment of an analog containing a 2-carbomethoxy group does not give significant conversion (Eq. 14).[3] However, it is possible to achieve a 66% yield of the lactam upon extended exposure to trifluoroacetic acid. It would be extremely unlikely that the rate of decomposition to a nitrene would be affected by the presence of a distant ester group (Eq. 15). In addition, the recovery of intact ester-substituted azide under conditions sufficient for the complete reaction of the unsubstituted version rules out nitrene intervention in at least the intramolecular reaction. Another unlikely mechanism is conversion of an azidohydrin to an oxaziridine via O–N bond formation (Eq. 16). Although oxaziridines can undergo thermal rearrangements to lactams,[43] they rearrange under acidic conditions to afford nitrones rather than amides.[44] Neither oxaziridines nor nitrones have ever been reported as products from the reactions of azides and carbonyl compounds.

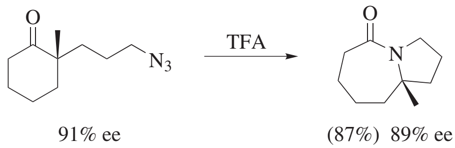


(Eq. 15)



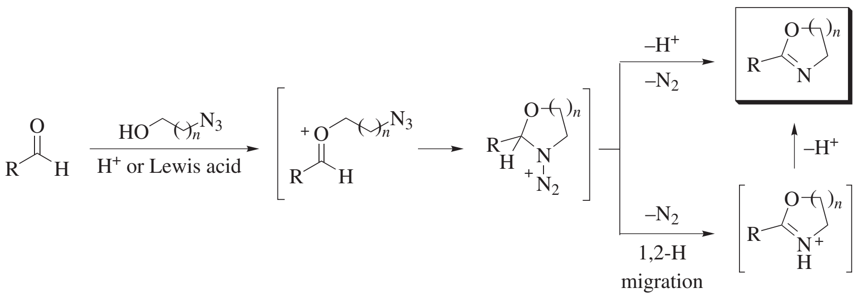
(Eq. 16)

The intramolecular Schmidt reaction of alkyl azides and ketones proceeds with retention of configuration of the migrating carbon atom (Eq. 17).[29]



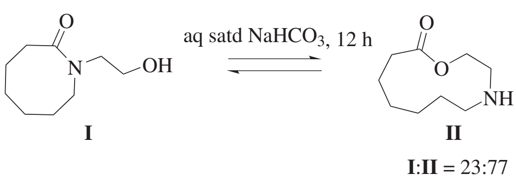
(Eq. 17)

Hydroxyalkyl azides react with aldehydes or ketones under acidic conditions to afford oxocarbenium ions. Once formed, the cation is intercepted by the nucleophilic azido group to afford an azidohydrin-like intermediate that rearranges with loss of nitrogen to afford an iminium ether as the primary product. In the case of aldehydes, where the initial product is a protonated imino ether, loss of both a proton and nitrogen ensue to provide oxazolines or dihydrooxazines when $n = 1$ or 2, respectively (Scheme 6).[45] It is not known whether the proton is lost in concerted elimination reaction or if a 1,2-hydride migration precedes deprotonation.

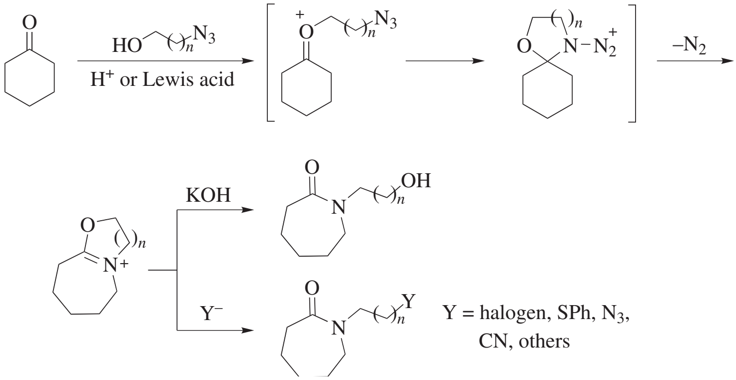


Scheme 6

For ketones, the reaction results in an iminium ether as the initial product (Scheme 7). Most often, the iminium ether is converted into an amide by the addition of hydroxide ion. In addition, it may be combined with a variety of other nucleophiles to afford terminally substituted *N*-alkyl lactams.[46] *N*-(Hydroxyalkyl)amides or lactams derived from acyclic or medium-ring ketones are subject to reorganizations to afford amine-substituted esters or lactones, respectively (Eq. 18).[47,48] These reactions are highly structure- and condition-dependent.

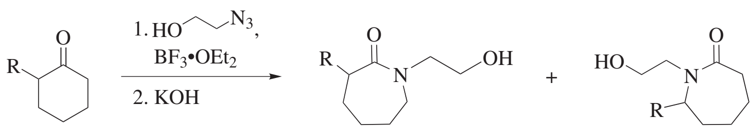


(Eq. 18)



Scheme 7

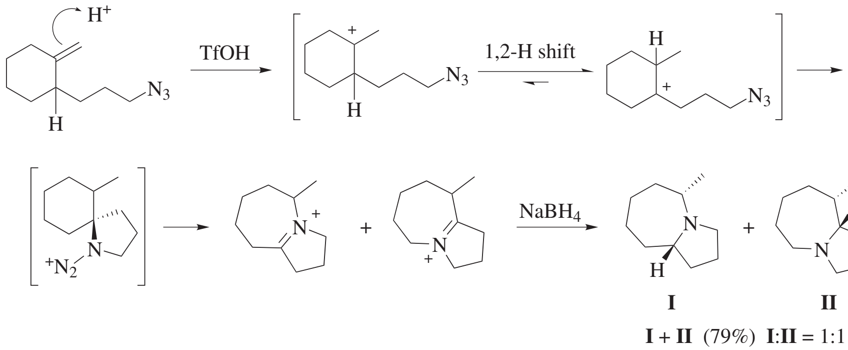
The constitutional outcome of the reactions of unsymmetrical cyclohexanones has been briefly studied (Eq. 19).[49] The extent of migration of the substituted carbon increases with the size of the ketone α-substituent. Interestingly, several ketones bearing an electron-withdrawing group afford a high proportion of the product resulting from migration of the unsubstituted methylene group. These observations have been analyzed by consideration of competing conformational and electronic factors in the azide adducts.[49]



I **II** (Eq. 19)

R	Yield (%) I + II	I:II
Me	83	45:55
i-Pr	80	21:79
t-Bu	11	13:87
Br	58	>95:5

Alkyl azides also react with carbocations derived from precursors such as alkenes or alcohols. The mechanism of this reaction is analogous to the related reactions of hydrazoic acid, with a key difference being that an intramolecular version is possible for azides. In the reaction shown (Scheme 8),[50,51] the initially generated intermediate is in equilibrium with an isomeric carbocation via a 1,2-hydride migration. Because both are of roughly equal stability, it is likely that the length of the chain between each cation and the azide determines which one will lead to product. In this example, two different carbon-to-nitrogen migration reactions occur to afford a pair of iminium ions as the primary products of the reaction. Because of the small energetic difference between the two possible iminium intermediates in this reaction, a roughly 1:1 mixture of isomers is observed. The addition of an exogenous reducing agent ultimately affords the reduced heterocyclic products via the least sterically hindered direction of hydride attack. The use of other cation precursors will be described in the "Scope and Limitations" section.



Scheme 8

SCOPE AND LIMITATIONS

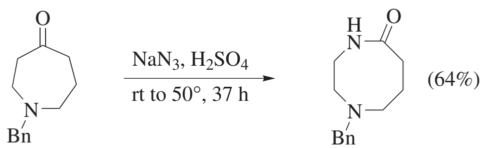
The reaction scope varies greatly with each version of the Schmidt reaction. In general, the reactions of hydrazoic acid with various electrophiles accommodate a broad range of substrates whereas the various Schmidt reactions involving alkyl azides are often more limited.

Schmidt Reactions of Hydrazoic Acid

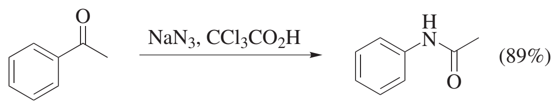
Reactions with Ketones and Aldehydes. The most commonly used Schmidt reaction is the conversion of a ketone into an amide or lactam with hydrazoic acid. The corresponding reactions of aldehydes are less important because they bifurcate into nitriles or insertion products depending on substrates and conditions. Also less useful from a preparative perspective is the use of Schmidt conditions for the conversion of carboxylic acids to provide amines bearing one fewer carbon. In this case, the reaction suffers in comparison with the Curtius rearrangement,[18,52] which carries out the same transformation under milder conditions.

The main practical issues pertinent to ketone/hydrazoic acid reactions are (1) site selectivity, and (2) the formation of tetrazole side products (which can often be minimized by changing the reaction conditions). Many more ketones undergo Schmidt reactions than do not; the most problematic examples are ketones that provide serious steric obstacles to nucleophilic addition to the carbonyl group.

The fact that structurally diverse ketones are so readily available also contributes to the popularity of the Schmidt reaction in synthesis. A noteworthy application is the synthesis of medium-size rings that are hard to make by direct cyclization. Thus, readily available 6- and 7-membered ring ketones are attractive precursors to the corresponding 7- and 8-membered lactams (Eq. 20).[53–56] In contrast, application of the Schmidt reaction to acylic ketones is less common because acyclic amides are effectively made by a passel of coupling methods. The useful application of the Schmidt reaction on an acyclic substrate is the synthesis of aromatic amides from ketone precursors (Eq. 21).[1]

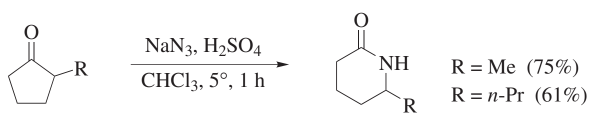


(Eq. 20)

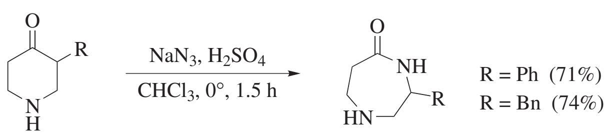


(Eq. 21)

A significant remaining limitation of the Schmidt reaction is that no variant reliably inserts into an α-monosubstituted ketone with migration of the less substituted carbon. For reasons discussed in the previous section, the most substituted α-carbon generally migrates in the reactions of unsymmetrical ketones. Two illustrative examples are shown in Eq. 22[16,53] and Eq. 23.[57]

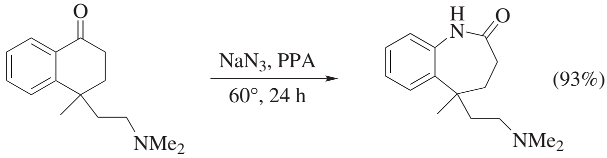


(Eq. 22)

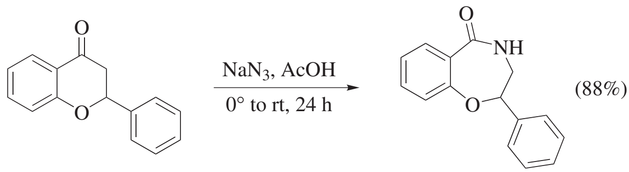


(Eq. 23)

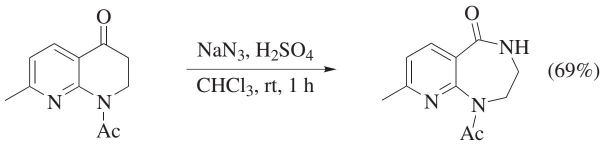
Aromatic ketones often react via migration of the aromatic group (Eq. 24),[58] but exceptions are known. In some cases, these reactions are readily understandable mechanistically; for example, electron-rich aromatic rings should migrate more readily than an alkyl group.[59,60] As discussed in the previous section, the steric demands of the alkyl group also play a role.[7] Other examples are harder to explain; for example, compare Eqs. 24 and 25.[61–64] The migratory preferences in reactions involving heteroaromatic ketones are particularly difficult to predict (Eqs. 26[65] and 27[66]).



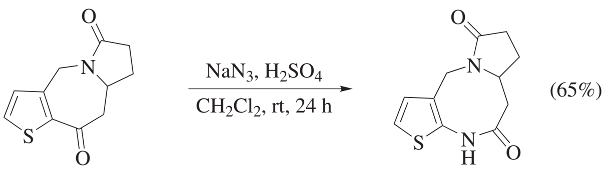
(Eq. 24)



(Eq. 25)

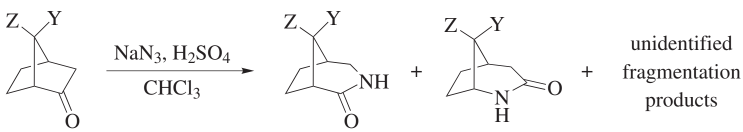


(Eq. 26)



(Eq. 27)

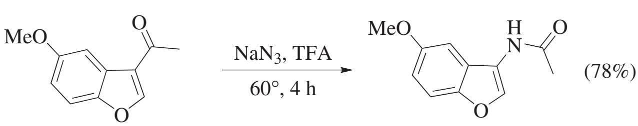
The Schmidt reactions of bicyclic ketones tend to proceed with poor site selectivity and are often accompanied by fragmentation byproducts.[16,67] A few systems, such as norcamphor, react with high selectivity for a particular isomer but the reactions are not necessarily high yielding (Eq. 28).[68]



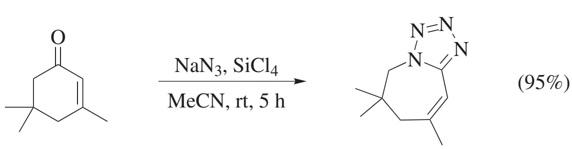
(Eq. 28)

Y = Z = H	(35%)	(<2%)	(63%)
Y = OTs, Z = H	(21%)	(31%)	(48%)
Y = H, Z = OTs	(14%)	(26%)	(60%)

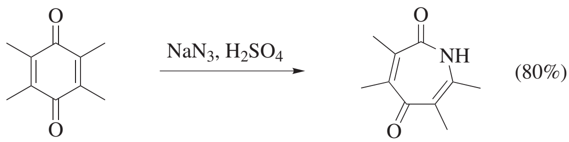
The reaction is also tolerant of α,β-unsaturation with many cases of enones reacting under standard Schmidt conditions. Often a simple enone containing a single adjacent double bond affords a product resulting from migration of the sp^2-hybridized α-carbon (Eq. 29),[69] but exceptions do exist (Eq. 30).[70] Quinones and other compounds containing only adjacent sp^2-hybridized carbons are perfectly competent Schmidt reaction substrates (Eq. 31).[71]



(Eq. 29)

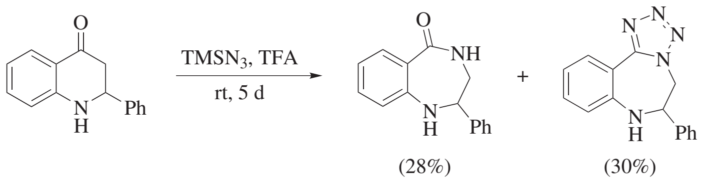


(Eq. 30)

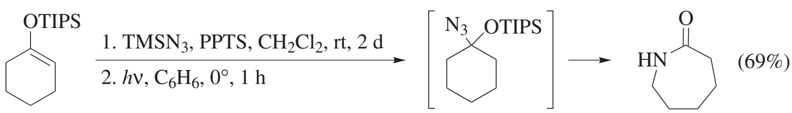


(Eq. 31)

Besides the use of sodium azide and hydrazoic acid in the Schmidt reaction, trimethylsilyl azide provides an alternative source with diminished explosive properties.[72] This reagent reacts with ketones and their enol ethers under acidic conditions (Eq. 32)[73] or irradiation (Eq. 33)[74] to yield lactams. As with the reactions of hydrazoic acid, tetrazoles are often isolated as byproducts in the acid-promoted reactions.

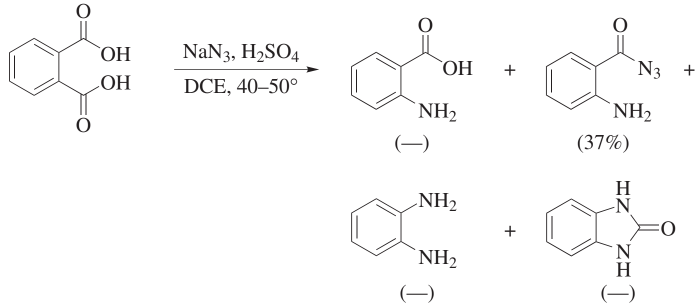


(Eq. 32)



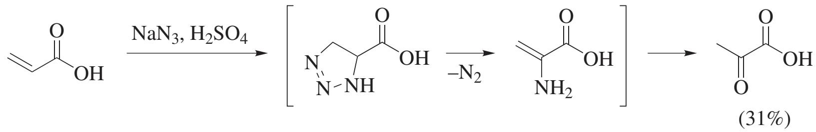
(Eq. 33)

Unusual Reactions and Alternative Electrophiles. A variety of interesting pathways have been reported in the nearly 100 years since the Schmidt reaction was first described.[75–77] This diversity is not surprising given the involvement of high-energy reactive intermediates and does not really detract from the overall utility of the reaction. For example, reaction of phthalic acid affords aniline products from one and two standard Schmidt reactions, respectively, along with a presumed acyl azide intermediate and a urea resulting from intramolecular trapping of an isocyanate (Eq. 34).[78,79] Instead of a Schmidt reaction, acrylic

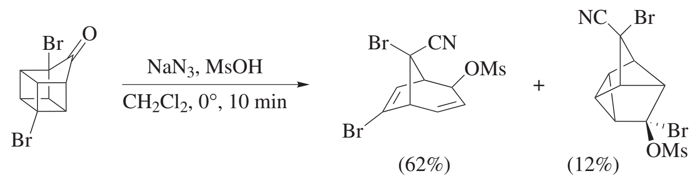


(Eq. 34)

acid undergoes a formal dipolar addition of azide to the double bond followed by acid-promoted decomposition to pyruvic acid (Eq. 35).[80] Similar cycloaddition reactions of alkyl azides are used to effect conversions of α,β-unsaturated ketones into aziridines (see "Schmidt Reactions of Alkyl Azides with Ketones and Aldehydes" section). Highly strained compounds often undergo skeletal rearrangements when exposed to HN_3 (Eq. 36).[81]

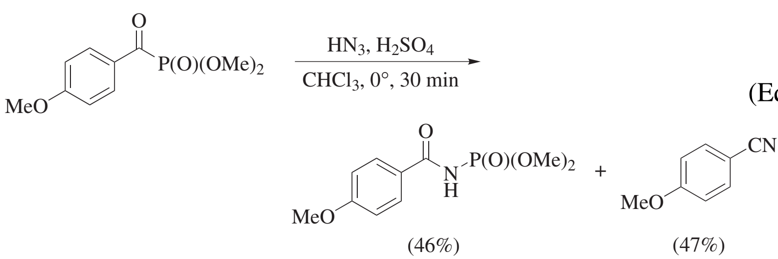


(Eq. 35)

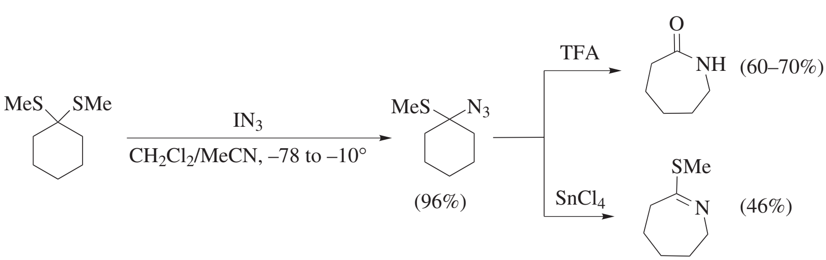


(Eq. 36)

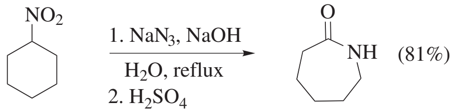
Schmidt reactions also can be carried out with O,O-dialkyl acylphosphonates (Eq. 37).[28,82] In addition, a version of the Schmidt reaction is known in which a dithioketal is activated by treatment with iodine azide to afford an α-azido sulfide (Scheme 9). This intermediate is converted into the corresponding ring-expanded lactam or thioimino ether upon treatment with trifluoroacetic acid or stannic chloride, respectively.[83] Finally, a little-used variation employs nitroalkanes as a carbonyl equivalent. Treatment of nitroalkanes with basic sodium azide affords amides in moderate to good yields (Eq. 38).[84]



(Eq. 37)



Scheme 9

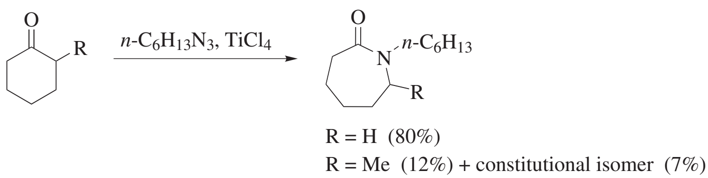


(Eq. 38)

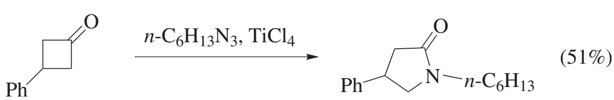
Schmidt Reactions of Alkyl Azides

The reactions of electrophiles with alkyl azides are considerably less general than those with hydrazoic acid. This section is organized according to the electrophile, beginning with a discussion of the reactions of azides with carbonyl groups and their equivalents and moving onto the reactions of alkyl azides with carbocations generated from double bonds or other precursors.

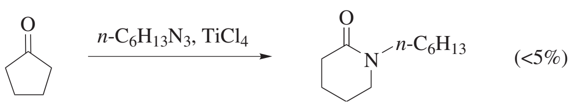
Reactions with Ketones and Aldehydes. The transformation of largest scope in this category involves intramolecular reactions of azidoalkyl-substituted ketones. Intermolecular reactions of azides and ketones have been only sparingly examined to date.[22,85] The known examples of this variation are poorly site selective, often poorly efficient, and limited by even moderate steric hindrance or the size of the ketone ring. The different yields obtained from reactions of *n*-hexyl azide either with cyclohexanone or with 2-methylcyclohexanone (Eq. 39)[22] exemplify the sensitivity of the reaction to additional steric bulk near the reacting carbonyl. Good yields are obtained in a few cases using a strong Lewis acid such as $TiCl_4$.[22,85] Even under these conditions, the reactions are severely limited (Eqs. 40–42). The reaction of alkyl azides with acyclic ketones is of similarly narrow utility.[85]



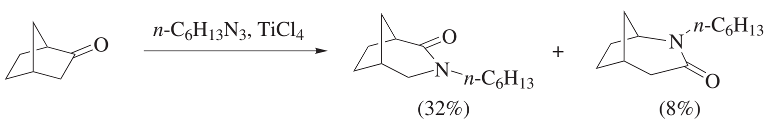
(Eq. 39)



(Eq. 40)

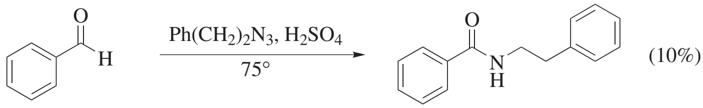


(Eq. 41)



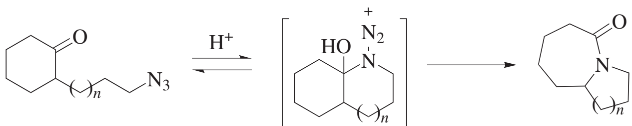
(Eq. 42)

Azides and aldehydes afford amides under protic acid conditions, but only from a few substrates, and in poor yields (Eq. 43).[21]



(Eq. 43)

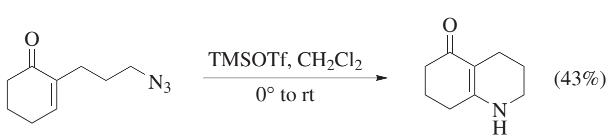
The intramolecular reactions are substantially superior in terms of scope, yields, allowable conditions, and selectivity—nearly every characteristic that one typically associates with synthetic utility. The prime restriction is that the distance between the carbonyl and azide groups must usually be 4 or 5 atoms for high yields. The former is preferred, presumably because it involves the formation of a six-membered cyclic intermediate. Examples involving five carbons typically require stronger Lewis acids (Eq. 44).[3]



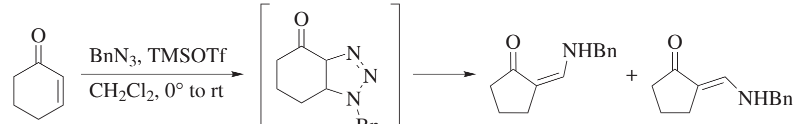
(Eq. 44)

n = 0, no reported examples
n = 1, TFA, 10 min (93%)
n = 2, TFA, 24 h, no conversion
n = 2, $TiCl_4$, 16 h (91%)
n = 3, no reported examples

The intramolecular process accommodates a great deal of variation in the ketone component such that successful reactions can be achieved with various ring sizes (reactions of cyclic 4–12 membered ketones have been reported[29]) and with acyclic versions. Apart from alkyl substituents, little work has been done to determine which functional groups are tolerated when adjacent to the ketone or the azide group. Electron-withdrawing substituents adjacent to the ketone slow down the reaction but are tolerated.[3] α,β-Unsaturated ketones containing appropriately tethered azides do not provide lactam products but instead afford products of apparent conjugate addition reactions (Eq. 45).[86] In a few cases, lactams have been prepared from α,β-unsaturated ketones upon irradiation (see "Comparison with Other Methods" section). The intermolecular version of this reaction also leads to non-amide products (Eqs. 46[87] and 47[88,89]). Similarly, unsaturated imides react to afford aminohydroxylation products (Eq. 48).[88] Presumably, the Lewis acid activates the enone so that it is more susceptible to 1,3-dipolar cycloaddition rather than 1,2-addition of azide to the ketone.[87]



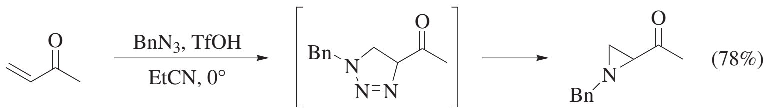
(Eq. 45)



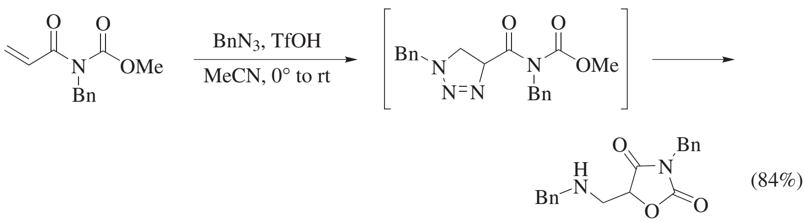
I II

I + **II** (68%) **I**:**II** = 3:2

(Eq. 46)

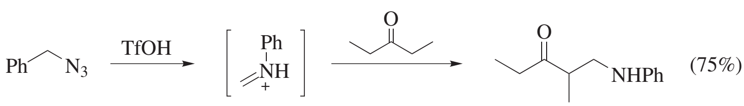


(Eq. 47)



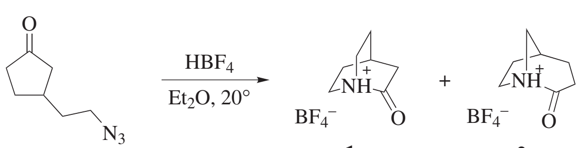
(Eq. 48)

Benzylic azides are unreliable partners with saturated ketones in both intermolecular[85] and intramolecular[90] versions of the Schmidt reaction. Thus, in cases where the Schmidt reaction is retarded due to steric crowding or the use of non-optimal tether lengths, the benzylic azides may undergo conversion into iminium ions under the reaction conditions. In such cases, products of Mannich-like processes have been reported (Eq. 49).[85]



(Eq. 49)

Although possible, reactions affording bridged lactams are rare. One important example entails the reaction of a ketone that bears an azidoalkyl side chain non-adjacent to the carbonyl group, a situation that necessitates bridged lactam formation. One of the two lactams formed is the long-sought "twisted" amide 2-quinuclidone (**1**) (Eq. 50).[91]



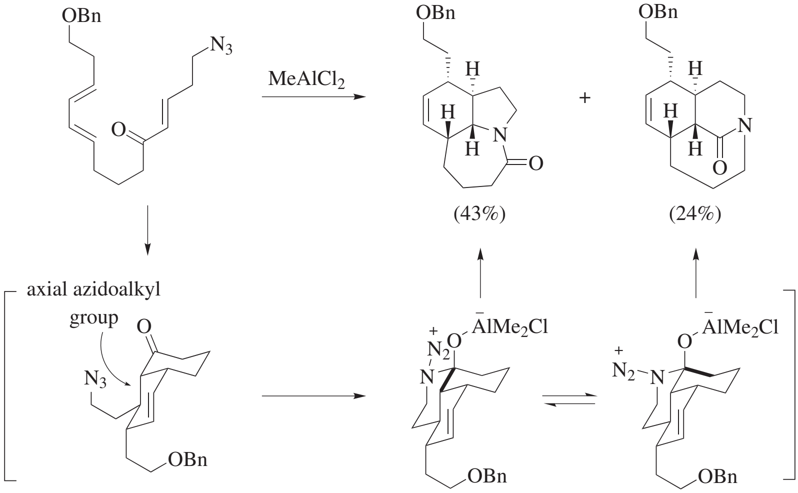
1 **2**

1:**2** = 76:24

1 (38%) after recrystallization

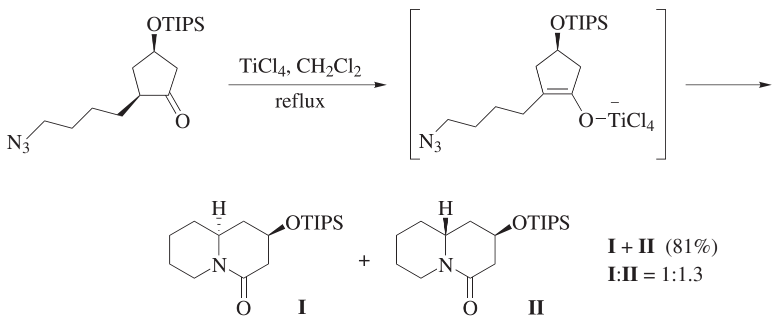
(Eq. 50)

In another example, intramolecular Schmidt reaction of a complex ketone containing an azidoalkyl group in an axial orientation gives a bridged lactam as a minor product (Scheme 10).[92] The Schmidt substrate is formed by an *endo*-selective intramolecular Diels–Alder reaction (an *exo* Diels–Alder pathway that affords another lactam product in 12% yield is omitted from the scheme). Presumably, two stereoisomeric azidohydrins can form from the intermediate shown, each of which leads to a lactam by antiperiplanar carbon–carbon bond migration with synchronous loss of nitrogen. In this system, one of these intermediates affords the usual fused lactam product whereas the other affords the bridged product.



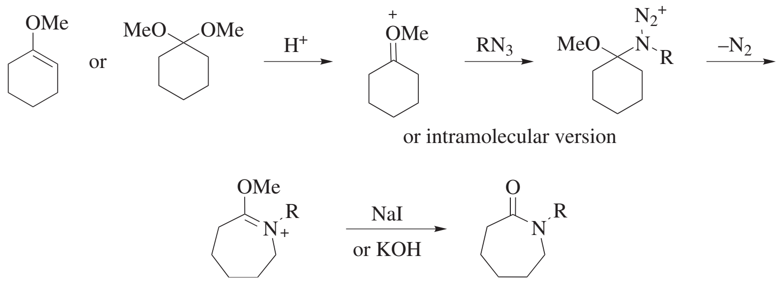
Scheme 10

As noted in the previous section, the intramolecular Schmidt reaction of alkyl azides generally occurs with retention of configuration. However, non-stereoselective reactions are observed in examples in which the carbon α to the carbonyl group undergoes reversible enolization under the reaction conditions (Eq. 51).[93]



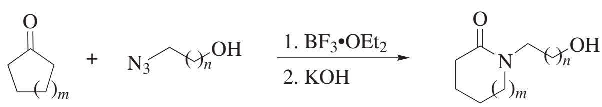
(Eq. 51)

Reactions of Enol Ethers, Ketals, or Hydroxyalkyl Azides. Ketals or enol ethers undergo a closely related reaction with alkyl azides to afford iminium ethers (Scheme 11).[94] In many cases, these intermediates can be isolated and characterized, but are more frequently converted into lactams by treatment of the iminium ether with aqueous base or sodium iodide. The former reaction proceeds via addition of hydroxide to the C=N bond and breakdown of the tetrahedral intermediate, while the latter involves direct S_N2 attack on the *O*-alkyl group. As with the reactions of alkyl azides and carbonyl groups, these reactions are most efficiently carried out intramolecularly.



Scheme 11

In a related process, 1,2- or 1,3-hydroxyalkyl azides react with cyclic ketones to afford lactams after hydrolysis of the primary iminium ether products (Eq. 52).[95,96] These reactions provide practical synthetic equivalents to the direct reactions of alkyl azides with ketones, despite the mechanistic differences (see previous section). This reaction works well for 5- to 7-membered cyclic ketones and is generally tolerant of substitution. Other products resulting from transamidation/transacylation processes may be obtained in reactions of ketones having 7 or more ring atoms (Eq. 18).[47,48]

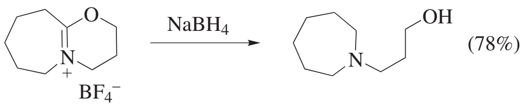


m	*n*	Yield (%)
1	1	96
1	2	98
2	1	98
2	2	90
3	1	68

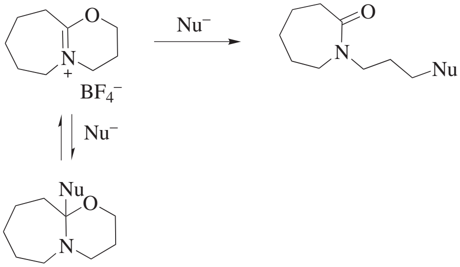
(Eq. 52)

The iminium ether intermediates in these reactions can react with nucleophilic species other than hydroxide. Depending on the nucleophile, reactions at two positions are possible.[46] The site selectivity is rationalized on the basis of reversibility of the initial addition reaction.[97] Thus, kinetic attack occurs at the formal cationic center as exemplified by the irreversible addition of hydride (Eq. 53).[46] However, most nucleophiles react reversibly at this center until they carry out an irreversible S_N2 displacement to afford an ω-functionalized *N*-substituted lactam

(Eq. 54).[46] In the examples shown, the iminium ether intermediate is isolated prior to treatment with the nucleophile (yields are from the iminium ether).



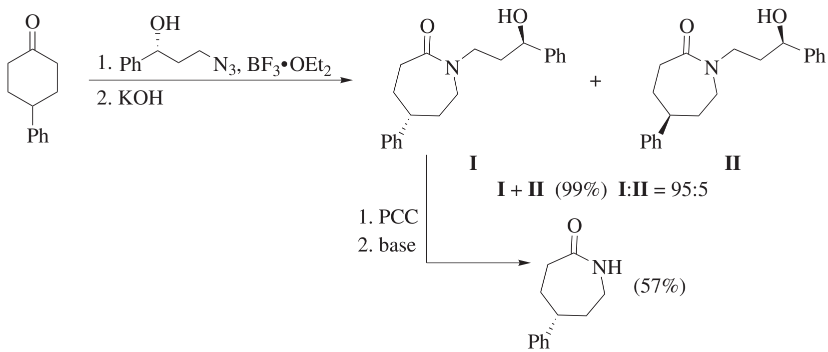
(Eq. 53)



Nu	Yield (%)
PhS	95
PhO	41
F	59
NC	82
N_3	85

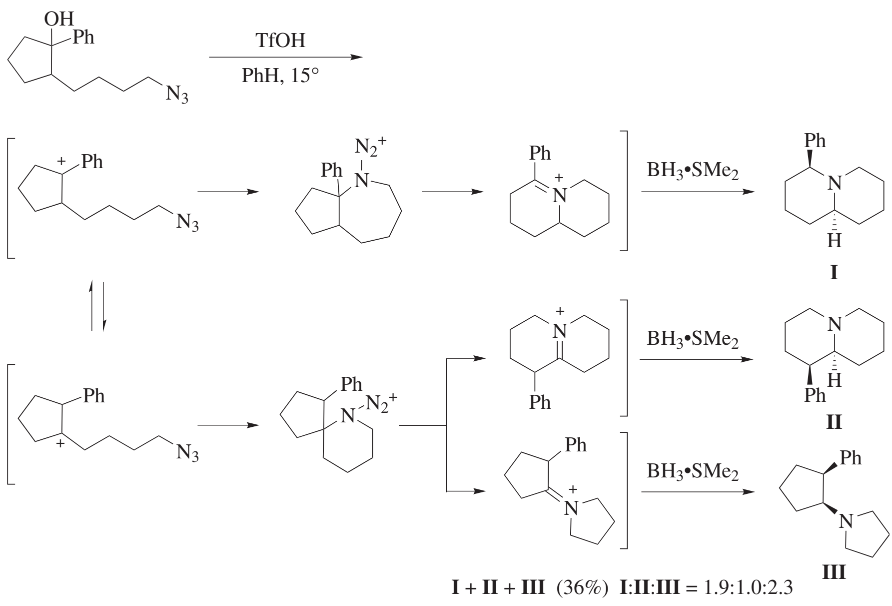
(Eq. 54)

The site selectivity of the Schmidt reaction in 2-substituted cycloalkanones is complex and depends on the substituent (see Eq. 22). However, an interesting mode of selectivity becomes possible in the reactions of symmetrically substituted ketones, such as 4-phenylcyclohexanone, with chiral hydroxyalkyl azides (Scheme 12).[95,98,99] In these cases, the methylene groups adjacent to the ketone are enantiotopic, so that stereoisomeric lactams result depending on which methylene group migrates. These reactions afford up to 95:5 ratios of diastereoisomers in favorable cases. Following separation of the diastereomeric lactams, removal of the nitrogen substituent affords the enantiomerically pure lactam.

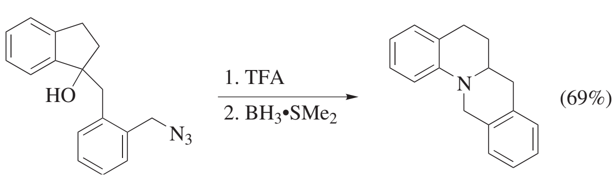


Scheme 12

Reactions with Alkenes, Alcohols, and Other Carbocation Precursors. The reactions of alkyl azides with carbocations, followed by a hydride reduction step, provide amines rather than lactams.[17,23,24,51,100–103] The reaction scope appears to be quite broad for intramolecular reactions. Most of the substrates have four carbons between the azide and the initial site of attack, with examples of both fused and bridged intermediates being reported. In some cases, multiple products are observed due to the intervention of carbocationic rearrangements prior to azide attack (Scheme 13).[101] In addition, each azide adduct is in principle subject to up to six possible alkyl, aryl, or hydride migrations in the ensuing step. In practice, however, only a few of the possible products are generally observed and in many cases careful synthetic planning can steer the reaction toward a single product in high yield (Eq. 55).[102]

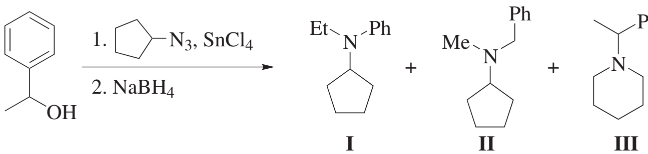


Scheme 13



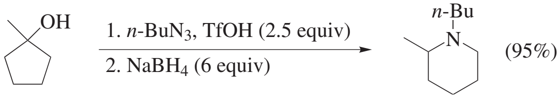
(Eq. 55)

The reactions of benzylic or tertiary carbocations with alkyl azides are also feasible in an intermolecular sense. As in the preceding cases, multiple products resulting from the migration of various groups are often observed (Eq. 56),[17] but in favorable cases the reactions can result in a single product (Eq. 57).[17,24] Epoxides are also effective cation precursors (Eq. 58).[104] As above, the primary product in each of these reactions is an iminium ion that is reduced to afford a tertiary amine.

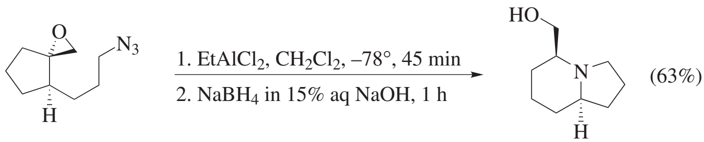


I + **II** + **III** (57%) **I**:**II**:**III** = 2.5:1:2

(Eq. 56)



(Eq. 57)



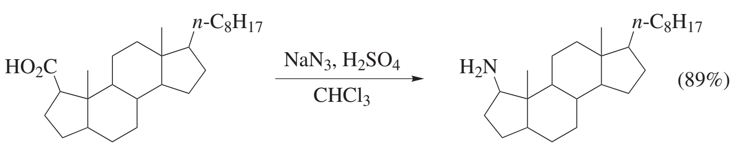
(Eq. 58)

Double bonds are also converted into cation equivalents through the addition of an electrophilic mercury salt (Scheme 14).[50] Attack of azide upon the mercuronium species affords an intermediate that loses nitrogen and undergoes a carbon-to-nitrogen migration. Subsequent addition of reducing agents affords products similar to those obtained when the reaction is promoted by proton sources. In some cases, useful differences in site selectivity are obtained using Hg(II) promotion in comparison to the acid-mediated conversions. Thus, with Hg(II), only products resulting from aryl migration are observed. In contrast, reaction of the same azide under protic conditions affords an approximately equal quantity of products from aryl and alkyl migrations (Scheme 14).[50]

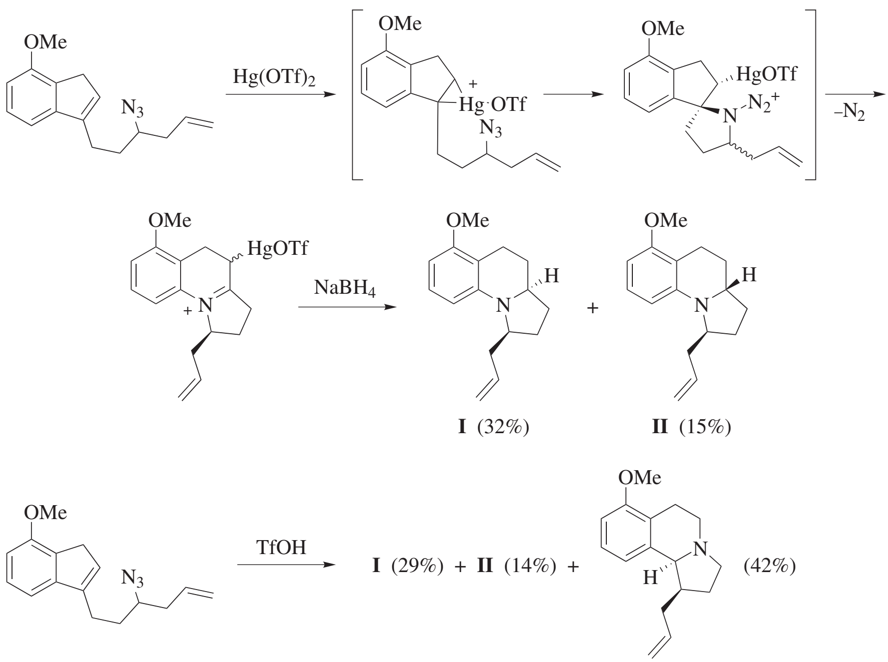
Metal activation of a triple bond provides another electrophilic species that is subject to azide attack (Scheme 15).[105] Thus, treatment of tethered azide-containing alkynes with a gold salt leads to pyrroles via attack of azide. A mechanistic hypothesis involving gold(I)-induced activation of the alkyne toward addition by the proximal nitrogen of the azide is shown. Subsequent loss of dinitrogen produces a cationic intermediate that is stabilized by electron donation from gold. A formal 1,2-shift regenerates the cationic gold(I) catalyst and produces a $2H$-pyrrole that tautomerizes to the observed product.

APPLICATIONS TO SYNTHESIS

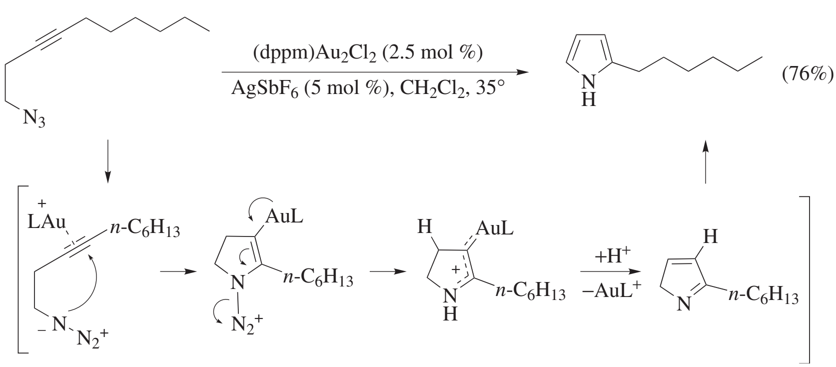
Both inter- and intramolecular Schmidt reactions are encountered as key steps in syntheses of alkaloids and other biologically interesting molecules. Simple examples are found in a route toward bisnorsteroids (Eq. 59)[106] and as a key, albeit poorly selective, step in a total synthesis of lycoramine (Scheme 16).[107]



(Eq. 59)

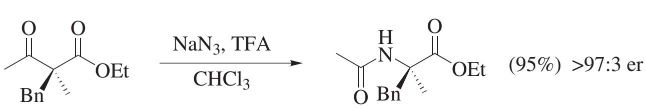


Scheme 14

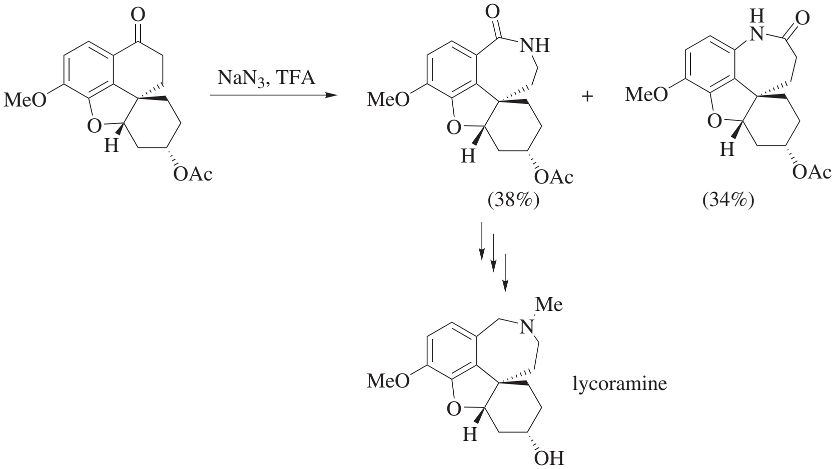


Scheme 15

Several groups have taken advantage of the stereospecificity of the Schmidt reaction en route to non-natural, quaternary amino acid derivatives.[108,109] In this approach, an α,α-disubstituted β-keto ester, prepared by asymmetric alkylation, is subjected to hydrazoic acid to afford the N-acetylamino ester with high enantiomeric purity (Eq. 60).[108,109]

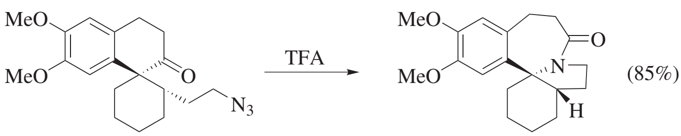


(Eq. 60)



Scheme 16

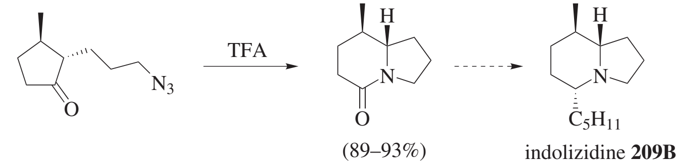
More recent work has used intramolecular Schmidt reactions in routes to multicyclic alkaloid skeletons. An early example was directed toward the homoerythrina spirocyclic ring system (Eq. 61).[110] Instructively, neither Beckmann nor HN_3-mediated Schmidt reaction conditions succeed in converting the corresponding keto mesylate into the lactam. Presumably, the location of the ketone adjacent to a quaternary center limits the facility of intermolecular azidohydrin formation in the latter case.



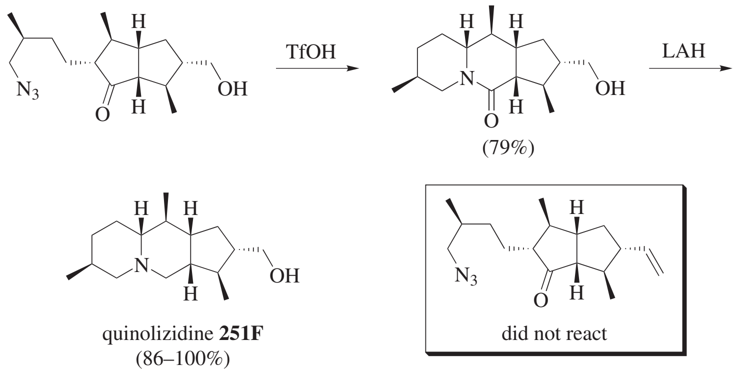
(Eq. 61)

Several applications of the Schmidt reaction have been directed toward alkaloids isolated from South American frogs. The first example, used to synthesize indolizidine **209B**, contains the ideal arrangement of four carbons between the azide and carbonyl groups (Scheme 17).[111] Accordingly, simple dissolution of the azide in trifluoroacetic acid initiates a smooth ring expansion process. On the other hand, the formation of a quinolizidine ring system requires harsher conditions; in the example shown in Scheme 18, triflic acid is needed.[112] Subsequent treatment of the lactam with LAH affords the quinolizidine **251F** (Scheme 18). Notably, the analog with an alkene in place of the terminal alcohol (box) could not be made to react with the azide in this system.

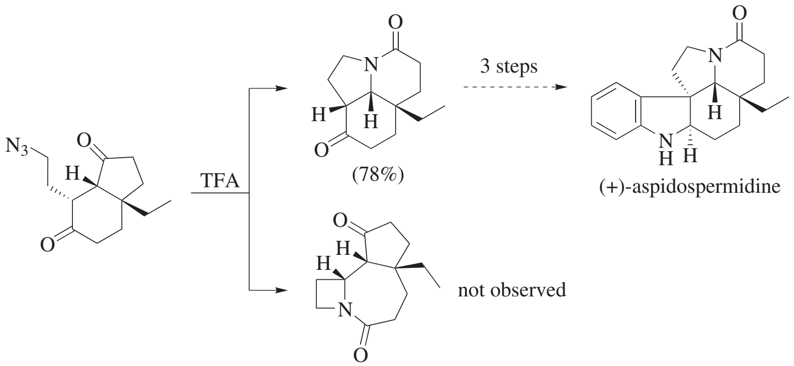
An interesting competition was examined in a route to aspidospermidine (Scheme 19).[113,114] Two lactams can be formed depending on which carbonyl group is attacked by the azide, but only the ketone bearing a 1,6-relationship with the azide reacts. The alternative pathway, which would lead to a product containing a four-membered ring, is not observed.



Scheme 17



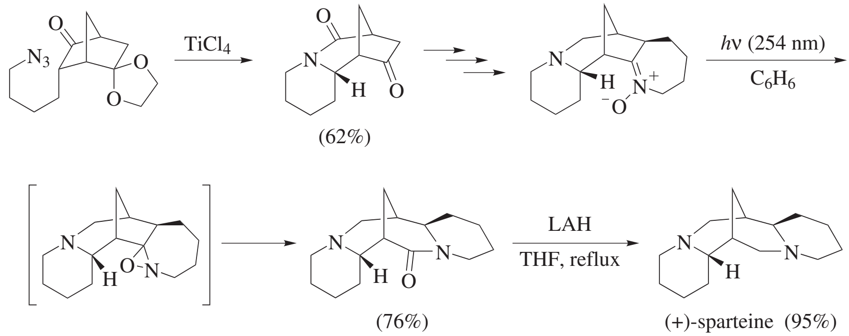
Scheme 18



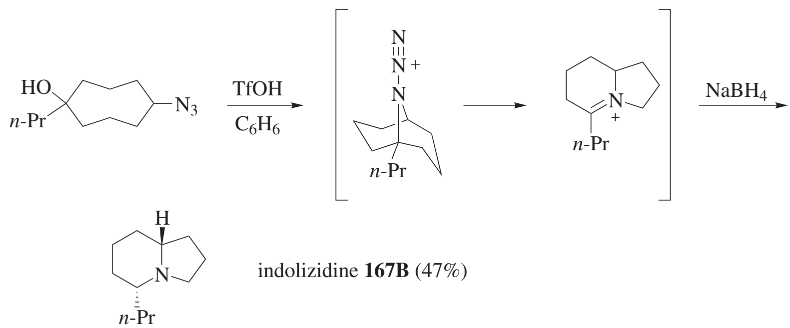
Scheme 19

An intramolecular Schmidt reaction in a bridged ring system is used in the context of a total synthesis of (+)-sparteine (Scheme 20).[115] In this synthesis, the initial Schmidt reaction proceeds smoothly, but it is not possible to use an analogous Schmidt reaction to create the rest of the ring system. A photochemical nitrone rearrangement is ultimately used to complete the synthesis.

An elegant example of a cation-mediated Schmidt reaction is used in a route to another South American frog toxin (Scheme 21).[51,104] In this case, carbocation formation is followed by transannular attack of azide. Only one iminium



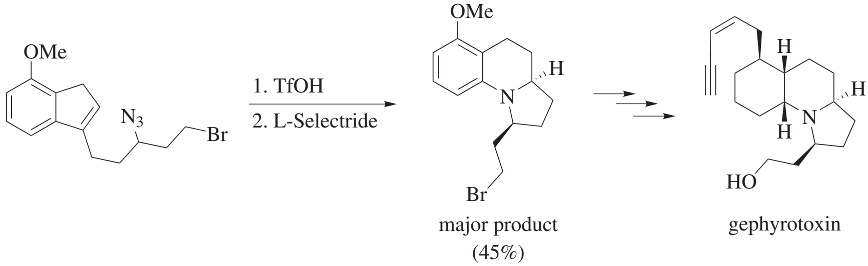
Scheme 20



Scheme 21

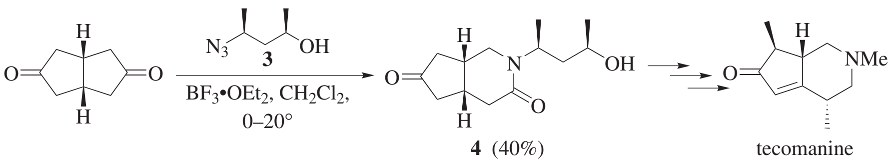
ion can be formed following carbon-to-nitrogen migration because of symmetry. Reduction of this ion occurs stereoselectively to afford indolizidine **167B**.

An additional application of the cation-initiated Schmidt reaction is directed toward a formal synthesis of gephyrotoxin as shown in Scheme 22.[102] The major product involves migration of the phenyl group (a small amount of the alternative alkyl migration product, not shown, is also obtained).



Scheme 22

An asymmetric, hydroxyalkyl-azide-mediated Schmidt reaction is employed in the synthesis of tecomanine.[116] In the key step, the *meso* [3.3.0] bicyclic dione reacts with chiral azide **3** (Scheme 23). Two lactams are formed in a ca. 2:1 ratio; the major isomer **4** is isolated in 40% yield. Removal of the nitrogen substituent and additional modification leads to the natural product.

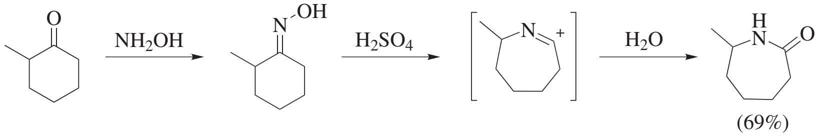


Scheme 23

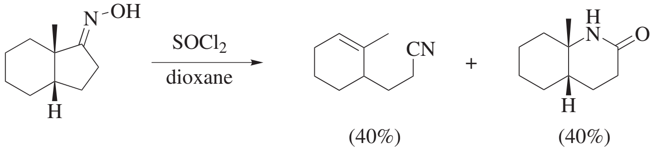
COMPARISON WITH OTHER METHODS

The Schmidt reaction of hydrazoic acid with ketones and the Beckmann reaction are often compared due to the similarity of the electrophiles employed and the products (Scheme 24).[33,117] Unlike the Schmidt reaction, the Beckmann reaction involves two steps: the preparation of an oxime from the starting carbonyl compound followed by either acid treatment or conversion of the hydroxyl group to a leaving group, e.g., by treatment with $POCl_3$. Like the Schmidt reaction using hydrazoic acid, the Beckmann rearrangement is limited to the synthesis of *N*-unsubstituted lactams.

The two reactions are comparable in scope, site selectivity, and synthetic utility. Very often, both Schmidt and Beckmann conditions are investigated when a nitrogen insertion is needed. Although it could be argued that the need for two steps to execute a Beckmann rearrangement is a drawback, in practical terms oxime formation is usually easy and sufficiently high yielding that it does not appreciably detract from using the process. Both sets of procedures have broad scope. Like the Schmidt reaction, the Beckmann rearrangement is also subject to competing nitrile formation from aldehydes. In addition, ketones bearing a cation-stabilizing group in the β position undergo Beckmann fragmentation reactions. Although these reactions have themselves been used to considerable advantage in synthesis, fragmentation when ring expansion is desired is clearly a drawback (Eq. 62).[118,119]

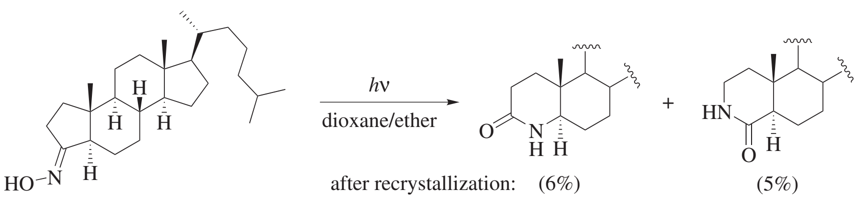


Scheme 24

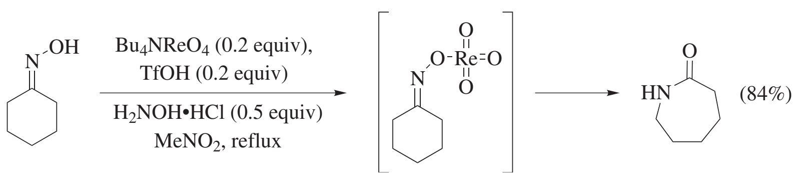


(Eq. 62)

Although exceptions exist, the Schmidt and Beckmann reactions generally afford the same constitutional isomer, i.e., that resulting from migration of the more highly substituted carbon. For the Beckmann reaction, this outcome is due to the preferential formation of the more stable oxime (OH group *anti* to the more bulky group) coupled with stereospecific migration of the antiperiplanar group in the rearrangement step. The similarity of product profiles for a given substrate in the Schmidt and Beckmann reactions has been often used to imply the intermediacy of diazoiminium ethers in the former reaction. Oximes can also be rearranged to provide lactams under photochemical conditions that obviate the need for highly acidic reaction conditions (the photo-Beckmann rearrangement, Eq. 63).[120] Another modification of the Beckmann reaction is promoted by a combination of tetrabutylammonium perruthenate and triflic acid (Eq. 64).[121,122]

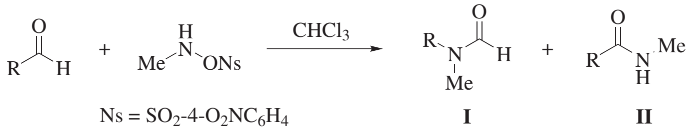


(Eq. 63)



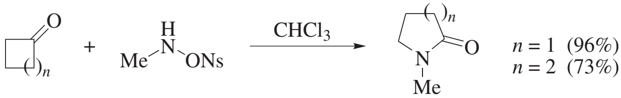
(Eq. 64)

Relatively few alternatives exist to the Schmidt reactions of alkyl azides. One way of directly converting an aldehyde or ketone into an *N*-alkylated amide is to treat the substrate with a reagent of the type $RNHOSO_2Ar$. The initial carbonyl addition step leads to a species that is pre-activated for loss of sulfonate and rearrangement (Eqs. 65[123] and 66[124−127]). Like the intermolecular Schmidt reaction of alkyl azides promoted by $TiCl_4$, this protocol does not have a particularly broad scope but has been usefully employed in particular contexts.



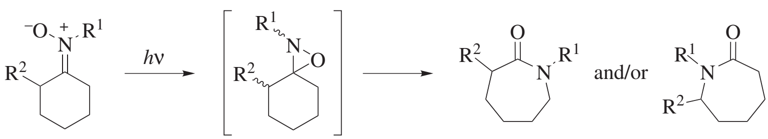
(Eq. 65)

R	Yield (%) I + II	I:II
Ph	96	23:1
4-BrC_6H_4	82	2:1
Et	64	1:7

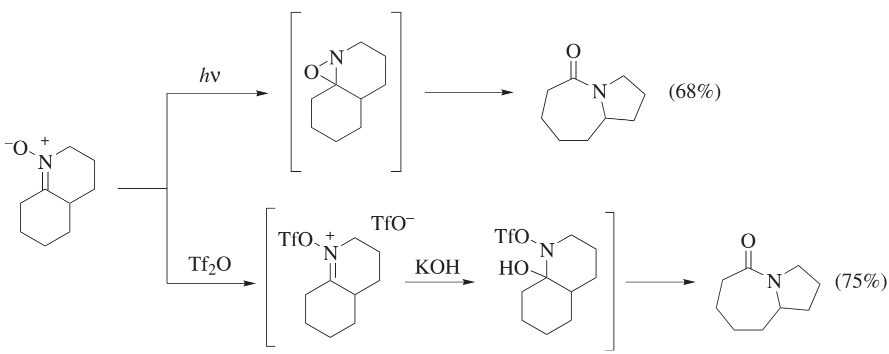


(Eq. 66)

The photochemical rearrangement of nitrones to amides (Eq. 67),[128–131] which also provides *N*-substituted lactams, probably proceeds via the initial rearrangement of the nitrone to the corresponding oxaziridine. This heterocycle then undergoes photochemically mediated in situ rearrangement to the lactam. This reaction has also been explored in the intramolecular context to provide a variety of ring systems.[130,132–136] The reaction can also be promoted by converting the nitrones into their *O*-trifluoromethanesulfonyl derivatives followed by base-mediated rearrangement (Scheme 25).[136] Like the photo-Beckmann reaction, this reaction is useful for cases in which strongly acidic conditions are not desirable.[93,115]



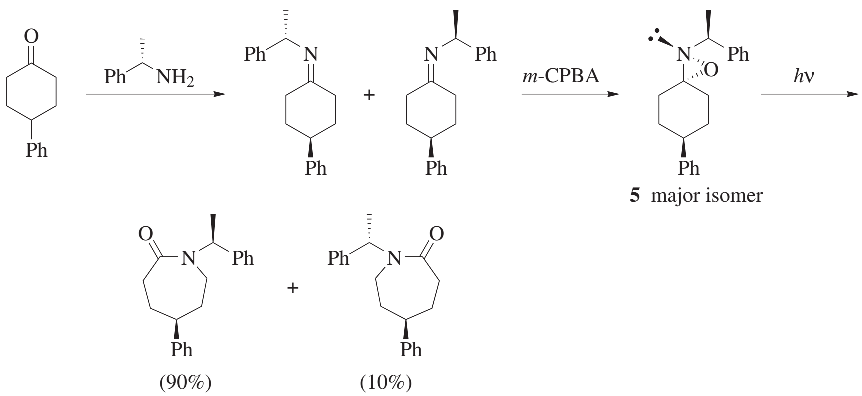
(Eq. 67)



Scheme 25

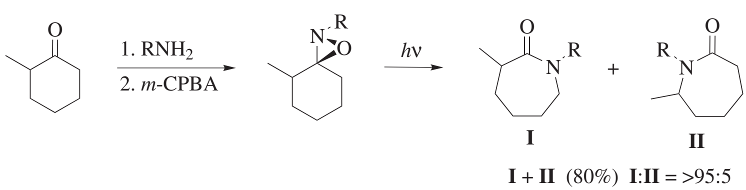
Oxaziridines can also be prepared from ketones or aldehydes via the corresponding imine derivatives, which are oxidized using *m*-CPBA or other common oxidants.[43,137–140] In addition to their likely involvement in photo-Beckmann reactions, oxaziridines are useful precursors to lactams in their own right, via photolytic rearrangement.[78,141–143] Rearrangements can also be induced by treatment with certain low-valent metal salts (iron(II) or copper(I)).[131,144–146]

The photochemical oxaziridine rearrangement is subject to a stereoelectronic effect that has an important synthetic ramification. Chiral oxaziridine **5** (Scheme 26) undergoes stereoselective rearrangement to afford the lactam with 9:1 stereoselectivity. In general, the predominant product from such photochemical rearrangements results from migration of the bond antiperiplanar to the lone pair on the oxaziridine nitrogen atom (which is non-invertable under the reaction conditions).[147,148]



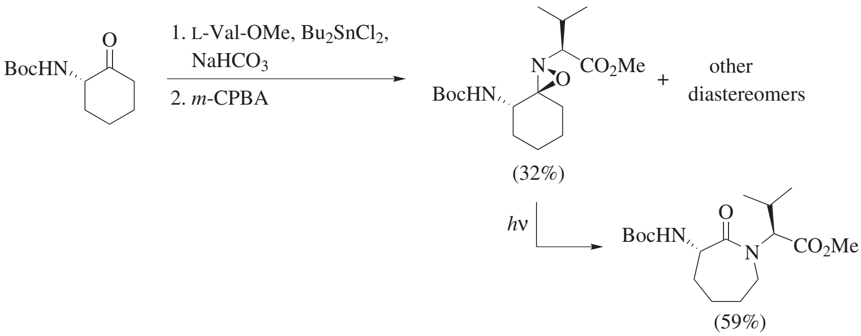
Scheme 26

Because of this effect, the oxaziridine rearrangement reaction is the only nitrogen insertion reaction known that provides a reliable route to lactams resulting from migration of the less substituted carbon in unsymmetrical cycloalkanones (Scheme 27).[149–151] Thus, the oxaziridine intermediate that is generally formed places the *N*-alkyl group away from the more highly substituted carbon on the ketone.[142] An example using this strategy to prepare a series of peptide analogs is shown in Scheme 28.[152]



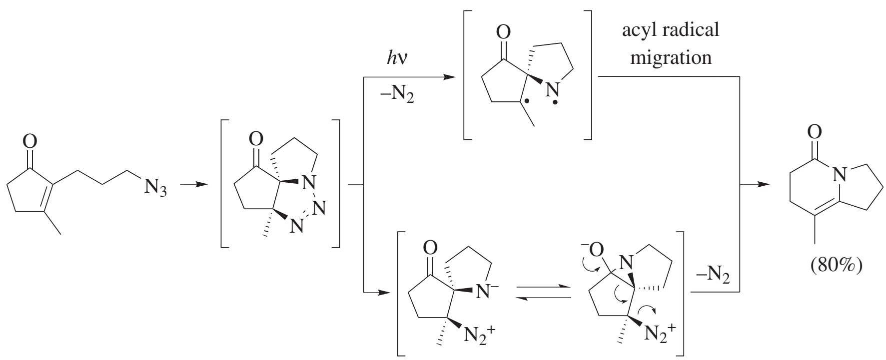
Scheme 27

A significant limitation of the intramolecular Schmidt reaction of alkyl azides is its inapplicability to unsaturated ketones (Eq. 45). In contrast, insertion products



Scheme 28

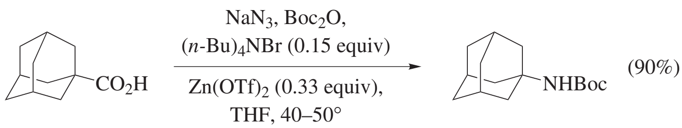
of azides appended to such partners are observed under irradiation.[153–156] These reactions are proposed to involve a thermally allowed [3+2] cycloaddition onto the enone, photochemical generation of a diradical with loss of dinitrogen, and finally molecular reorganization to afford the final products (Scheme 29).[86] An ionic mechanism may also be operative in this case.



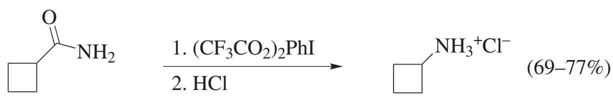
Scheme 29

As noted earlier, the Schmidt reactions of hydrazoic acid with carboxylic acids or with aldehydes are rarely used by synthetic chemists. In the former case, the Curtius reaction of carboxylic acids, which involves the conversion of the carboxylic acid into an acyl azide that is then subjected to thermal rearrangement, is the most common reaction for the synthesis of amines from acids. The acyl azide can be prepared via the acyl chloride (typically readily made from the acid), other kinds of activated acids,[157] or directly from the acid via in situ activation, e.g., by reaction with diphenyl phosphoryl azide.[158]

The Curtius reaction has been widely adopted because its conditions are relatively mild and do not require the use of the toxic and explosive hydrazoic acid as a reagent. In addition, the thermal acyl azide rearrangement provides as its initial product an isocyanate; hydrolysis of this species with water affords the amine. Even better, the isocyanate can be combined with alcohols or amines to afford carbamates or ureas, respectively. A one-pot version of the Curtius reaction that provides *N*-Boc amines in 50–94% yields has also been reported (Eq. 68).[159] Another widely used reaction that does not involve the formation of N_3-containing species is the Hofman rearrangement of amides to afford amines (Eq. 69).[160]



(Eq. 68)



(Eq. 69)

EXPERIMENTAL CONDITIONS

Schmidt reactions using hydrazoic acid are generally accomplished by generating HN_3 in situ from NaN_3, i.e., by adding it to sulfuric acid, HCl, or polyphosphoric acid.[161] Cosolvents such as chloroform or DME may be used. In some cases, an additional protic or Lewis acid such as $SnCl_4$, trichloroacetic acid, or $BF_3{\bullet}OEt_2$ is added. Heating is often required. Some older procedures involve preparation of stock solutions of HN_3 in chloroform or other solvents, although these are rarely used nowadays.[11]

The use of hydrazoic acid is hazardous, as it is both explosive and toxic. Proper precautions that include safety shields and an efficient hood are essential. Typically, the workup of the reaction involves a basic extraction step that makes it possible to remove hydrazoic acid in the aqueous layer (as NaN_3 for example). For reasons discussed below, it is best not to use methylene chloride as the organic solvent in such extractions.

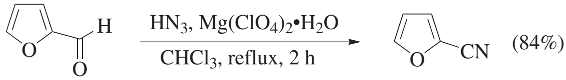
Intermolecular Schmidt reactions in which alkyl azides react with carbonyl compounds are generally carried out in methylene chloride using commercial solutions of $TiCl_4$. Intramolecular reactions can be carried out under similar conditions, although a wider range of Lewis acids are usable for these more reactive substrates. Alternatively, protic acid conditions can be used, with neat trifluoroacetic acid or triflic acid/methylene chloride being most common in this context. Similar conditions can be employed for the reactions of azides with cations derived from olefins or alcohols.

Either protic or Lewis acids can be used to facilitate the intermolecular reactions of hydroxyalkyl azides with ketones; a comparative study suggests that $BF_3{\bullet}OEt_2$ is the most effective promoter for this reaction.[96] The key difference between these reactions and those noted above is that the initial product is not a lactam or amide but rather an iminium ether. These salts can be isolated using standard workup conditions and in some cases have been chromatographed. Treatment with an aqueous base like KOH or $NaHCO_3$ is commonly used to convert these initial products into lactams.

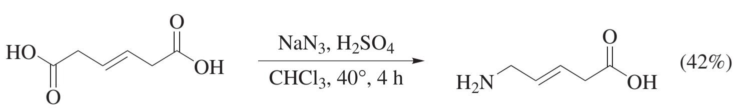
Two safety considerations come into play for the reactions with alkyl azides. The first is the nature of the azide itself. *The authors advise readers to assume that any alkyl azide is a possible explosion hazard and to treat azides having low formula weights with particular caution.* Specific manipulations to be avoided include heating (especially in the absence of solvent), vacuum distillation, preparing on large scale, or allowing exposure to metals.

A second consideration should be heeded when preparing azides from sodium azide. *NaN_3 is believed to pose a particular hazard when heated or evaporated in methylene chloride solutions; the formation of diazidomethane is possible under these conditions and explosions have been documented.*[162] One can also prepare alkyl azides via halogen displacement or epoxide opening by azidotrimethylsilane activated by fluoride or a Lewis acid.[163,164] However, *azidotrimethylsilane has been associated with toxic reactions, possibly by environmental hydrolysis to form hydrazoic acid.*[165] Finally, a variation of the Mitsunobu reaction using $Zn(N_3)_2$ can be used to prepare azides directly from alcohols.[166]

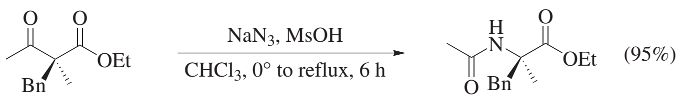
EXPERIMENTAL PROCEDURES



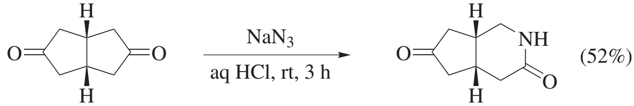
Furan-2-carbonitrile [Schmidt Reaction of an Aldehyde with Hydrazoic Acid to Afford a Nitrile].[167] To a three-necked flask with a mechanical stirrer and a reflux condenser were added 2-furaldehyde (9.61 g, 0.1 mol), a solution of HN_3 in $CHCl_3$ (15 mL, 0.11 mol), and $Mg(ClO_4)_2$ (25.0 g, 0.1 mol). The release of gaseous nitrogen began after 5 min. The flow of nitrogen became strongest after 10 to 15 min. When the release of nitrogen had stopped, the reaction mixture was brought to its boiling point and kept there for 2 h. The contents of the flask were cooled to rt, water was added, and the mixture was filtered. The organic layer was washed twice with water, dried (Na_2SO_4), and evaporated. The residue was distilled under vacuum to give the desired product (7.82 g, 84%): bp 147°; ^1H NMR (300 MHz, $CDCl_3$) δ 6.63 (dd, $J = 1.8, 3.7$ Hz, 1H), 7.33 (d, $J = 3.7$ Hz, 1H), 7.82 (d, $J = 0.75$ Hz, 1H); IR (neat) 3110, 2200, 1575 cm^{-1}. Anal. Calcd for C_5H_3NO: C, 64.52; H, 3.25; N, 15.05. Found: C, 64.44; H, 3.61; N, 14.91.



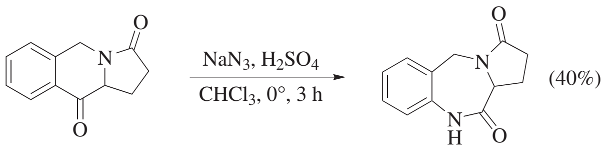
(*E*)-5-Aminopent-3-enoic Acid [Schmidt Reaction of a Carboxylic Acid with Hydrazoic Acid to Afford an Amine].[168] (*E*)-2-Butene-1,4-dicarboxylic acid (1.4 g, 9.71 mmol) was suspended in $CHCl_3$ (40 mL), and concentrated sulfuric acid (4.0 mL) was added. NaN_3 (0.65 g, 10 mmol) was added in small amounts over 30 min while the mixture was stirred rapidly. After a further 4 h at 40° the $CHCl_3$ layer was decanted from the viscous residue which was washed again with $CHCl_3$ (30 mL). The residue was dissolved in water (150 mL), filtered, and added to a column of Dowex 50 W (H^+) ion-exchange resin (50 mL). The column was washed with water to neutral pH and then the amino acid was eluted with aqueous pyridine (300 mL, 1 M). Evaporation of the solvent afforded an oil (600 mg) that slowly solidified. Recrystallization from water/ethanol gave the desired product as white needles (0.437 g, 42%): mp 165–167°; IR (nujol) 3500–2400, 2180, 1625 cm^{-1}; ^1H NMR (89.6 MHz, D_2O/DCl) δ 3.64 (d, J = 6.1 Hz, 2H), 4.03 (d, J = 5.7 Hz, 2H), 6.28 (m, 2H); MS (EI) m/z: $[M + H]^+$ 116 (100), 99 (86), 98 (11), 85 (10), 70 (13). Anal. Calcd for $C_5H_9NO_2$: C, 52.2; H, 7.9; N, 12.2. Found: C, 52.0, H, 7.9; N, 12.4.



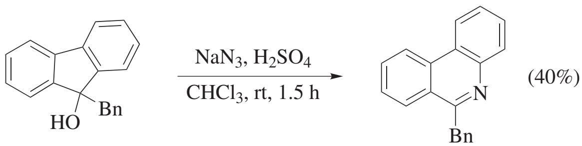
(*R*)-Ethyl 2-Acetamido-2-methyl-3-phenylpropanoate [Schmidt Reaction of an Acyclic Ketone with Hydrazoic Acid to Afford an Amide].[109] Methanesulfonic acid (0.73 mL, 10.0 mmol) was added dropwise to the stirred solution of ethyl (*S*)-2-benzyl-2-methylacetoacetate (234 mg, 1.00 mmol) in $CHCl_3$ (5 mL) at 0°, and then NaN_3 (325 mg, 5.0 mmol) was added. After being refluxed for 6 h, the reaction mixture was cooled to rt, diluted with H_2O, neutralized with diluted aqueous NH_3, extracted with Et_2O, and dried over $MgSO_4$. Removal of the solvent afforded an oily residue, which was purified by column chromatography on silica gel (hexane/EtOAc 9:1) to give the desired product as a colorless oil (237 mg, 95%): $[\alpha]^{25}_D - 63.8$ (c 1.10, $CHCl_3$), lit. $[\alpha]_D - 47.8$ (>97.5:2.5 er); ^1H NMR ($CDCl_3$) δ 1.35 (t, J = 3.0 Hz, 3H), 1.66 (s, 3H), 1.96 (s, 3H), 3.21 (d, J = 13.5 Hz, 1H), 3.60 (d, J = 13.5 Hz, 1H), 4.29 (m, 2H), 6.09 (br s, 1H), 7.02–7.08 (m, 2H), 7.18–7.30 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 14.1, 23.4, 24.0, 41.0, 61.2, 61.8, 126.8, 128.2, 129.8, 136.6, 169.5, 173.9; IR (neat) 3300 (br), 1720, 1660 cm^{-1}. FABMS m/z: $[M + H]^+$ 250.



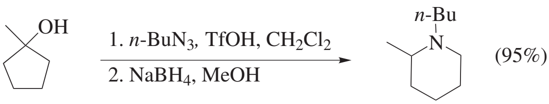
(1*R, 6*S**)-3-Azabicyclo[4.3.0]nona-4,8-dione [Schmidt Reaction of a Cyclic Ketone with Hydrazoic Acid to Afford a Lactam].[116]** Sodium azide (0.60 g, 9.1 mmol) was added portionwise over 20 min to a solution of *cis*-bicyclo[3.3.0]octane-3,7-dione (1.0 g, 7.2 mmol) in 36% aqueous HCl (20 mL), while keeping the temperature below 35°. The mixture was stirred for 3 h at rt and then brought to pH 10 with 20% aqueous NaOH at 0°. Precipitated NaCl was filtered off and the aqueous layer was extracted continuously with $CHCl_3$ for 48 h. Drying the organic phase over $MgSO_4$, followed by removal of solvent, furnished a residue that was separated on a silica gel column (30 g). Elution with CH_2Cl_2/acetone (85:15) gave unreacted diketone (240 mg) and the desired product (576 mg, 52%): mp 120–122°; ^{1}H NMR ($CDCl_3$) δ 2.10–2.30 (m, 3H), 2.40–2.90 (m, 5H), 3.21 (ddd, J = 3.0, 6.8, 13.0 Hz, 1H), 3.52 (ddd, J = 3.5, 5.8, 13.0 Hz, 1H), 6.3 (br s, 1H); ^{13}C NMR (D_2O) δ 30.7 (d), 31.3 (d), 31.9 (t), 40.9 (t), 41.9 (t), 43.6 (t), 175.4 (s), 223.7 (s); IR (neat) 3246, 2935, 1735, 1667, 1638 cm^{-1}; MS m/z: M^+153 (100), 125 (10), 112 (33), 96 (35), 82 (53), 68 (33), 54, (82), 41 (78). Anal. Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.76; H, 7.21; N, 9.11.



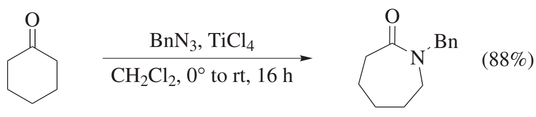
10,11a-Dihydro-1*H*-benzo[*e*]pyrrolo[1,2-*a*][1,4]diazepine-3,11(2*H*,5*H*)-dione [Schmidt Reaction of a Heterocyclic Ketone with Hydrazoic Acid to Afford a Lactam].[169] To a solution of 1,2-dihydropyrrolo[1,2-*b*]isoquinoline-3,10(5*H*,10a*H*)-dione (1.5 mmol) in $CHCl_3$ (30 mL) at 0°, was added concentrated sulfuric acid (24.3 mL). NaN_3 (214 mg, 3.3 mmol) was added portionwise and the mixture was stirred for 3 h at this temperature. Ice (250 g) was then added. The mixture was extracted with CH_2Cl_2 (3 × 50 mL), and the organic extracts were washed with water (2 × 25 mL) and dried over $MgSO_4$. After evaporation under vacuum, the crude product was purified by chromatography on a silica gel column (240–400 mesh) using CH_2Cl_2/MeOH (99:1, v/v) as eluent to give the desired product (40%): mp 202–204°; ^{1}H NMR ($CDCl_3$) δ 2.00–2.10 (m, 2H), 2.40–2.70 (m, 2H), 4.18 (q, J = 7.1 Hz, 1H), 4.28 (d, J = 14 Hz, 1H), 4.77 (d, J = 14 Hz, 1H), 7.09 (d, J = 8 Hz, 1H), 7.22 (d, J = 8 Hz, 1H), 7.35 (d, J = 8 Hz, 1H), 7.37 (d, J = 8 Hz, 1H), 8.06 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.75, 29.9, 44.6, 57.8, 122.1, 126.4, 127.3, 129.6, 130.4, 136.8, 169.3, 173.4; IR (neat) 3160, 1670 cm^{-1}; MS m/z: M^+ 216. Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.95. Found: C, 66.39; H, 5.47; N, 13.18.



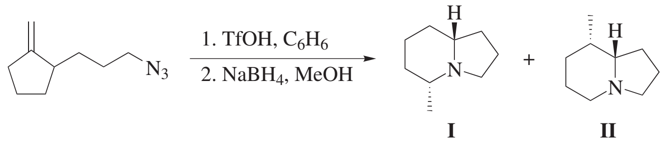
9-Benzylphenanthridine [Schmidt Reaction of an Alcohol and Hydrazoic Acid to Afford an Imine].[170] To a suspension of NaN_3 (7.3 g, 11.0 mmol) in $CHCl_3$ (15 mL), cooled in ice, was added dropwise sulfuric acid (98%, 29 mL) with stirring that was continued for 10 min at 0°. The ice bath was replaced by a water bath maintained at rt, and a solution of 9-benzylfluoren-9-ol (2.0 g, 7.3 mmol) in $CHCl_3$ (20 mL) was added during 1 h to the vigorously stirred mixture. Stirring was continued for a further hour; the mixture was then poured on ice (1.2 kg) and shaken. From the aqueous acidic solution, and from the sulfate (which frequently separated), the base was liberated by addition of 2 N NaOH. The product was filtered off, washed, and dried. The desired product was obtained after crystallization from ethanol and short-path distillation at 130°/0.4 mm as yellow needles (0.8 g, 40%): mp 112°. Anal. Calcd for $C_{20}H_{15}N$: C, 89.2; H, 5.6; N, 5.2. Found: C, 88.7; H, 5.7; N, 5.15.



1-(*n*-Butyl)-2-methylpiperidine [Schmidt Reaction of an Alcohol with an Alkyl Azide to Afford an Amine].[24] Triflic acid (0.959 g, 6.33 mmol) was added to a solution of 1-methylcyclopentan-1-ol (0.250 g, 2.49 mmol) and *n*-butyl azide (1.48 g, 15.0 mmol) in CH_2Cl_2 at 0° over 10 min. Sodium borohydride (1.25 g, 38.0 mmol) in MeOH (10 mL) was added at 0°. After stirring at rt overnight, 2 N HCl (10 mL) was added and the mixture was washed with ether (2 × 20 mL), then basified with aqueous 15% NaOH (30 mL) and extracted with ether (2 × 20 mL). The combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, and concentrated to afford the desired product as a clear oil (0.369 g, 95%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, $J = 7.3$ Hz, 3H), 1.06 (d, $J = 6.3$ Hz, 3H), 1.20–1.33 (m, 4H), 1.35–1.50 (m, 2H), 1.52–1.68 (m, 4H), 2.12 (dt, $J = 3.0$, 10.6 Hz, 1H), 2.21–2.30 (m, 1H), 2.31–2.38 (m, 1H), 2.58–2.72 (m, 1H), 2.80–2.90 (m, 1H); ^{13}C NMR (90 MHz, $CDCl_3$, JMOD) δ 14.0, 19.1, 20.9, 24.1, 26.2, 27.2, 34.6, 52.1, 53.8, 55.70; IR (neat) 2859 (s), 2786 (s), 2592 (w), 1455 (m), 1372 (m), 1330 (w), 1277 (w), 1132 (w), 1076 (w), 900 (w) cm^{-1}; MS (EI) m/z: M^+ 155 (12.6), 140 (59.4), 126 (5.3), 112 (100), 98 (9.7), 84 (20.1), 70 (6.1), 55 (18.1), 44 (18.5). HRMS m/z: calcd for $C_{10}H_{21}N$, 155.1674; found, 155.1669.

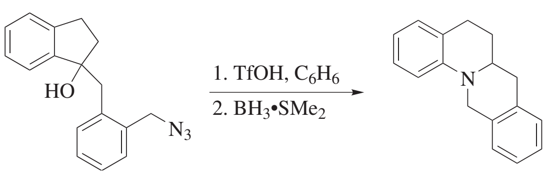


1-Benzyl-2*H*-hexahydroazepin-2-one [Intermolecular Schmidt Reaction of a Ketone with an Alkyl Azide to Afford an Amide].[85] To a solution of cyclohexanone (0.100 g, 1.02 mmol) and benzyl azide (0.271 g, 2.04 mmol) in CH_2Cl_2 (2.5 mL), in an ice bath, was added dropwise $TiCl_4$ (0.484 g, 2.55 mmol). The reaction mixture was allowed to warm to rt (with gas evolution). A precipitate formed after 15 min, and the suspension was stirred for a total of 16 h, at which time it was diluted with EtOAc (20 mL) and partitioned between EtOAc (200 mL) and saturated $NaHCO_3$ solution (30 mL). The organic layer was washed with brine (30 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent followed by silica gel chromatography (hexanes/EtOAc 4:1) gave the desired product as a clear oil (0.365 g, 88%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46–1.53 (m, 2H), 1.70–1.75 (m, 4H), 2.64–2.66 (m, 2H), 3.26–3.33 (m, 2H), 4.60 (s, 2H), 7.26–7.32 (m, 5H); ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 23.4, 28.0, 29.9, 37.1, 48.8, 51.0, 127.2, 128.1, 128.4, 137.8, 175.9; IR (neat) 2923, 1637 cm^{-1}; MS (EI) m/z: M$^+$ 203, 106, 91, 55. HRMS m/z: calcd for $C_{13}H_{17}NO$, 203.1310; found, 203.1313.



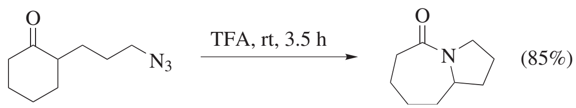
I + II (71%) **I**:**II** = 1:1

(5*R,8a*R**)-5-Methylindolizidine and (8*S**,8a*S**)-8-Methylindolizidine [Intramolecular Schmidt Reaction of an Azidoalkyl Alkene to Afford an Amine].[51]** Triflic acid (1.250 g, 8.34 mmol) was added to a cooled (5°) solution of 1-(3-azidopropyl)-2-methylenecyclopentane (0.920 g, 5.56 mmol) in benzene (55 mL). After 45 min, $NaBH_4$ (0.631 g, 16.7 mmol) was added via a pressure equalizing solid addition funnel. Methanol (10 mL) was immediately added, and the resulting mixture was stirred for 10 h. Aqueous NaOH (25 mL, 15% w/v) was added, and the resulting mixture was extracted with ether (3 × 15 mL). The combined organic extracts were washed with brine (2 × 25 mL) and water (2 × 25 mL), then dried ($MgSO_4$) and concentrated. Silica gel was deactivated by the addition of 20% by weight of hexamethyldisilazane to a suspension of SiO_2 in hexane. Chromatography on the deactivated silica gel (hexane/acetone 88:12) afforded a 1:1 mixture of the title compounds (0.546 g, 71%) as an inseparable mixture as determined by GC analysis: ^{1}H NMR (on mixture, 360 MHz, $CDCl_3$) δ 0.84 (s, 1H), 0.86 (s, 1H), 0.95 (dd, 1H), 1.07 (s, 1H), 1.09 (s, 1H), 1.1–2.1 (m, 18H), 2.95–3.1 (m, 2H), 3.15–3.25 (m, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.9, 20.5, 21.1, 23.3, 24.7, 25.8, 29.1, 30.6, 31.1, 33.5, 34.3, 36.9, 51.8, 52.9, 54.6, 58.9, 64.8, 70.9; IR (on mixture, neat) 2928 (s), 2779 (s), 2370 (m), 2274 (m), 1457 (m), 1328 cm^{-1}. Data for (5*R**,8a*R**)-5-methylindolizidine: MS (EI) m/z: M$^+$ 139, 138, 124 (100), 110, 97, 96, 70, 69, 68, 57, 56, 55, 54, 42, 41, 39. GCMS data for (8*S**,8a*S**)-8-methylindolizidine: MS (EI) m/z: M$^+$ 139, 138, 124, 111, 110, 97, 96 (100), 84, 83, 82, 70, 69, 68, 67, 56, 55, 54, 53, 43, 42, 41, 40, 39.



(67%)

6,6a,7,12-Tetrahydro-5*H*-12a-azabenzo[*a*]anthracene [Intramolecular Schmidt Reaction of an Azidoalkyl Alcohol to Afford an Amine].[102] Triflic acid (0.339 g, 2.26 mmol) was added to a solution of 1-[2′-(azidomethyl)benzyl]-2,3-dihydro-1*H*-inden-1-ol (0.544 g, 1.95 mmol) in benzene (30 mL) at rt. After 10 min, the solution was cooled to 0° and treated with borane dimethyl sulfide complex (3.0 mL of a 2.0 M solution in THF, 6.0 mmol). After the mixture was warmed to rt with stirring for 14 h, 15% aqueous NaOH (15 mL) was added, and the resulting mixture was extracted with ether (3 × 15 mL). The combined organic extracts were washed with brine, then dried ($MgSO_4$) and concentrated. Chromatography (hexane/ether 7:1) afforded the desired compound (0.307 g, 67%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.87–1.96 (m, 1H), 2.01–2.11 (m, 1H), 2.65–2.96 (m, 4H), 3.30–3.38 (m, 1H), 4.22 (d, J = 15.8 Hz, 1H), 4.76 (d, J = 15.8 Hz, 1H), 6.66–6.71 (m, 1H), 6.83 (d, J = 8.2 Hz, 1H), 7.00 (d, J = 7.3 Hz, 1H), 7.12–7.21 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.7, 29.7, 37.5, 50.3, 53.1, 112.1, 117.2, 125.2, 126.0, 126.1, 126.3, 127.1, 128.2, 128.3, 134.2, 134.8, 146.1; IR (neat) 1603 cm^{-1}; MS (EI) m/z: M$^+$ 235 (100), 220, 84; HRMS m/z: calcd for $C_{17}H_7N$, 235.1361; found, 235.1352.



Hexahydro-1*H*-pyrrolo[1,2-*a*]azepin-5(6*H*)-one [Intramolecular Schmidt Reaction of an Azidoalkyl Ketone to Afford a Lactam].[29] 2-(3-Azidopropyl) cyclohexanone (0.099 g, 0.55 mmol) was dissolved in TFA (5 mL) at rt, and the solution was stirred. After 3.5 h, the solution was concentrated under vacuum. Ether (100 mL) was added, and the solution was washed with $NaHCO_3$ (1 × 25 mL) and brine (1 × 25 mL). The organic layer was dried over Na_2SO_4 and concentrated to give an oil. The crude product was purified by silica gel chromatography (Et_2O, then EtOAc) to give the desired product (0.071 g, 85%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30–1.46 (m, 1H), 1.46–1.56 (m, 2H), 1.56–1.76 (m, 2H), 1.77–1.90 (m, 3H), 1.90–2.02 (m, 1H), 2.15–2.29 (m, 1H), 2.36–2.47 (m, 1H), 2.56 (dd, J = 6.9, 15.0 Hz, 1H), 3.37 (dt, J = 7.2, 11.8 Hz, 1H), 3.62–3.76 (m, 2H); ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 23.2, 29.6, 34.8, 35.6, 38.0, 46.7, 58.7, 173.9; IR (neat) 2922, 1635 cm^{-1}. MS (EI) m/z: M$^+$ 153, 124, 96, 84, 70 (100), 55. HRMS m/z: calcd for $C_9H_{15}NO$, 153.1154; found, 153.1154.

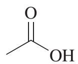
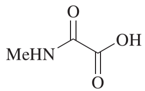
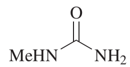
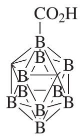
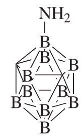
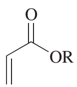
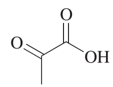
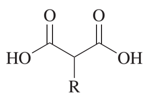
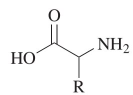
TABULAR SURVEY

The tables contain literature references for each of the Schmidt reaction variants discussed in this chapter. The coverage is from 1946 (when the previous *Organic Reactions* chapter on the Schmidt reaction was published)[11] to the end of 2009. In the tables, all carbon counts include protecting groups. The substrates are divided among the tables based on the reacting center, grouped by mechanism and oxidation state. For example, Table 1, “Schmidt Reactions of Carboxylic Acids with HN_3”, also includes esters and anhydrides. Compounds that contain both a reacting carboxylic acid and an acyclic ketone are placed in Table 3, “Schmidt Reactions of Acyclic Ketones with HN_3”. Compounds that contain both a reacting cyclic and acyclic ketone are placed in Table 4, “Schmidt Reactions of Carbocyclic Ketones with HN_3”. Table 5, “Schmidt Reactions of Heterocyclic Ketones with HN_3”, only contains substrates in which the heterocyclic ketone is the reacting center, not just present in the molecule. Ketones that react via initial carbocation formation are placed in Tables 8 and 10, along with alcohols, alkenes, alkynes, and epoxides that react with a similar mechanism.

The following abbreviations are used in the tables:

BINOL	1,1′-bi(2-naphthol)
dppm	bis(diphenylphosphino)methane
eq	equivalent(s)
g	gas
MW	microwave irradiation
PNB	4-nitrobenzyl
s	secondary
t	tertiary

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_2			
	NaN_3, H_2SO_4 or AcOH	$MeNH_2$ (89)	171
C_3			
	NaN_3, H_2SO_4, PhH, 80°, 4 h	 (—)	172
	HN_3, H_2SO_4	 (—)	173
C_{3-5}			
	NaN_3, H_2SO_4, 40°, 17 h	 R: H (31); Me (32); Et (35)	80
C_{3-9}			
	1. HN_3, H_2SO_4, $CHCl_3$, 50°, 8 h 2. Amberlite IR-4B	 R: H (49); Me (83); Et (89); *n*-Pr (61); *i*-Pr (68); *n*-Bu (50); *s*-Bu (66); *t*-Bu (67); *n*-C_5H_{11} (54); *i*-C_5H_{11} (59); *n*-C_6H_{13} (38)	174

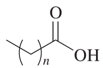
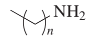
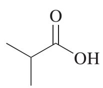
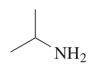
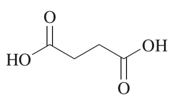
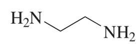
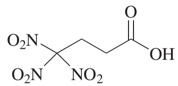
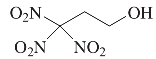
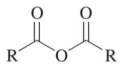
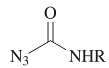
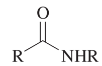
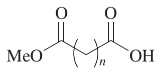
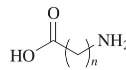
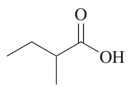
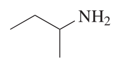
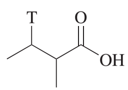
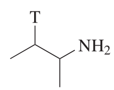
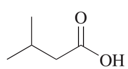
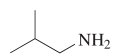
C_{3-18}					
		NaN_3, H_2SO_4, PhH, 50–60°		*n*	
				1 (—)	175–181
				2 (—)	177, 181, 177a, 179
				3 (—)	182
				4 (72)	183
				5 (—)	177
				6 (—)	182
				7 (—)	182
				8 (70)	184
				10 (81)	184, 182
				12 (80)	184
				14 (85)	184, 185
				16 (90)	184, 183
C_4					
		NaN_3, H_2SO_4, 40°		(96)	171
		NaN_3, H_2SO_4		(—)	186

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4			
	1. NaN_3, TFA 2. $NaNO_2$	 (88)	187
C_{4-10}			
	NaN_3, H_2SO_4, $CHCl_3$, 60°	 **I** +  **II** **I** + **II** (—) R: Me, *n*-Pr, *n*-Bu	188
C_{4-11}			
	1. HN_3, H_2SO_4, $CHCl_3$, 60° 2. H_2O, reflux	 *n* = 1 (58)	189
		2 (79)	189
		4 (74)	189
		6 (—)	190
		7 (81)	189
		8 (83)	189
C_5			
	NaN_3, H_2SO_4, PhH, 50–60°	 (—)	175
	HN_3, H_2SO_4, $CHCl_3$	 (—)	191
	NaN_3, H_2SO_4	 (—)	192

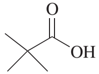
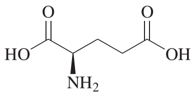
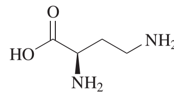
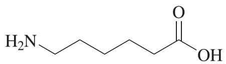
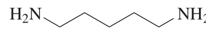
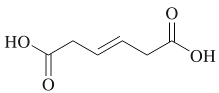
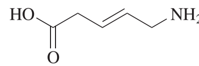
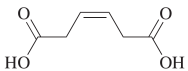
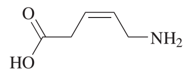
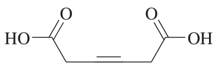
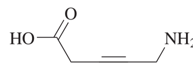
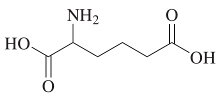
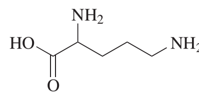
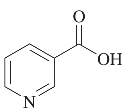
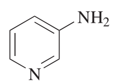
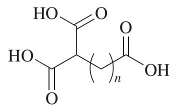
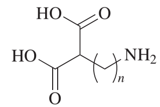
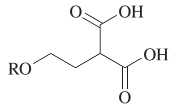
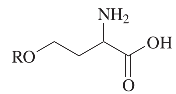
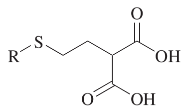
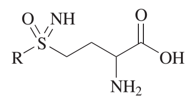
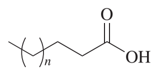
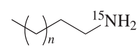
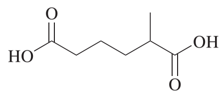
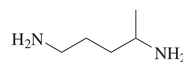
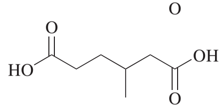
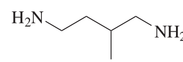
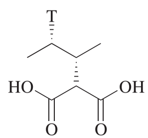
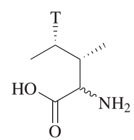
		NaN_3, H_2SO_4, 40°, 30 min	 (91)	193
		HN_3	 (—)	194
C_6		NaN_3, H_2SO_4, $CHCl_3$, 40°, 40 min	 (—)	195
		NaN_3, H_2SO_4, $CHCl_3$, 40°, 4 h	 (42)	168
		NaN_3, H_2SO_4, $CHCl_3$, 50°, 1 h	 (3)	168
		NaN_3, H_2SO_4, $CHCl_3$, 40°, 4 h	 (—)	168
		HN_3	 (77)	178
		NaN_3, 30% oleum, 95°, 6 h	 (69)	196

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-9} 	HN_3, H_2SO_4, $CHCl_3$, 60°, 2 h	 *n* / 2 (39) / 3 (42) / 4 (44) / 5 (—)	197 / 197 / 197 / 190
	HN_3, H_2SO_4, PhH, 50°, 3 h	 R / Me (23) / Et (29) / *n*-Pr (13) / *n*-Bu (15)	198
	HN_3, H_2SO_4, PhH, 50°, 3 h	 R / Me (25) / Et (29) / *n*-Pr (25) / *n*-Bu (30)	199
C_{6-18} 	$Na^{15}N_3$, PPA, 50°, 8 h	 *n* / 2 (72) / 14 (98)	183
C_7 	HN_3	 (—)	200
	HN_3	 (83)	200
	HN_3, H_2SO_4, $CHCl_3$, rt to 55°, 4 h	 (34)	191

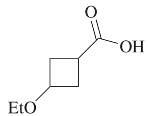
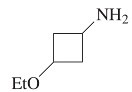
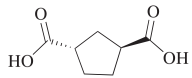
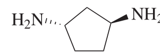
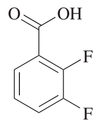
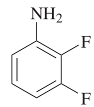
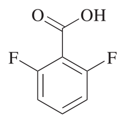
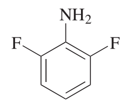
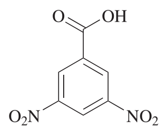
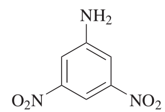
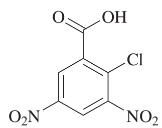
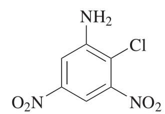
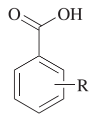
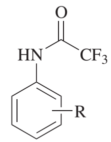
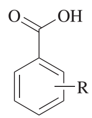
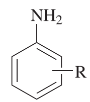
	HN_3		(—)	201
	NaN_3, H_2SO_4, $CHCl_3$, 60°, 4 h		(12)	202
	HN_3		(77)	203
	HN_3		(86)	203
	NaN_3, H_2SO_4, DCE, 80°, 3 h		(93)	204
	NaN_3, 20% oleum, DCE, 80°, 3 h		(92)	205

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)				Refs.
C_{7-8} 	NaN_3, TFA, TFAA, 48 h		R			
			H		(72)	206
			2-Br		(95)	
			3-Br		(0)	
			4-Br		(0)	
			2-O_2N		(62)	
			3-O_2N		(0)	
			4-O_2N		(0)	
			2-Me		(87)	
			3-Me		(79)	
			4-Me		(71)	
C_{7-11} 	A: NaN_3, H_2SO_4, 40–50°, 2–12 h B: NaN_3, PPA, rt C: NaN_3, H_2SO_4, $CHCl_3$, rt, 2–24 h		R	Conditions		
			H	C	(97)	2
			2-F	A	(59)	207
			2-Cl	C	(80)	2
			2-Br	C	(73)	2
			2-I	C	(81)	2
			2-O_2N	C	(98)	2
			3-Cl	C	(71)	2
			3-Br	C	(70)	2
			3-O_2N	A	(100)	208
			4-F	A	(92)	208
			4-Cl	A	(99)	208
			4-Br	A	(96)	208

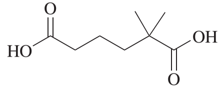
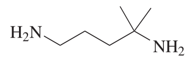
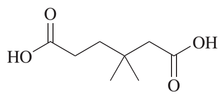
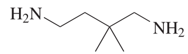
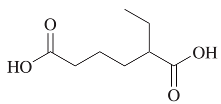
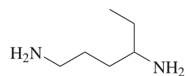
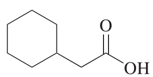
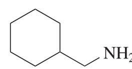
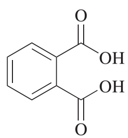
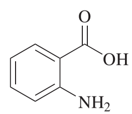
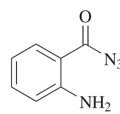
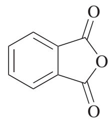
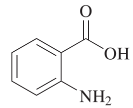
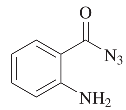
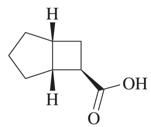
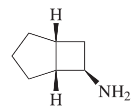
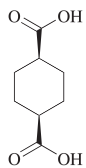
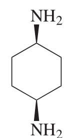
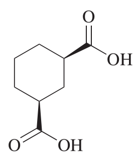
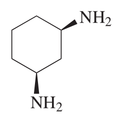
			4-O_2N	A	(99)	208
			2-Me	C	(86)	2
			3-Me	C	(84)	2
			4-Me	C	(50)	2
			4-NC	A	(73)	208
			4-CF_3	A	(41)	208
			4-MeO	B	(80)	161
			2-Et	C	(83)	2
			2-*i*-Pr	C	(87)	2
			2-*t*-Bu	C	(82)	2
			2,4,6-Me_3	B	(91)	161
C_8		HN_3			(—)	200
		HN_3			(—)	200
		HN_3			(—)	200
		NaN_3, H_2SO_4, $CHCl_3$, 55°, 12 h			(86)	209
		NaN_3, H_2SO_4, DCE, 40°, 2 h	 (—) + 		(37)	78

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	NaN_3, H_2SO_4, 110°, 30 min	 (73)	210
	NaN_3, AcOH, 50°, 3 h	 (12)	78
	HN_3	 (—)	211
	NaN_3, H_2SO_4, $CHCl_3$, 15–50°, 8 h	 (22)	212
	HN_3, H_2SO_4, $CHCl_3$, 15–50°, 8 h	 (44)	35, 213

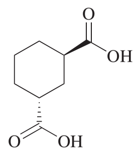
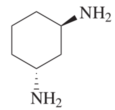
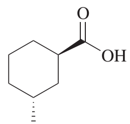
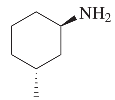
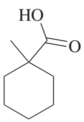
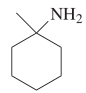
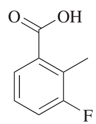
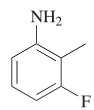
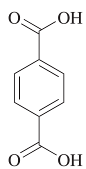
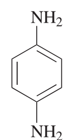
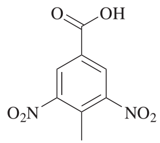
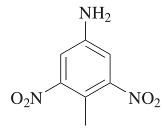
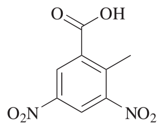
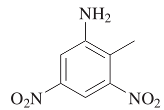
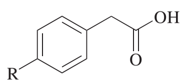
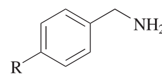
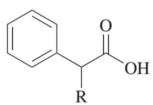
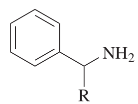
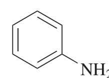
	HN_3, H_2SO_4, $CHCl_3$, 15–50°, 8 h		(44)	35
	NaN_3, H_2SO_4, $CHCl_3$, 15–50°, 8 h		(34)	214
	NaN_3, H_2SO_4, 55°, overnight		(45)	209
	HN_3		(76)	215
	NaN_3, H_2SO_4		(—)	216

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	NaN_3, H_2SO_4, 0–60°, 4 h	 (90)	217
	NaN_3, H_2SO_4, 0–60°, 4 h	 (98)	217
C_{8-9} 	NaN_3, H_2SO_4, $CHCl_3$, 80°, 3 h	 R: O_2N (70); Cl (51); H (77); Me (5)	218
C_{8-12} 	NaN_3, PPA, 50°, 8 h	 **I** +  **II** R / **I** / **II**: H (68) (0); *n*-Bu (49) (46)	219

C_9

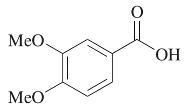
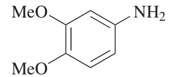
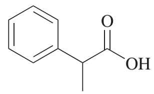
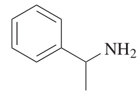
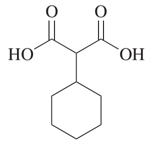
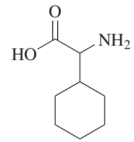
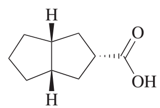
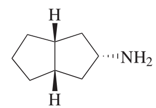
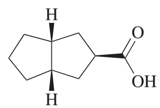
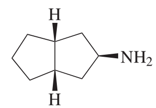
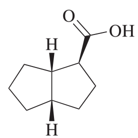
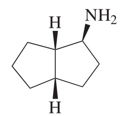
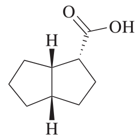
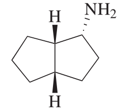
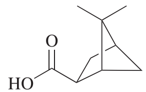
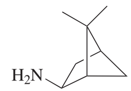
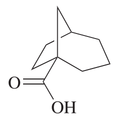
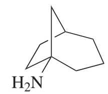
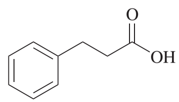
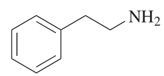
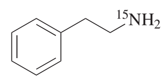
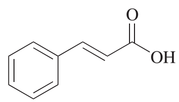
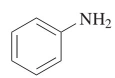
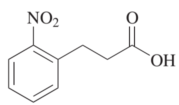
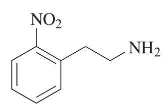
	HN_3		(—)	220
	NaN_3, H_2SO_4, $CHCl_3$, rt to 45°, 1 h		(84)	221
	NaN_3, H_2SO_4, PhH, 50°, 5 h		(56)	222
	NaN_3, H_2SO_4, $CHCl_3$, 50°		(91)	223
	NaN_3, H_2SO_4, $CHCl_3$, 50°		(—)	224
	NaN_3, H_2SO_4, $CHCl_3$, 50°		(—)	225

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	NaN_3, H_2SO_4, $CHCl_3$, 50°	 (—)	226
	NaN_3, H_2SO_4, $CHCl_3$, 50°, 2 h	 (61)	227
	HN_3	 (63)	228
	NaN_3, H_2SO_4, $CHCl_3$, rt to 45°, 2 h	 (—)	229
	$Na^{15}N_3$, PPA, 50°	 (71)	183
	NaN_3, H_2SO_4	 (—)	230
	HN_3, H_2SO_4, $CHCl_3$, 45°	 (83)	231

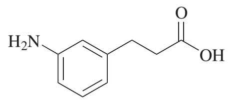
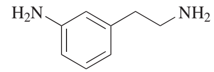
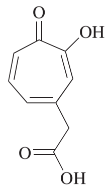
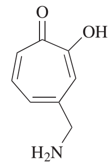
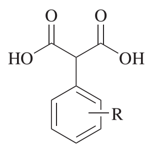
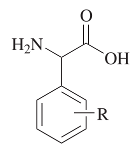
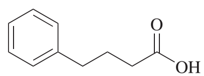
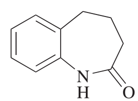
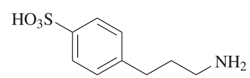
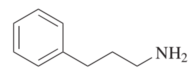
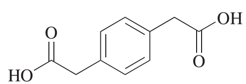
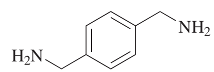
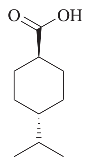
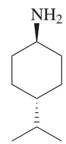
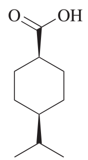
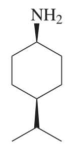
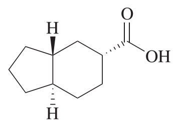
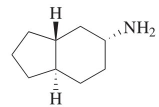
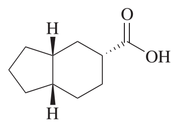
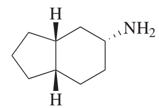
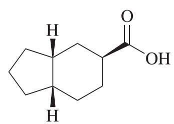
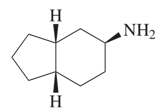
	HN_3, H_2SO_4, $CHCl_3$, 45°	 (75)	231
	NaN_3, H_2SO_4, $CHCl_3$, 40°	 (70)	232
C_{9-10}			
	NaN_3, H_2SO_4, PhH, 50°, 5 h	 R: H (46); 2-Cl (27); 2-Br (30); 2-Me (38); 3-Me (50); 4-Me (0)	222
C_{10}			
	NaN_3, H_2SO_4, $CHCl_3$, 40°, 1 h	 **I** (50) +  (40)	75
	NaN_3, PPA, 85°, 2 h	**I** (40) +  (24)	75
	NaN_3, H_2SO_4	 (—)	216

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	NaN_3, H_2SO_4, $CHCl_3$, 55°, 30 min	 (85)	233
	NaN_3, H_2SO_4, $CHCl_3$, 55°, 30 min	 (81)	233
	HN_3	 (—)	234
	HN_3	 (—)	234
	HN_3	 (—)	234

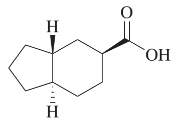
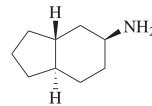
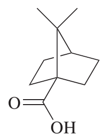
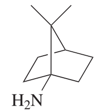
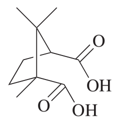
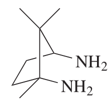
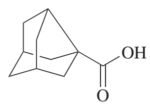
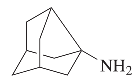
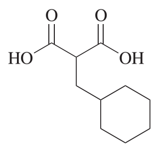
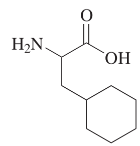
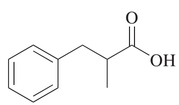
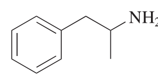
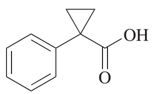
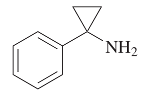
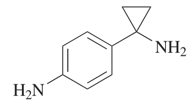
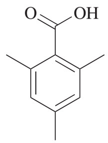
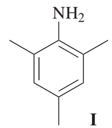
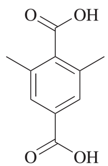
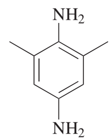
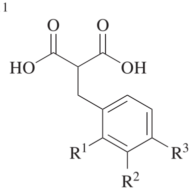
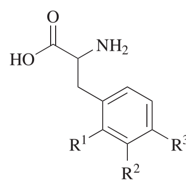
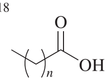
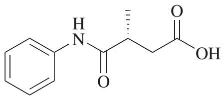
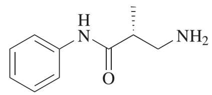
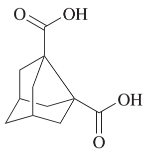
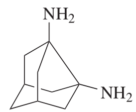
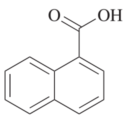
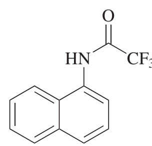
	HN_3	 (—)	234
	NaN_3, H_2SO_4, PhH, 50°, 2 h	 (—)	235
	NaN_3, H_2SO_4, $CHCl_3$, 55–65°, 1 h	 (76)	236
	NaN_3, H_2SO_4, $CHCl_3$, 45°, 2 h	 (63)	237
	NaN_3, H_2SO_4, PhH, 50°, 5 h	 (50)	222
	HN_3	 (—)	235

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	NaN_3, H_2SO_4, $CHCl_3$, 80°, 3 h	 (16) +  (5)	218
	NaN_3, H_2SO_4, 0°	 **I** (51)	238
	NaN_3, PPA, rt	**I** (91)	161
	NaN_3, H_2SO_4, $CHCl_3$, rt	 (87)	238
C_{10-11} 	NaN_3, H_2SO_4, PhH, 50°, 5 h		222

R^1	R^2	R^3	
H	H	H	(19)
Cl	H	H	(37)
Br	H	H	(30)
I	H	H	(0)
H	Cl	H	(19)
H	Br	H	(20)
H	H	Cl	(36)
H	H	Br	(25)
H	H	I	(0)

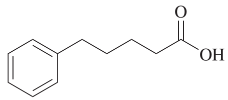
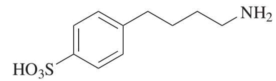
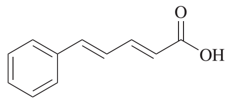
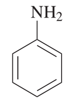
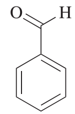
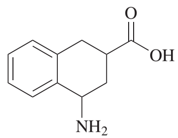
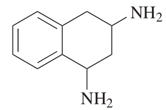
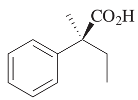
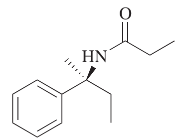
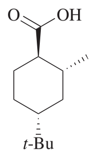
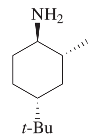
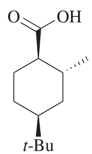
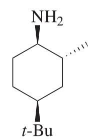
H	H	O_2N	(32)
Cl	H	Cl	(22)
H	Cl	Cl	(21)
Me	H	H	(0)
MeO	H	H	(0)
H	H	Me	(0)

Carbon No.	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10-18}		NaN_3, H_2SO_4, PhH, 50–60°		184
C_{11}		NaN_3, H_2SO_4, $CHCl_3$, 50°, 3 h	 (32)	239
		NaN_3, H_2SO_4, $CHCl_3$, 45°, 2 h	 (13)	240
		NaN_3, TFA/TFAA, 48 h		206

n		*n*	
8	(70)	14	(85)
10	(81)	16	(90)
12	(80)		

TFA/TFAA		TFA/TFAA	
10:0	(0)	4:6	(92)
9:1	(76)	3:7	(57)
8:2	(85)	2:8	(28)
7:3	(98)	1:9	(12)
6:4	(97)	0:10	(0)
5:5	(97)		

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
	NaN_3, H_2SO_4, $CHCl_3$, 40°, 1 h	 (80)	75
	HN_3, H_2SO_4, $CHCl_3$, 50°, 1 h	 (6) +  (13)	241
	NaN_3, $CHCl_3$, 45°, 20 h	 (55)	242
	1. NaN_3, MsOH, 0° to reflux 2. EtCOCl	 (64)	243
C_{12}			
	NaN_3, H_2SO_4, $CHCl_3$, 55°, 30 min	 (88)	233
	NaN_3, H_2SO_4, $CHCl_3$, 55°, 30 min	 (78)	244

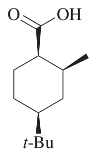
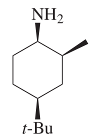
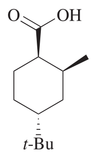
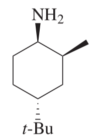
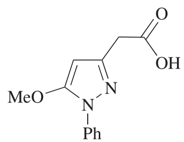
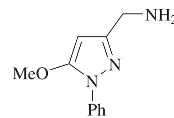
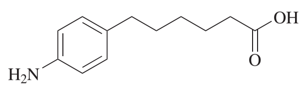
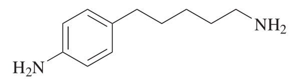
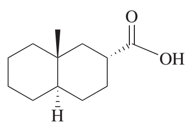
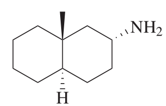
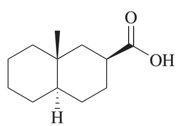
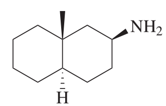
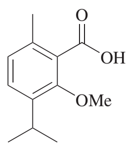
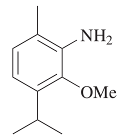
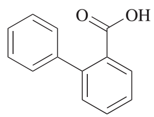
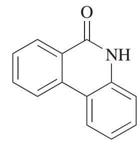
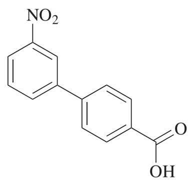
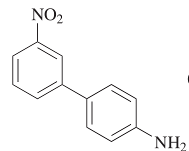
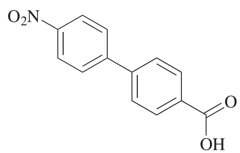
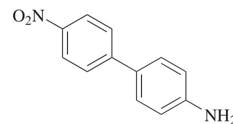
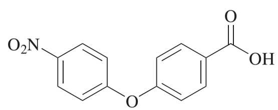
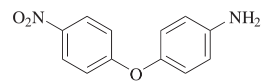
	NaN_3, H_2SO_4, $CHCl_3$, 55°, 30 min		(66)	233
	NaN_3, H_2SO_4, $CHCl_3$, 55°, 30 min		(78)	233
	HN_3, $CHCl_3$, 45°, 10 h		(35)	245
	HN_3, H_2SO_4, $CHCl_3$, 45°		(60)	231
	NaN_3, H_2SO_4, $CHCl_3$, 55°, 30 min		(51)	233
	NaN_3, H_2SO_4, $CHCl_3$, 55°, 30 min		(57)	233

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12} 	HN_3, PhH, 40°, 1 h	 (48)	246
C_{13} 	NaN_3, H_2SO_4, $CHCl_3$	 (84)	218
	HN_3, 50°, 30 min	 (—)	247
	HN_3, 50°, 30 min	 (—)	247
	HN_3	 (—)	248

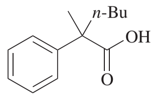
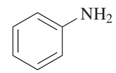
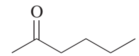
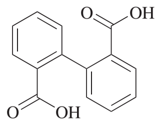
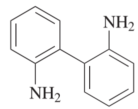
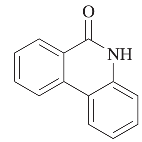
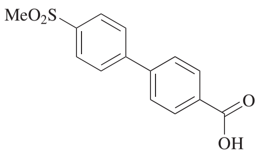
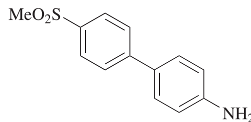
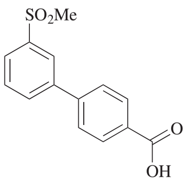
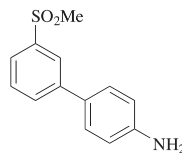
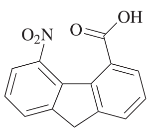
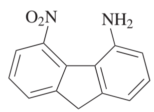
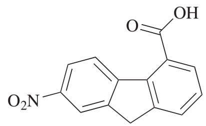
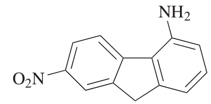
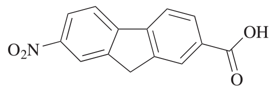
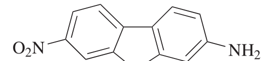
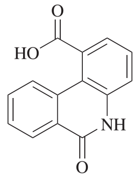
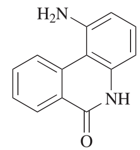
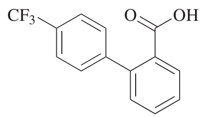
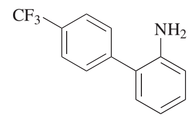
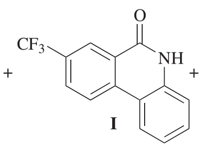
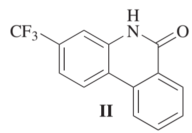
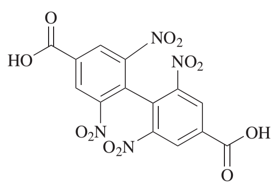
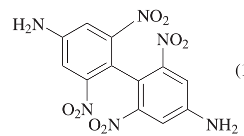
	NaN_3, PPA, 50°, 8 h	 (58) +  (—)	219
C_{14}			
	NaN_3, H_2SO_4, DCE, 40°, 2.5 h	 (43) +  (6)	78
	HN_3, 50°, 30 min	 (38)	247
	HN_3, 50°, 30 min	 (23)	247
	NaN_3, H_2SO_4, $CHCl_3$, 40°, 2 h	 (67)	249

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	NaN_3, H_2SO_4, $CHCl_3$, 40°, 2 h	 (70)	250
	NaN_3, H_2SO_4, $CHCl_3$	 (—)	251
	NaN_3, H_2SO_4, $CHCl_3$, 40°, 2 h	 (—)	252
	NaN_3, H_2SO_4, $CHCl_3$	 (22) +  **I** +  **II** **I + II** (21)	218
	NaN_3, DCE, reflux, 5 h	 (100)	253

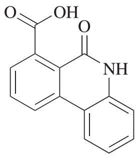
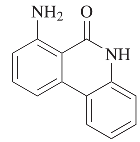
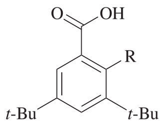
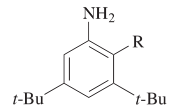
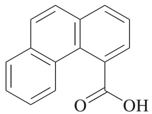
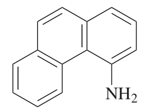
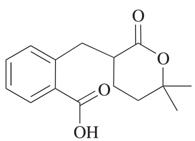
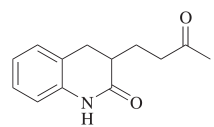
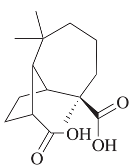
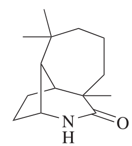
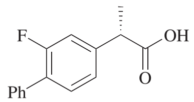
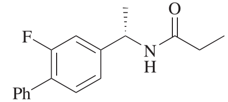
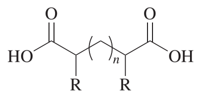
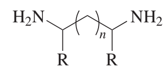
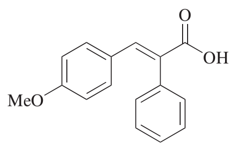
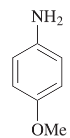
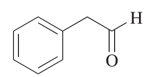
C_{15}				
	NaN_3, H_2SO_4, $CHCl_3$		(—)	254
	NaN_3, H_2SO_4, $CHCl_3$, rt		R	
			H (86)	2
			O_2N (79)	2
			Cl (87)	2
			Br (90)	2
			I (96)	255
	1. NaN_3, TFA, TFAA 2. KOH		(81)	256
	—		(—) + CO_2	257
	HN_3, H_2SO_4, $CHCl_3$, rt, 1 h		(96)	258

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	1. NaN_3, MsOH 2. EtCOCl	 (—)	243
$C_{15–24}$			
	NaN_3, H_2SO_4, PhH, rt		259

n	R	
3	*n*-Bu	(60)
3	*i*-Bu	(75)
3	*n*-C_5H_{11}	(78)
3	*i*-C_5H_{11}	(80)
3	*n*-C_6H_{13}	(75)
3	2-ethyl-1-hexyl	(35)
4	*n*-Bu	(60)
4	*n*-C_5H_{11}	(60)
4	*i*-C_5H_{11}	(76)
4	*n*-C_6H_{13}	(80)
4	2-ethyl-1-hexyl	(87)
5	*n*-Bu	(79)
5	*i*-Bu	(55)
5	*n*-C_6H_{13}	(80)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}			
	HN_3, H_2SO_4, $CHCl_3$, 55°, 1 h	 (34) +  (35)	241

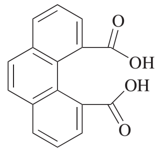
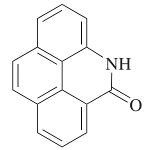
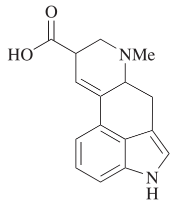
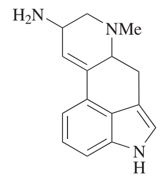
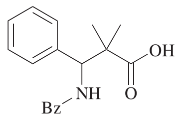
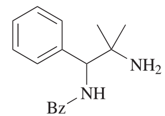
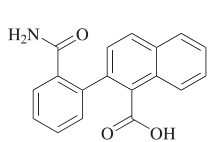
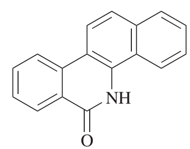
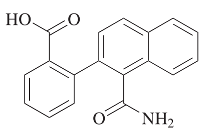
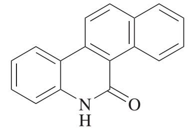
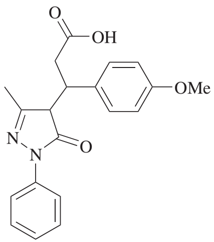
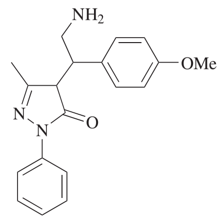
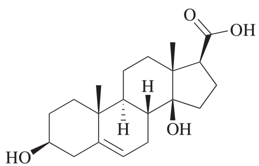
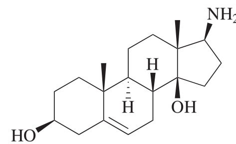
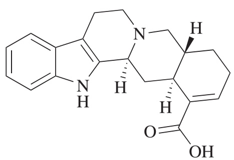
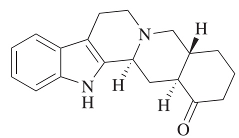
Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
	NaN_3, H_2SO_4, DCE, 40°, 2.5 h	 (67)	78
	HN_3	 (—)	260
C_{18}			
	NaN_3, H_2SO_4, $CHCl_3$, 55°, 1.5 h	 (41)	261
	NaN_3, H_2SO_4, 60°, 1 h	 (—)	262

TABLE 1. SCHMIDT REACTIONS OF CARBOXYLIC ACIDS WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18}			
	NaN_3, H_2SO_4, 60°, 1 h	 (95)	262
C_{20}			
	NaN_3, H_2SO_4, $CHCl_3$, 0–50°, 5 h	 (64)	263
	HN_3	 (—)	264
	HN_3, H_2SO_4, $CHCl_3$	 (20)	265

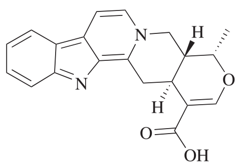
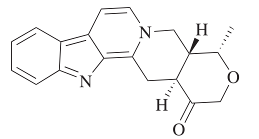
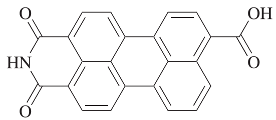
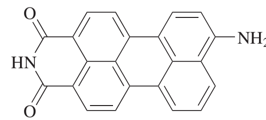
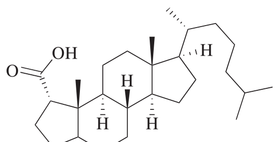
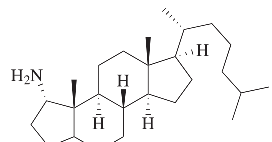
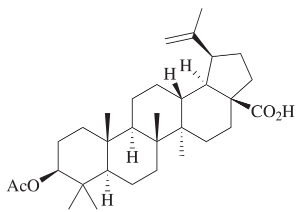
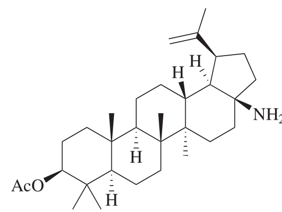
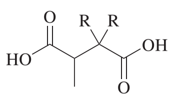
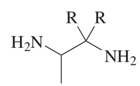
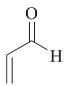
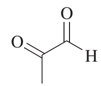
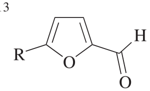
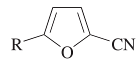
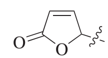
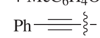
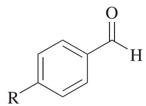
	HN_3		(—)	266
C_{23}				
	NaN_3, H_2SO_4, 50°, 4 h		(50)	267
C_{27}				
	NaN_3, H_2SO_4, $CHCl_3$		(89)	106
	HN_3, PhH, 0° to rt		(85)	268
C_{41}				
 R = n-$C_{18}H_{37}$	HN_3		(—)	269

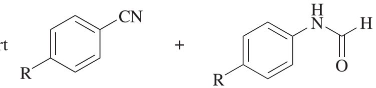
TABLE 2. SCHMIDT REACTIONS OF ALDEHYDES WITH HN_3

Substrate	Conditions	Product(s) and Yield(s) (%)			Refs.
C_3					
	NaN_3, HCl, rt	 (37)			270
C_{5-13}					
	HN_3, $Mg(ClO_4)_2$•H_2O, $CHCl_3$, reflux, 2 h		R		167
			H	(84)	
			Br	(88)	
			I	(85)	
			O_2N	(96)	
			Me	(91)	
			MeS	(79)	
			$ClCH_2$	(96)	
			2-C_4H_3S	(90)	
			EtO_2CCH_2S	(78)	
				(89)	
			5-NC-2-C_4H_3S	(92)	
			Ph	(90)	
			PhO_2S	(98)	
			4-$O_2NC_6H_4$	(85)	
			4-ClC_6H_4O	(81)	
			2,4-$(O_2N)_2C_6H_3S$	(93)	
			4-MeC_6H_4O	(79)	
			PhCOS	(90)	
			3-BrC_6H_4COS	(91)	
			4-$MeC_6H_4O_2S$	(98)	
				(94)	

C_{7-8}



NaN$_3$, H$_2$SO$_4$ (x eq), PhH, 0° to rt

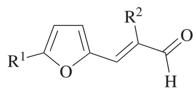


I + **II**

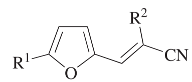
R	x	**I**	**II**
H	2	(32)	(14)
H	6.6	(10)	(59)
Cl	2	(55)	(12)
Cl	6.6	(15)	(48)
O$_2$N	2	(72)	(2)
O$_2$N	6.6	(46)	(23)
Me	2	(50)	(6)
Me	6.6	(13)	(43)
MeO	2	(86)	(0)
MeO	6.6	(64)	(0)

36

C_{7-14}



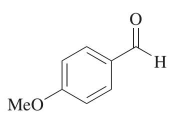
HN$_3$, Mg(ClO$_4$)$_2$•H$_2$O, CHCl$_3$, rt to reflux, 2 h



R^1	R^2	
H	H	(84)
H	Me	(92)
O$_2$N	H	(95)
Me	H	(92)
Me	Me	(82)
Ph	H	(95)
Ph	Me	(92)
2,4,6-Cl$_3$C$_6$H$_2$	H	(93)

271

C_8



NaN$_3$, H$_2$SO$_4$, CHCl$_3$, 0–45°, 3 h

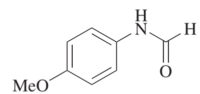
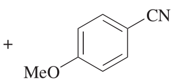
 (60) +  (7)

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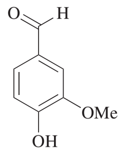
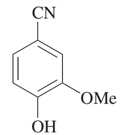
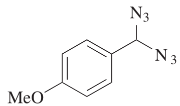
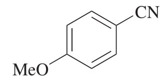
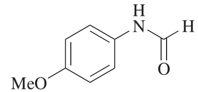
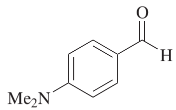
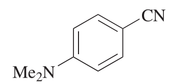
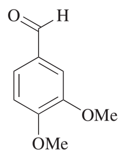
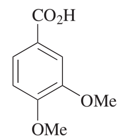
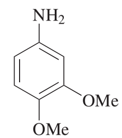
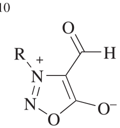
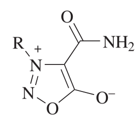
TABLE 2. SCHMIDT REACTIONS OF ALDEHYDES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	NaN_3, H_2SO_4, 0°, 2 h	 (70)	272
	H_2SO_4, MeCN	 (86) +  (2)	27
C_9 	NaN_3, H_2SO_4, 10°	 (61)	273
	NaN_3, H_2SO_4, 0°, 2 h	 (84) +  (6)	272
C_{9-10} 	NaN_3, H_2SO_4, rt, 10 h	 R: Ph (74); 4-BrC_6H_4 (63); 2-MeC_6H_4 (60); 4-MeC_6H_4 (68); 4-$MeOC_6H_4$ (47)	274

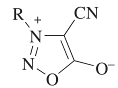
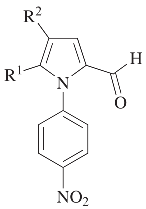
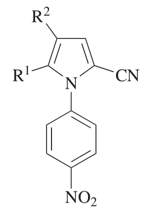
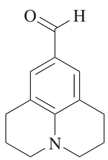
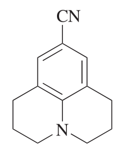
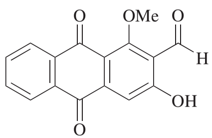
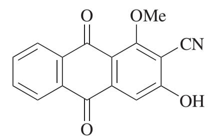
Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
	NaN$_3$, aq H$_2$SO$_4$, rt, 10 h	 R: Ph (77); 4-BrC$_6$H$_4$ (67); 2-MeC$_6$H$_4$ (71); 4-MeC$_6$H$_4$ (73); 4-MeOC$_6$H$_4$ (72)	274
C$_{11}$ 	HN$_3$, Mg(ClO$_4$)$_2$•H$_2$O, CHCl$_3$, rt to reflux, 3 h	 R^1 H, R^2 H (97); R^1 Br, R^2 H (98); R^1 Br, R^2 Br (98)	275
C$_{13}$ 	NaN$_3$, H$_2$SO$_4$, 10°	 (77)	273
C$_{16}$ 	HN$_3$	 (—)	276

TABLE 2. SCHMIDT REACTIONS OF ALDEHYDES WITH HN_3 (*Continued*)

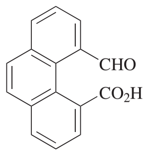
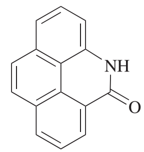
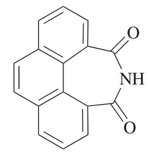
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}			
	NaN_3, H_2SO_4, DCE, 40°, 2.5 h	 (—) +  (—)	78

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3

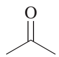
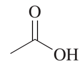
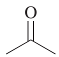
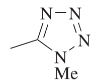
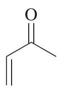
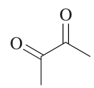
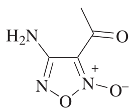
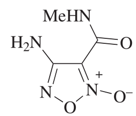
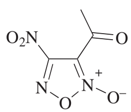
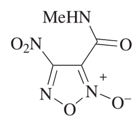
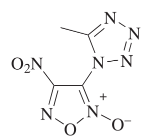
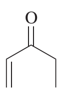
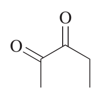
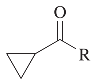
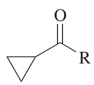
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3			
	NaN_3, H_2SO_4, PhH	 (—) + $MeNH_2$ (—)	277
	$SiCl_4$, NaN_3, MeCN, rt, 12 h	 (98)	70
C_4			
	NaN_3, HCl, rt	 (8)	270
	NaN_3, PPA, rt, 48 h	 (21)	278
	NaN_3, PPA, rt, 48 h	 (12) +  (12)	278
C_5			
	NaN_3, HCl, rt	 (50)	270

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-10} 	A: NaN_3, 89% H_2SO_4, $CHCl_3$ B: NaN_3, 83% H_2SO_4, $CHCl_3$ C: NaN_3, 69% H_2SO_4, $CHCl_3$ D: NaN_3, 50% H_2SO_4, $CHCl_3$ E: NaN_3, CCl_3CO_2H, 63°	 **I** + **II**	30

R	Conditions	**I + II**	**I:II**
Me	A	(88–100)	73:27
Me	B	(88–100)	74:26
Me	C	(88–100)	44:56
Me	D	(—)	10:90
Me	E	(88–100)	27:73
Et	B	(88–100)	82:18
Et	C	(88–100)	82:18
Et	D	(—)	26:74
Et	E	(88–100)	26:74
i-Pr	B	(88–100)	92:8
i-Pr	C	(88–100)	96:4
i-Pr	D	(—)	82:18
i-Pr	E	(88–100)	48:52
Ph	A–C, E	(88–100)	7:93

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-12} 	NaN_3, H_2SO_4, $CHCl_3$, rt	**I + II**	279

R	**I + II**	**I:II**
Me	(75)	1:3.3
Ph	(76)	1:19
2-MeC_6H_4	(85)	1:19
4-MeC_6H_4	(61)	1:19
(*E*)-PhCH=CH	(35)	1:10

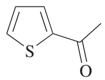
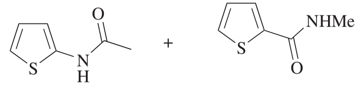
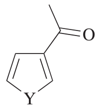
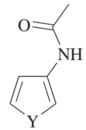
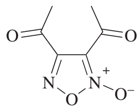
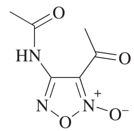
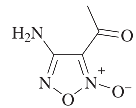
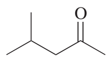
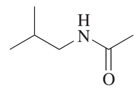
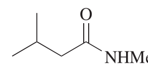
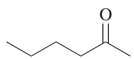
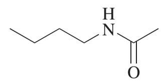
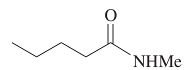
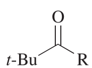
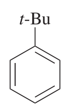
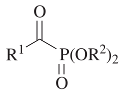
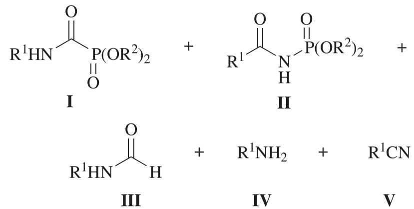
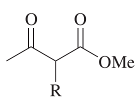
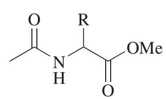
C_6 	HN_3, H_2SO_4, $CHCl_3$, 0°, 15 min	 I + II (—)	280
	HN_3, H_2SO_4, $CHCl_3$, 0°, 15 min	 Y: O (20); S (80); Se (75)	281
	NaN_3, H_2SO_4, CH_2Cl_2, 0°, 3 h	 (—) +  (63)	278
	NaN_3, silica sulfuric acid,[a] 60°, 20 min	 (66) +  (26)	282
	NaN_3, silica sulfuric acid,[a] 60°, 20 min	 (69) +  (23)	282
C_{6-9} 	NaN_3, H_2SO_4, PhH, rt	 I + t-BuNH$_2$ II; R = Me: I (30), II (3); R = t-Bu: I (23), II (9)	283

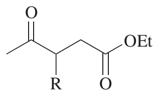
TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-14} 	HN_3, H_2SO_4, $CHCl_3$, 0°, 30 min		28
	NaN_3, MsOH, DME, –30° to rt, 3 h		56

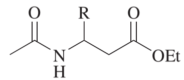
R^1	R^2	I	II	III	IV	V
i-Pr	Me	(0)	(0)	(57)	(0)	(0)
3-ClC_6H_4	Me	(0)	(1)	(39)	(7)	(0)
4-$MeOC_6H_4$	Me	(0)	(46)	(0)	(0)	(47)
4-$MeOC_6H_4$[b]	Me	(0)	(45)	(0)	(0)	(51)
Ph	Et	(9)	(3)	(53)	(14)	(0)
4-ClC_6H_4	Et	(19)	(2)	(65)	(4)	(0)
4-MeC_6H_4	Et	(11)	(3)	(70)	(7)	(7)
4-$MeOC_6H_4$	Et	(0)	(30)	(0)	(0)	(62)
4-$MeOC_6H_4$[c]	Et	(0)	(31)	(0)	(0)	(54)
3-$MeOC_6H_4$	Et	(0)	(2)	(59)	(9)	(6)
3,4-$(OCH_2O)C_6H_3$	Et	(0)	(28)	(0)	(0)	(51)
2,6-$(MeO)_2C_6H_3$	Et	(0)	(0)	(0)	(0)	(62)
2,4,6-$Me_3C_6H_2$	Et	(0)	(0)	(0)	(43)	(0)
2,6-Me_2-4-$MeOC_6H_2$	Et	(0)	(0)	(0)	(50)	(0)

R	
Me	(47)
Bn	(26)
$Ph(CH_2)_2$	(100)
(*E*)-PhCH=$CHCH_2$	(79)

C$_{7-14}$



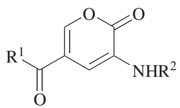
NaN$_3$, H$_2$SO$_4$, CHCl$_3$, 5°



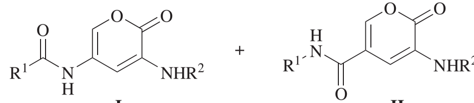
R	
H	(49)
Me	(70)
Et	(29)
Bn	(19)

284

C$_{7-19}$



A: NaN$_3$, H$_2$SO$_4$, –10 to 0°, 3 h; then rt, 2 h
B: NaN$_3$, H$_2$SO$_4$, 32–35°, 2 h

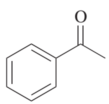


I + **II**

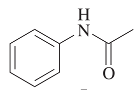
R^1	R^2	Conditions	**I + II**	**I:II**
Me	H	A	(96)	1:0
Me	H	B	(86)	1:0
Me	MeCO	A	(86)	1:0
Me	PhCO	A	(98)	1:0
Ph	H	A	(87)	3.9:1
Ph	H	B	(92)	3.6:1
Ph	MeCO	A	(72)	3.7:1
Ph	PhCO	A	(99)	3.5:1

285

C$_8$



NaN$_3$, MsOH, DME, –30° to rt, 3 h



I (80)

56

NaN$_3$, AcOH, HBr, 55–65° — **I** (21) — 1

NaN$_3$, CCl$_3$CO$_2$H, 55–65° — **I** (89) — 1

Azide, FeCl$_3$, DCE, rt — **I**

Azide	Time	
TMSN$_3$	30 min	(85)
NaN$_3$	2 h	(76)

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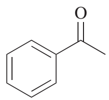
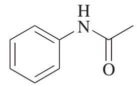
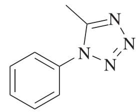
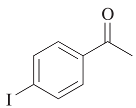
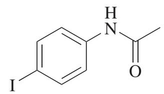
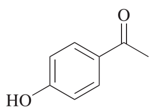
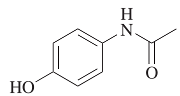
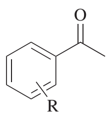
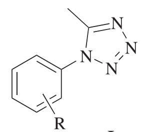
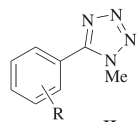
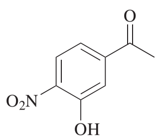
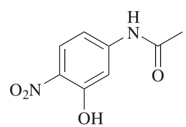
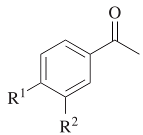
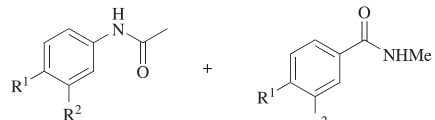
TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	NaN_3, PPA, 50°, 7 h	 (82)	54
	HN_3, $AlCl_3$, $PhNO_2$, PhH, rt	 (42)	272
	Azide, $FeCl_3$, DCE, rt	 Azide / Time: $TMSN_3$, 35 min (76); NaN_3, 3 h (68)	286
	Azide, $FeCl_3$, DCE, rt	 Azide / Time: $TMSN_3$, 33 min (72); NaN_3, 2.5 h (66)	286
	NaN_3, $SiCl_4$, MeCN, rt, 12 h	 **I** +  **II** R / **I** / **II**: H (87) (5); 4-Cl (87) (5); 3-O_2N (60) (5)	70
	NaN_3, MsOH, rt, 14 h	 (82)	287

C_{8-9}



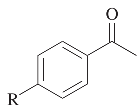
A: NaN_3, H_2SO_4, PhH, 60°
B: NaN_3, CCl_3CO_2H, 65°



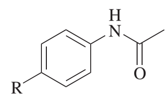
I + **II**

I + **II** (—) 59

R^1	R^2	Conditions	**I**:**II**
H	H	A	90:10
H	H	B	90:10
O_2N	H	A	90:10
O_2N	H	B	90:10
H	O_2N	A	90:10
H	O_2N	B	90:10
MeO	H	A	80:20
MeO	H	B	80:20



NaN_3, silica sulfuric acid,[a] 60°



I

R	Time (min)	
H	25	(95)
Cl	35	(92)
O_2N	45	(90)
Me	25	(91)

282

NaN_3, $Fe(HSO_4)_3$, grinding, 50°

I

R	Time (min)	
H	25	(92)
Cl	35	(91)
O_2N	25	(91)
Me	35	(94)

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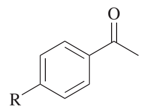
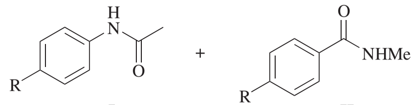
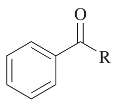
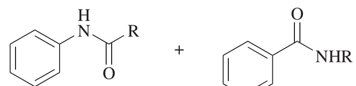
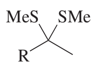
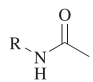
TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{8-9} 	NaN_3, P_2O_5–SiO_2, MW	 **I** **II**	289

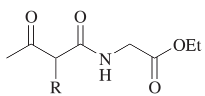
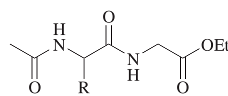
R	Time (min)	**I + II**	**I:II**
H	8	(90)	1:0
Cl	8	(90)	1:0
O_2N	10	(80)	4:1
Me	10	(85)	1:0
MeO	10	(83)	1:0

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{8-10} 	NaN_3, HCl (concd)	 **I** **II**	7

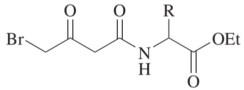
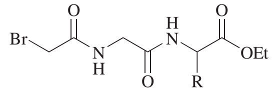
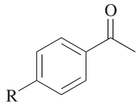
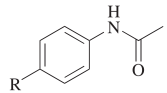
R	**I + II**	**I:II**
Me	(81)	95:6
Et	(80)	85:15
i-Pr	(57)	51:49

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. IN_3, CH_2Cl_2, –78 to –10°, 2 h 2. TFA, $CHCl_3$, rt, 2 h		83

R	
t-Bu	(62)
n-C_5H_{11}	(77)
c-C_6H_{11}	(59)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{8-15} 	HN_3, H_2SO_4		290

R	
H	(49)
Me	(56)
Et	(57)
n-Pr	(50)
n-Bu	(34)
Bn	(82)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	HN_3, H_2SO_4	 R = H (35); R = Bn (21)	291
C_{8-20}			
	A. NaN_3, AcOH, H_2SO_4, 70°, 2–6 h B. NaN_3, H_2SO_4		

R	Conditions		Refs.
H	A	(99)	292
O_2N	A	(70)	292
n-C_5H_{11}	A	(81)	293
Ph	A	(99)	292
PhO	A	(99)	292
PhS	A	(99)	292
PhOS	A	(60)	292
PhO_2S	A	(85)	292
4-$O_2NC_6H_4$	A	(80)	292
4-$O_2NC_6H_4O$	A	(50)	292
n-C_5H_{11}	B	(81)	294
Bn	A	(70)	292
n-C_7H_{15}	B	(—)	294
n-C_9H_{19}	B	(—)	294
n-$C_{10}H_{21}$	A	(93)	293
n-$C_{12}H_{25}$	A	(95)	293

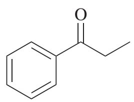
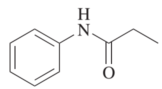
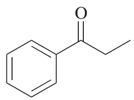
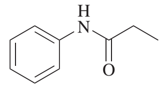
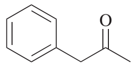
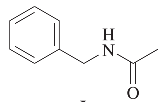
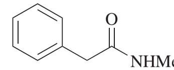
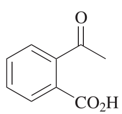
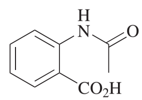
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	NaN_3, silica sulfuric acid,[a] 60°, 0.5 h	 **I** (95)	282
	NaN_3, P_2O_5–SiO_2, MW, 8 min	**I** (92)	289
	NaN_3, $Fe(HSO_4)_3$, 50°, 30 min	**I** (93)	288

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	Azide, $FeCl_3$, DCE, rt	 Azide / Time: $TMSN_3$, 35 min (78); NaN_3, 2 h (70)	286
	NaN_3, promoter	 **I** +  **II**	

Promoter	Solvent	Temp	Time (h)	**I + II**	**I:II**	Refs.
PPA	PPA	rt	8	(43)	100:0	295
H_2SO_4	Et_2O	0°	3	(—)	31:69	296
H_2SO_4	Et_2O	rt	3	(—)	40:60	296
H_2SO_4	PhH/Et_2O (1:9)	rt	3	(—)	44:56	296
H_2SO_4	PhH/Et_2O (1:1)	rt	3	(—)	64:36	296
H_2SO_4	PhH/Et_2O (9:1)	rt	3	(—)	78:22	296
H_2SO_4	PhH	0°	3	(—)	80:20	296
H_2SO_4	PhH	rt	3	(—)	79:21	296
PPA	PPA	20°	5	(—)	76:24	296
PPA	PPA	50°	3	(—)	72:28	296
PPA	PPA	100°	1	(—)	67:23	296
silica sulfuric acid[a]	—	60°	0.4	(91)	75:25	282
P_2O_5–SiO_2	—	MW	0.17	(91)	75:25	289
$Fe(HSO_4)_3$	—	50°	0.4	(90)	80:20	288

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	NaN_3, CCl_3CO_2H, 60°	 (65)	8

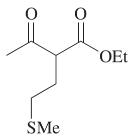
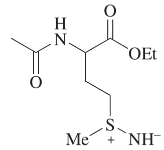
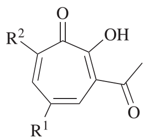
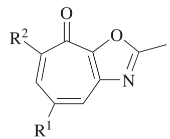
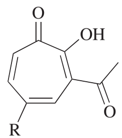
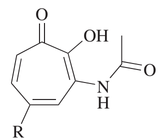
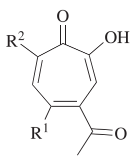
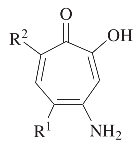
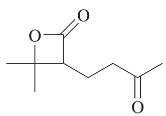
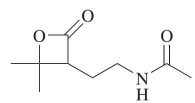
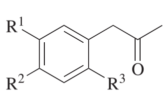
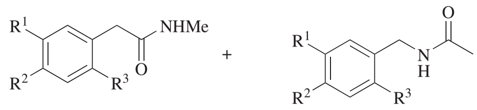
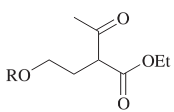
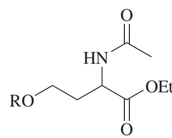
	HN_3, H_2SO_4, $CHCl_3$, PhH		(—)	297
	NaN_3, H_2SO_4, $CHCl_3$, rt, 2 h		R^1 R^2 H I (39) Br Br (69)	298
	NaN_3, H_2SO_4, $CHCl_3$, rt, 2 h		R H (66) O_2N (47)	299 298
	NaN_3, H_2SO_4, $CHCl_3$, rt, 2 h		R^1 R^2 H H (94) Br H (—) H O_2N (83) Br O_2N (—)	300
	HN_3, H_2SO_4, $CHCl_3$		(70)	301

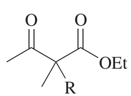
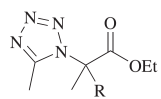
TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-10} 	A: NaN_3, PPA, 0°, 6 h B: NaN_3, H_2SO_4, PhH, rt, 6 h C: NaN_3, H_2SO_4, Et_2O, 0°, 6 h	 **I** + **II**	296

R^1	R^2	R^3	Conditions	**I + II**	**I:II**
H	H	H	A	(>95)	24:76
H	H	H	B	(>95)	20:80
H	H	H	C	(>95)	60:40
H	H	O_2N	A	(90)	27:73
H	H	O_2N	B	(100)	14:86
H	H	O_2N	C	(40)	67:33
H	O_2N	H	A	(90)	15:85
H	O_2N	H	B	(100)	14:86
H	O_2N	H	C	(60)	33:67
—OCH_2O—		H	A	(35)	90:10
—OCH_2O—		H	B	(—)	—
—OCH_2O—		H	C	(29)	43:57

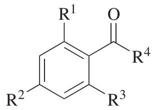
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-12} 	HN_3, H_2SO_4, PhH, 50°, 3 h		198

R	
Me	(85)
Et	(90)
n-Bu	(82)

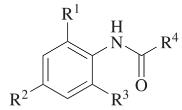
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-14} 	$TMSN_3$, $ZnBr_2$, 65°, 24 h		302

R	
Et	(90)
i-Bu	(78)
Ph	(40)
Bn	(70)

C_{9-19}

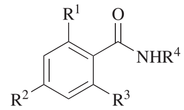


NaN$_3$, H$_2$SO$_4$, CCl$_3$CO$_2$H, 60°, 1–5 h



I

+

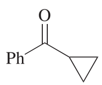


II

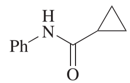
R^1	R^2	R^3	R^4	**I + II**	**I:II**
Me	H	H	Me	(—)	99:1
HO$_2$C	H	H	Me	(65)	91:9
Cl	H	H	Ph	(100)	30:70
Br	H	H	Ph	(100)	19:81
O$_2$N	H	H	Ph	(—)	70:30
Me	H	H	Ph	(34)	12:88
MeO	H	H	Ph	(88)	50:50
HO$_2$C	H	H	Ph	(—)	98:2
Me	Me	Me	Ph	(—)	95:5
Ph	H	H	Ph	(35)	95:5

8

C_{10}

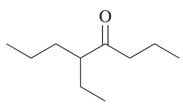


Azide, FeCl$_3$, DCE, rt

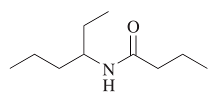


Azide	Time	
TMSN$_3$	45 min	(81)
NaN$_3$	3.5 h	(73)

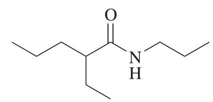
286



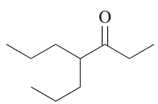
NaN$_3$, H$_2$SO$_4$, CHCl$_3$



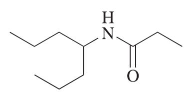
(—) +



(—) 303

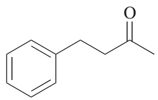
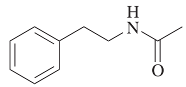
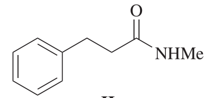
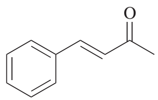
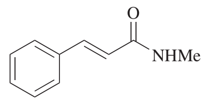
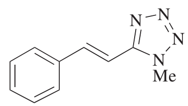
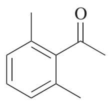
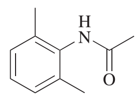
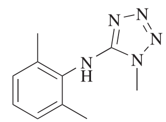
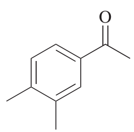
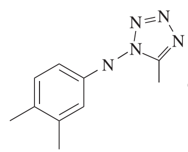


NaN$_3$, H$_2$SO$_4$, CHCl$_3$



(—) 303

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	NaN_3, PPA, rt, 8 h	 **I** (95) +  **II** (—)	54
	NaN_3, silica sulfuric acid,[a] 60°, 45 min	**I** + **II** (93), **I**:**II** = 5:1	282
	NaN_3, P_2O_5, SiO_2, MW, 10 min	**I** + **II** (93), **I**:**II** = 5:1	289
	NaN_3, $Fe(HSO_4)_3$, 50°, 25 min	**I** + **II** (90), **I**:**II** = 4:1	288
	NaN_3, PPA, rt, 8 h	 (58)	54
	$SiCl_4$, NaN_3, MeCN, rt, 12 h	 (95)	70
	NaN_3, H_2SO_4, 0° to rt, 14 h	 (—) +  (—)	304
	NaN_3, H_2SO_4	 (72)	305

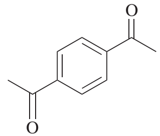
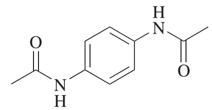
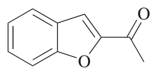
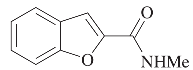
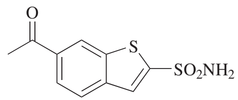
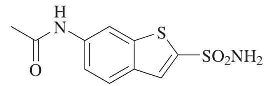
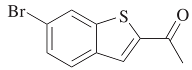
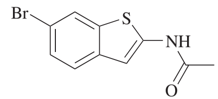
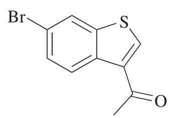
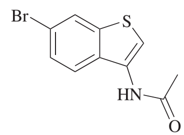
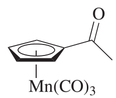
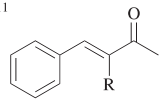
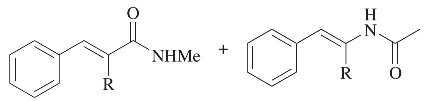
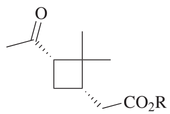
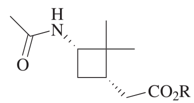
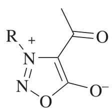
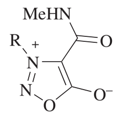
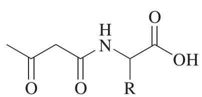
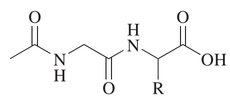
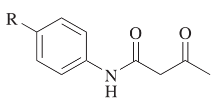
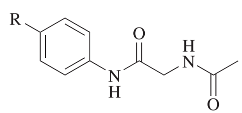
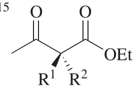
	NaN_3, H_2SO_4, $CHCl_3$	 (—)	216
	NaN_3, CCl_3CO_2H, $CHCl_3$, 50°, 3 h	 (80)	69
	NaN_3, AcOH, H_2SO_4, 80°, 3 h	 (28)	306
	HN_3, AcOH, 95°, 8 h	 (74)	307
	HN_3, AcOH, 95°, 8 h	 (70)	307
	NaN_3, PPA, 65°, 19 h	 **I** **II** **I + II** (73), **I**:**II** = 3:2	308, 309
	NaN_3, H_2SO_4	**I + II** (12), **I**:**II** = 3:2	308, 309
	NaN_3, TFA	**I + II** (50), **I**:**II** = 3:2	308, 309

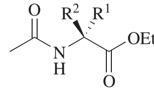
TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10-11}			
	NaN_3, CCl_3CO_2H	 I + II R, I, II H, (75), (0) Me, (0), (86)	7
C_{10-12}			
	HN_3, H_2SO_4, $CHCl_3$	 R H (89) Et (92)	301
	NaN_3, H_2SO_4, 0° to rt, 6 h	 R Ph (50) 4-BrC_6H_4 (74) 4-MeC_6H_4 (77) 4-$MeOC_6H_4$ (58) 4-$EtOC_6H_4$ (63)	310
C_{10-13}			
	HN_3, H_2SO_4	 R *i*-Bu (48) Bn (46)	290
	NaN_3, H_2SO_4, $CHCl_3$	 R H (57) H_2NO_2S (44) $(HO)_2AsO$ (70) EtO (35) EtO_2C (50)	311

C_{10-15}

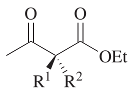


NaN_3, MsOH, HCl, 0° to reflux, 6 h

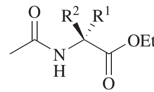


R^1	R^2		
allyl	Me	(44)	109
n-Pr	Me	(99)	109
i-Pr	Me	(50)	109
n-Bu	Me	(89)	109
i-Bu	Me	(80)	109
allyl	Et	(0)	109
n-Pr	Et	(48)	109
i-Pr	Et	(21)	109
n-Bu	Et	(37)	109
i-Bu	Et	(35)	312
Et	*i*-Bu	(40)	109
H	Bn	(90)	313
Bn	Me	(95)	109
Bn	Et	(52)	109

C_{10-20}

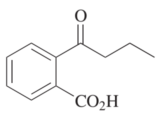


A. NaN_3, MsOH, $CHCl_3$, reflux, 1 h
B. NaN_3, H_2SO_4, DME, rt, 24 h

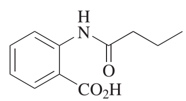


R^1	R^2	Conditions		
MeO_2CCH_2	Me	A	(88)	108
Bn	Me	A	(95)	108
Bn	Me	B	(82)	314
$4\text{-}BrC_6H_4CH_2$	Me	B	(63)	314
$4\text{-}BrC_6H_4CH_2$	Bu	B	(43)	314
$2\text{-}C_{10}H_7CH_2$	Me	A	(89)	108
$2\text{-}C_{10}H_7CH_2$	Me	B	(82)	314
$2\text{-}C_{10}H_7CH_2$	Bu	B	(41)	314

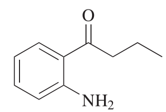
C_{11}



NaN_3, H_2SO_4, $CHCl_3$, rt, 3 h

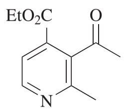
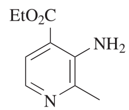
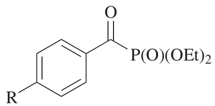
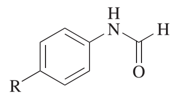
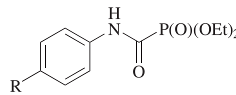
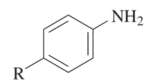
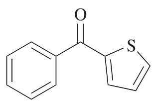
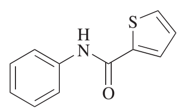
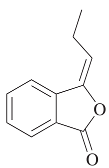
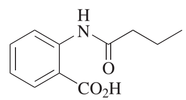
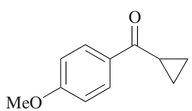
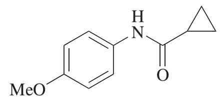


(77) +



(5) 315

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	1. NaN_3, H_2SO_4, $CHCl_3$, rt, 18 h 2. H_2O, reflux, 1.5h	 (94)	316
	HN_3, H_2SO_4, $CHCl_3$	 **I** +  **II** +  **III**	82
	NaN_3, H_2SO_4, CCl_3CO_2H, 50°, 3 h	 (49)	317
	NaN_3, H_2SO_4, $CHCl_3$, rt, 3 h	 (69)	315
	Azide, $FeCl_3$, DCE, rt		286

R	**I**	**II**	**III**
H	(53)	(9)	(14)
Cl	(65)	(19)	(0)

Azide	Time	
$TMSN_3$	49 min	(78)
NaN_3	3.5 h	(70)

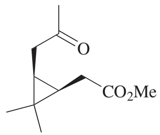
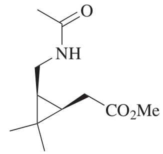
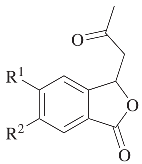
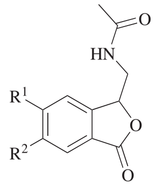
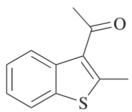
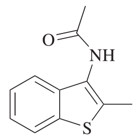
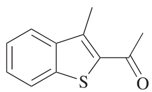
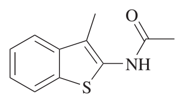
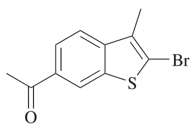
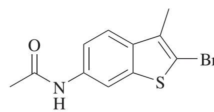
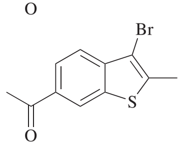
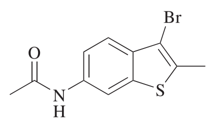
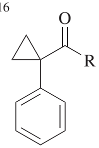
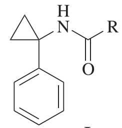
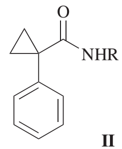
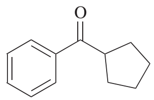
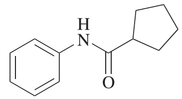
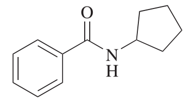
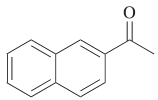
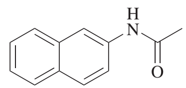
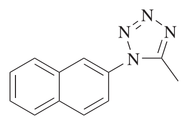
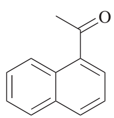
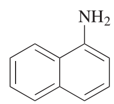
	NaN_3, MsOH, DME, –30° to rt		(68)	318
	NaN_3, PPA, 20–90°, 4 h		R^1 R^2 H H (40) Cl H (—) Cl Cl (80)	319
	HN_3, AcOH, 70°		(82)	320
	HN_3, AcOH, 70°		(50)	320
	HN_3, AcOH, 70°		(63)	320
	HN_3, AcOH, 70°		(71)	320

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11-16} 	NaN_3, H_2SO_4, $CHCl_3$, rt	 **I** +  **II** R / **I + II** / **I:II** Me / (81) / 3.3:1 Ph / (66) / 1.7:1	279
C_{12} 	NaN_3, $ClCH_2CO_2H$, 60°, 6 h	 (—) +  (—)	321
	NaN_3, MsOH, DME, –30° to rt, 3 h	 **I** (91)	56
	NaN_3, PPA, 55°, 12 h	**I** (81)	54
	NaN_3, CCl_3CO_2H, 60°	**I** (95)	1
	NaN_3, H_2SO_4	**I** (55)	1
	NaN_3, $POCl_3$, $CHCl_3$	**I** (42)	1
	NaN_3, $AlCl_3$, $PhNO_2$	 (73)	1
	1. NaN_3, *x*% H_2SO_4, 0°, 8 h 2. HCl, EtOH, reflux, 24 h	 *x* 75 (15) 85 (48) 90 (70) 95 (36)	5

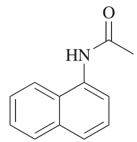
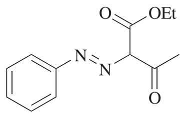
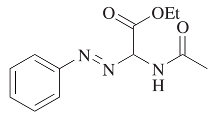
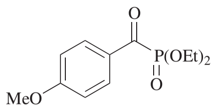
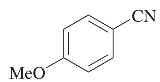
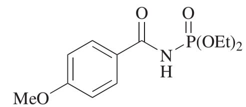
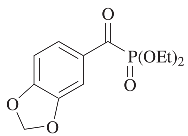
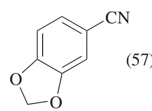
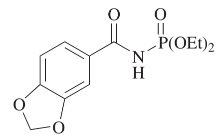
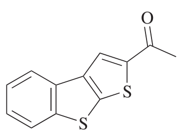
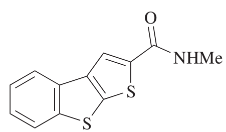
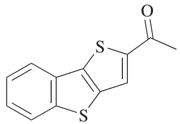
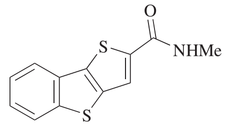
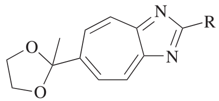
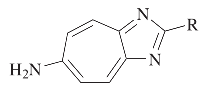
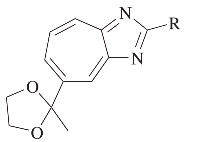
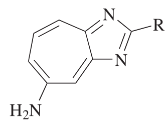
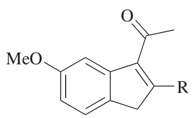
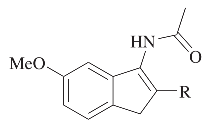
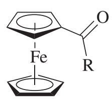
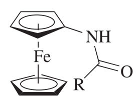
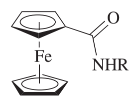
	NaN_3, PPA, 55°, 12 h	 (72) **I**	54
	NaN_3, CCl_3CO_2H, 60°	**I** (90)	1
	NaN_3, H_2SO_4, $CHCl_3$, 0–55°	 (71)	322
	HN_3, H_2SO_4, $CHCl_3$	 (65) +  (30)	82
	HN_3, H_2SO_4, $CHCl_3$	 (57) +  (28)	82
	NaN_3, H_2SO_4, AcOH, 100°, 8 h	 (67)	323

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}			
	NaN_3, H_2SO_4, AcOH, 100°, 8 h	 (60)	323
	NaN_3, H_2SO_4, rt, 2 h	 R / H (—) / H_2N (80)	324
C_{12-13}			
	NaN_3, H_2SO_4, rt, 2 h	 (—) R / H / H_2N / MeS	324
	NaN_3, TFA, $CHCl_3$, 60°, 4 h	 R / H (78) / Me (80)	69
C_{12-17}			
	NaN_3, PPA, 60°, 28 h	 **I** +  **II** R / **I** / **II** Me (20) (10) Ph (10) (5)	309

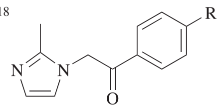
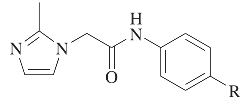
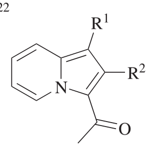
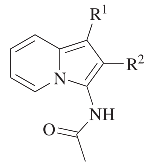
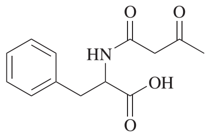
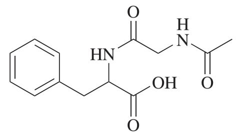
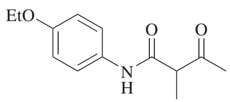
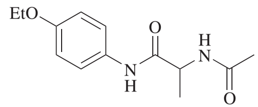
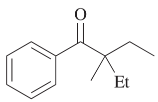
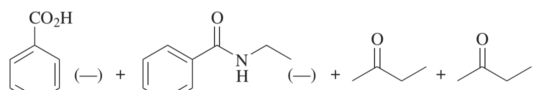
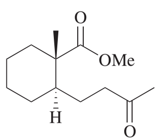
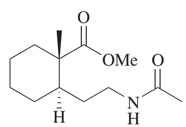
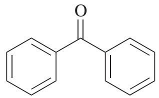
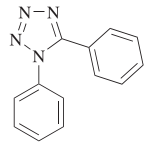
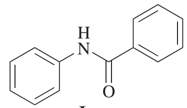
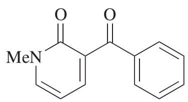
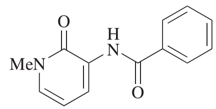
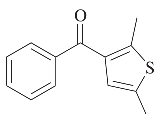
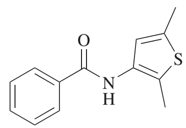
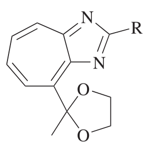
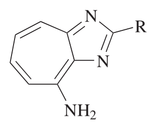
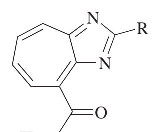
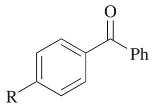
C_{12-18}		NaN_3, H_2SO_4, 60°	 R: Cl (78); Br (64); O_2N (71); Ph (68)	325
C_{12-22}		HN_3, H_2SO_4, $CHCl_3$, –5°, 45 min	 R^1, R^2: Me, Me (86); H, Ph (78); Ph, Ph (86)	326
C_{13}		NaN_3, H_2SO_4, $CHCl_3$	 (20)	311
		NaN_3, H_2SO_4, $CHCl_3$	 (45)	311
		NaN_3, H_2SO_4, 0–40°, 3 h	 (—) + (—) + (19) + (8)	327
		NaN_3, H_2SO_4, $CHCl_3$, 0°, 30 min	 (55)	328

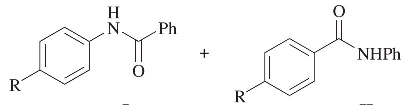
TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	$SiCl_4$, NaN_3, MeCN, rt, 15 h	 (97)	70
	A. NaN_3, H_2SO_4, CCl_3CO_2H B. NaN_3, PPA, 50°, 8.5 h C. NaN_3, MsOH, DME, rt	 **I** Conditions: A (99); B (99); C (57)	1 54 56
	Azide, $FeCl_3$, DCE, rt	**I** Azide / Time $TMSN_3$ 32 min (79) NaN_3 2.5 h (70)	286
	NaN_3, H_2SO_4, $CHCl_3$, 0–50°, 12 h	 (70)	329
	NaN_3, CCl_3CO_2H, H_2SO_4, 50°, 3 h	 (58)	317
$C_{13–18}$ 	NaN_3, H_2SO_4, rt, 2 h	 **I** +  **II** R / **I** / **II** Me (34) (0) Ph (84) (15)	330

C_{13-19}



NaN_3, CCl_3CO_2H, 60°, 8 h



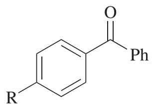
I + **II**

I + II (—)

R	**I:II**
Cl	3:2
O_2N	1:1
Me	1:1
MeO	3:2
Me_2N	1:1
Ph	1:1

7

C_{14}

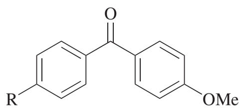


NaN_3, H_2SO_4, PhH, 50°, 8 h

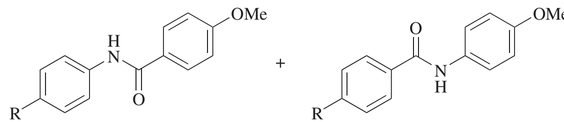
I + **II**

R	**I + II**	**I:II**
Me	(64)	1:1
MeO	(—)	2:1

331



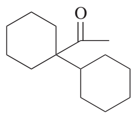
NaN_3, H_2SO_4, CCl_3CO_2H, 60°, 8 h



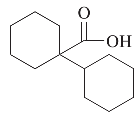
I + **II**

R	**I + II**	**I:II**
Cl	(97)	1:1
O_2N	(93)	1:1

6

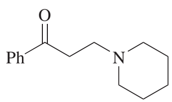


NaN_3, H_2SO_4, $CHCl_3$

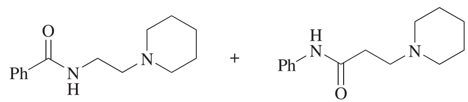


(75)

332



NaN_3, H_2SO_4

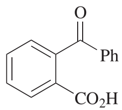
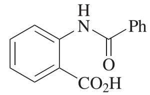
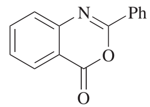
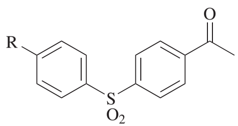
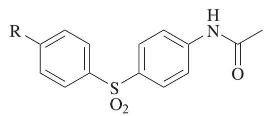
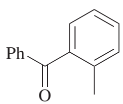
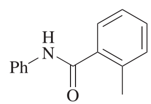
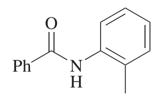
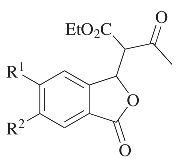
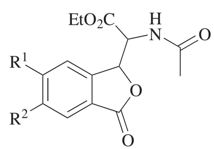


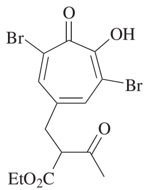
I + **II**

I + II (—), **I:II** = 1:1

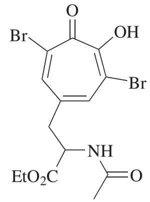
333

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	NaN_3, H_2SO_4, CCl_3CO_2H, 50°	 (91)	317
	NaN_3, H_2SO_4, $CHCl_3$	 (80)	334
	NaN_3, H_2SO_4	 (—) R: H, O_2N	248
	NaN_3, H_2SO_4, CCl_3CO_2H	 **I** +  **II** **I** + **II** (97), **I**:**II** = 12:88	6
	NaN_3, H_2SO_4, CH_2Cl_2, PhH, 20°, 1 h	 R^1 / R^2: H / H (87); H / Cl (84); Cl / H (80); Cl / Cl (82)	319



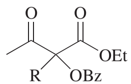
NaN_3, H_2SO_4, PhH, 0°, 1 h



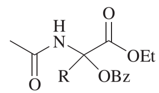
(97)

335

C_{14-17}

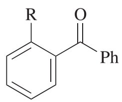


HN_3, H_2SO_4, CCl_4

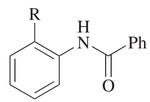


R	
Me	(58)
Et	(60)
n-Pr	(60)
n-Bu	(60)

336

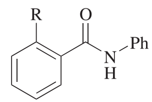


NaN_3, CCl_3CO_2H, 60°, 12 h



I

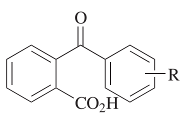
+



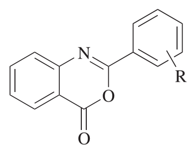
II

R	**I + II**	**I:II**
Me	(99)	24:76
HO_2C	(87)	100:0
Et	(96)	23:77
i-Pr	(96)	18:82

63

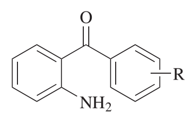


NaN_3, H_2SO_4, $CHCl_3$, rt, 3 h



I

+

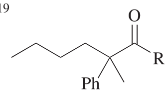
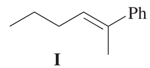
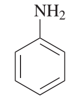
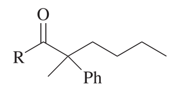
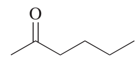
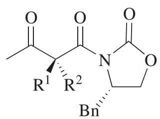
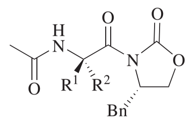
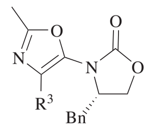
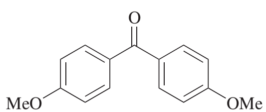
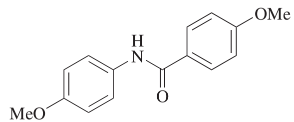


II

R	**I**	**II**
4-Cl	(84)	(3)
$3\text{-}O_2N$	(87)	(4)
4-MeO	(75)	(0)
$2,4,6\text{-}Me_3$	(29)	(0)

315

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14-19} 	NaN_3, PPA, 50°, 8 h	 **I** +  **II** +  **III** +  **IV**	337
C_{14-23} 	A: NaN_3, MsOH, DME, –30° to rt B: NaN_3, H_2SO_4, DME, –30° C: NaN_3, H_2SO_4, PhH, 5° to rt	 **I** +  **II**	56
C_{15} 	NaN_3, PPA, 50°, 8.5 h	 (91)	54

R	**I**	**II**	**III**	**IV**
Me	(8)	(41)	(25)	(29)
Ph	(8)	(24)	(58)	(—)

R^1	R^2	R^3	Conditions	**I**	**II**
H	H	H	A	(0)	(45)
H	Me	Me	A	(0)	(91)
Me	H	Me	C	(14)	(21)
H	Bn	Bn	A	(0)	(27)
H	Bn	—	B	(50)	(0)
H	Bn	—	C	(0)	(0)
$Ph(CH_2)_2$	H	$Ph(CH_2)_2$	A	(0)	(66)
H	(*E*)-PhCH=CHCH$_2$	(*E*)-PhCH=CHCH$_2$	A	(0)	(32)

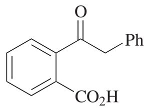
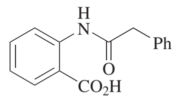
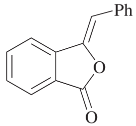
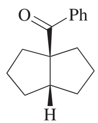
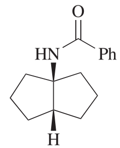
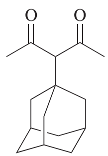
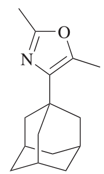
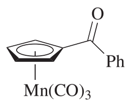
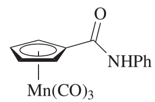
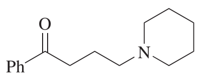
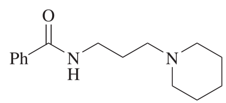
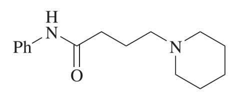
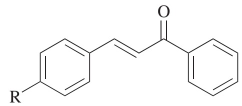
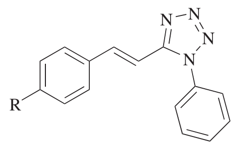
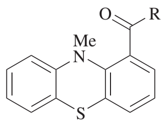
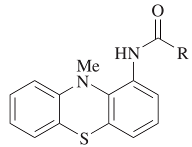
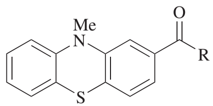
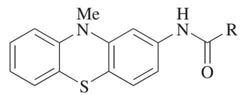
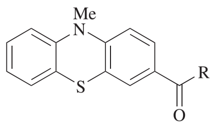
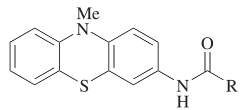
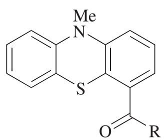
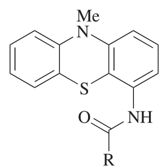
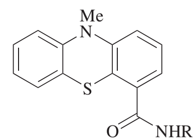
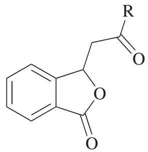
	NaN_3, H_2SO_4, $CHCl_3$, rt, 3 h	 **I** (85)	315
	NaN_3, H_2SO_4, $CHCl_3$, rt, 3 h	**I** (62)	315
	NaN_3, H_2SO_4, $CHCl_3$, 0°, 45 min	 (56)	338
	NaN_3, MsOH, DME, –30° to rt, 3 h	 (87)	56
	NaN_3, Promoter	 Promoter / Conditions PPA / 65°, 19 h / (67) H_2SO_4 / — / (15) TFA / — / (32)	308
	NaN_3, H_2SO_4	 **I** +  **II** **I** + **II** (—), **I**:**II** = 3:7	333

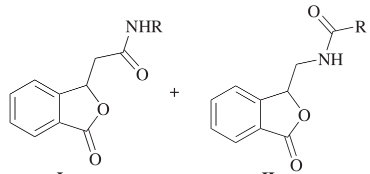
TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15-16}			
	NaN_3, $SiCl_4$, MeCN, rt, 12 h	 R: H (94); Cl (95); MeO (90)	70
C_{15-20}			
	NaN_3, H_2SO_4, PhH, 0°	 R: Me (83); Ph (16)	339
	NaN_3, H_2SO_4, PhH, 0°	 R: Me (67); Ph (53)	339
	NaN_3, H_2SO_4, PhH, 0°	 R: Me (31); Ph (63)	339
	NaN_3, H_2SO_4, PhH, 0°	 **I** +  **II** R / **I** / **II**: Me (72) (0); Ph (34) (24)	339

C_{16}



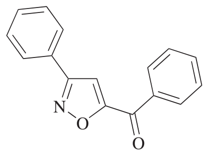
NaN_3, PPA, 20–90°, 4 h



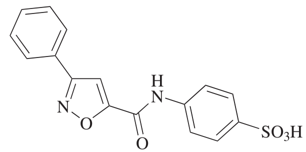
I + **II**

R	I	II
2-$O_2NC_6H_4$	(56)	(0)
4-$O_2NC_6H_4$	(92)	(—)

319

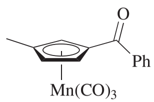


NaN_3, H_2SO_4, $CHCl_3$

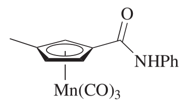


(100)

340



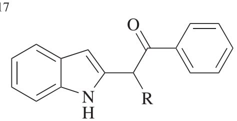
NaN_3, Promoter



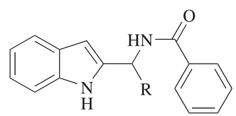
Promoter	Conditions	
PPA	65°, 19 h	(53)
H_2SO_4	—	(26)
TFA	—	(20)

308

C_{16-17}



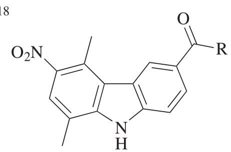
NaN_3, H_2SO_4, $CHCl_3$, rt



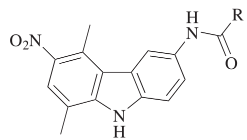
R	
H	(38)
Me	(56)

341

C_{16-18}



NaN_3, TFA, 100°, 5 h



R	
Me	(71)
Et	(70)
n-Pr	(72)

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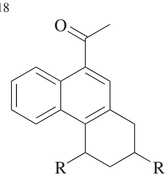
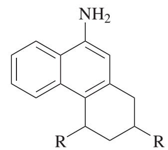
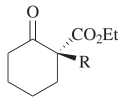
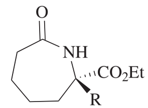
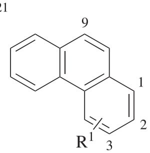
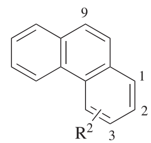
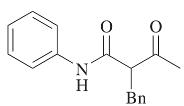
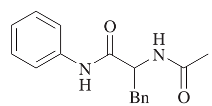
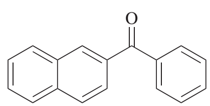
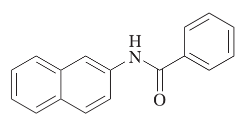
TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16-18} 	1. NaN_3, H_2SO_4, 60°, 8 h 2. Hydrolysis	 R: H (81); Me (82)	5
C_{16-20} 	NaN_3, MsOH, $CHCl_3$, reflux, 1 h	 R: Bn (97); 2-$C_{10}H_7CH_2$ (71)	108
C_{16-21} 	1. NaN_3, H_2SO_4, 60°, 8 h 2. Hydrolysis	 R^1, R^2: 2-Ac, 2-H_2N (88); 3-Ac, 3-H_2N (80); 9-Ac, 9-H_2N (73); 1-Bz, 1-BzHN (93)	5
C_{17} 	NaN_3, H_2SO_4, $CHCl_3$	 (40)	311
	NaN_3, PPA, 50°, 10 h	 (72)	54

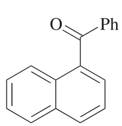
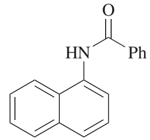
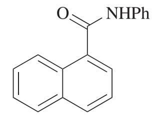
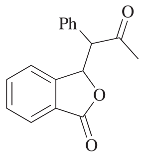
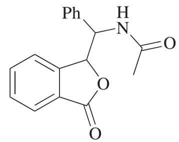
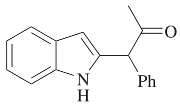
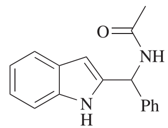
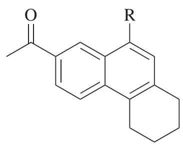
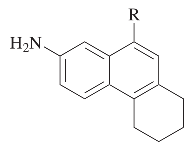
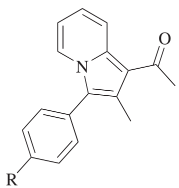
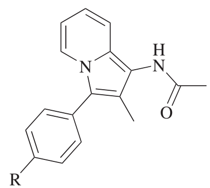
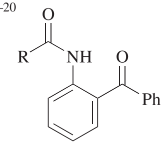
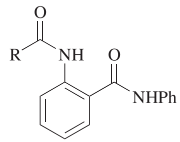
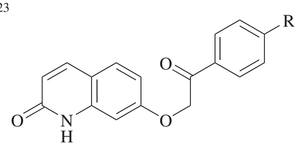
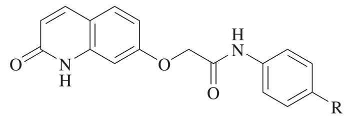
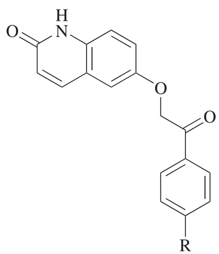
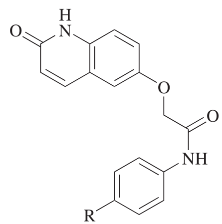
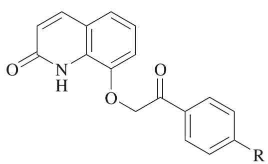
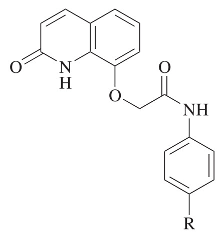
	NaN_3, CCl_3CO_2H, 60°, 12 h	 (29) +  (69)	63
	NaN_3, PPA, 0° to rt, 3 h	 (95)	343
	NaN_3, H_2SO_4, $CHCl_3$, rt	 (40)	341
C_{17-18}			
	1. NaN_3, H_2SO_4, 60°, 8 h 2. Hydrolysis	 R: Me (93); Et (99)	5
	HN_3, H_2SO_4, $CHCl_3$, 0°, 30 min	 R: H (64); Cl (77); O_2N (56); MeO (71)	344

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17-20} 	NaN_3, H_2SO_4, $CHCl_3$, rt, 12 h	 (—) R: *n*-Pr; Ph; 2-$O_2NC_6H_4$	345
C_{17-23} 	NaN_3, H_2SO_4, rt, 10 min	 R: H (94); F (92); MeO (80); Ph (98)	346
	NaN_3, H_2SO_4, rt, 10 min	 R: H (85); F (73); MeO (93); Ph (95)	346
	NaN_3, H_2SO_4, rt, 10 min	 R: H (96); F (92); MeO (96); Ph (75)	346

C_{18}

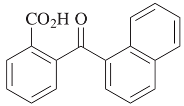
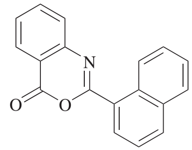
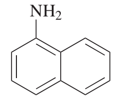
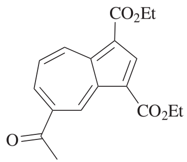
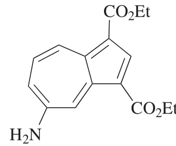
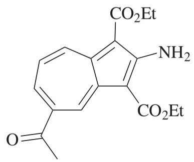
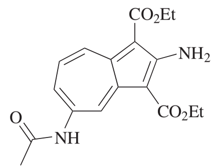
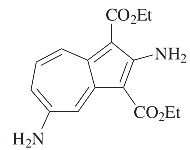
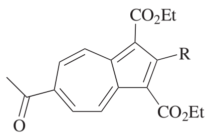
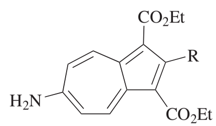
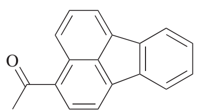
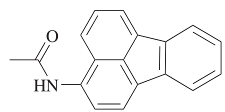
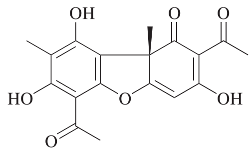
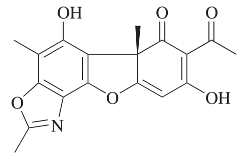
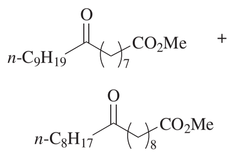
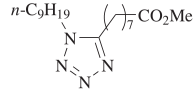
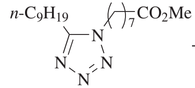
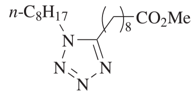
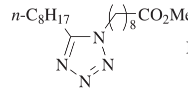
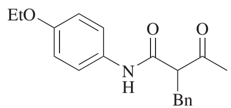
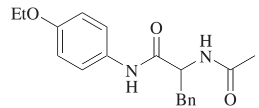
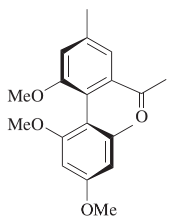
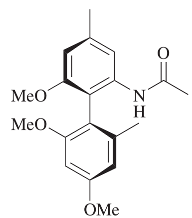
	NaN_3, H_2SO_4, $CHCl_3$, rt, 3 h	 (51) +  (7)	315
	NaN_3, H_2SO_4, $CHCl_3$, rt, 12 h	 (—)	347
	NaN_3, H_2SO_4, $CHCl_3$, rt, 12 h	 (—) +  (—)	347
	NaN_3, H_2SO_4, $CHCl_3$, rt, 12 h	 (—) R: H, H_2N	347
	NaN_3, TFA, 60°, 6 h	 (50)	348

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18} 	NaN_3, $CHCl_3$, 50–60°, 2 h	 (70)	349
C_{19} 	NaN_3, $TiCl_4$, MeCN, reflux, 5 h	 **I** +  **II** +  **III** +  **IV** **I** + **II** + **III** + **IV** (71)	350
	NaN_3, H_2SO_4, $CHCl_3$	 (53)	311
	NaN_3, TFA, 60°, 27 h	 (43)	351

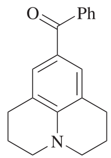
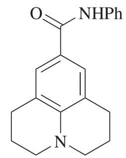
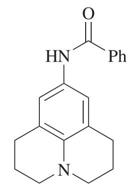
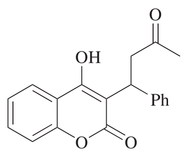
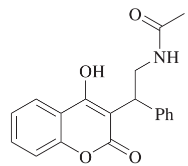
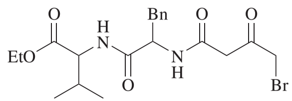
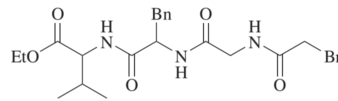
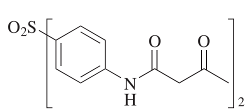
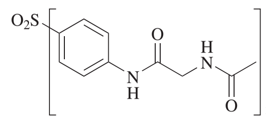
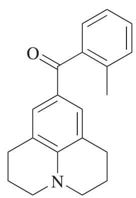
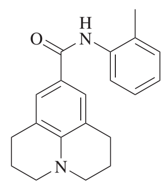
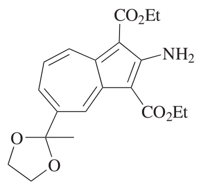
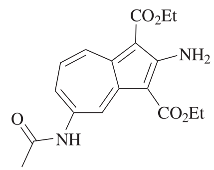
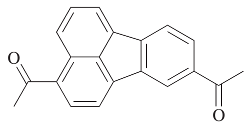
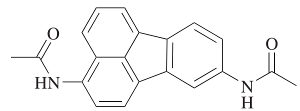
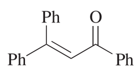
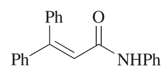
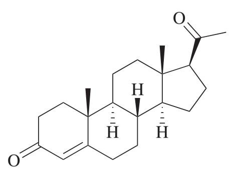
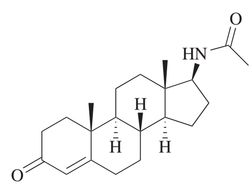
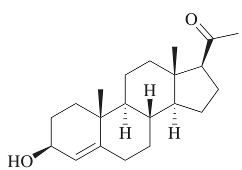
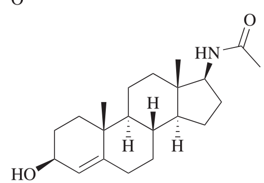
C_{20}		NaN_3, H_2SO_4, CCl_3CO_2H, 60°, 3 h	 (—) +  (—)	273
		NaN_3, H_2SO_4, $CHCl_3$, rt, 2 h	 (90)	352
		HN_3, H_2SO_4	 (31)	291
		NaN_3, H_2SO_4, $CHCl_3$	 (40)	311
		NaN_3, H_2SO_4, PhH, rt	 (76)	273

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{20}			
	NaN_3, H_2SO_4, $CHCl_3$, rt, 12 h	 (—)	347
	NaN_3, TFA, 60°, 6 h	 (99)	348
C_{21}			
	NaN_3, H_2SO_4, $CHCl_3$, 35°, 1 h	 (40)	353
	NaN_3 (1 eq), PPA, 50°, 10 h	 (35)	354
	HN_3, H_2SO_4, $CHCl_3$, rt, 30 min	 (82)	355

C$_{22}$

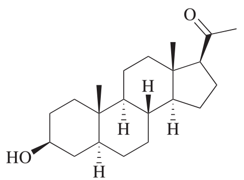
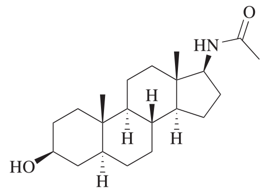
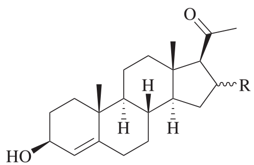
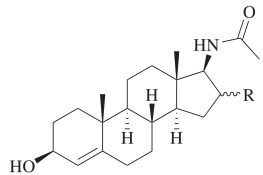
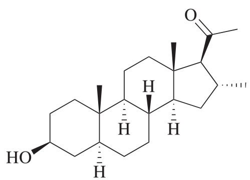
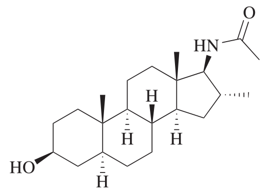
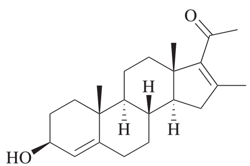
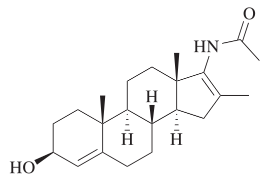
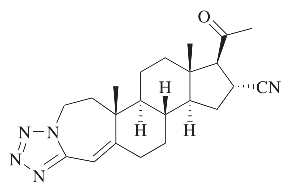
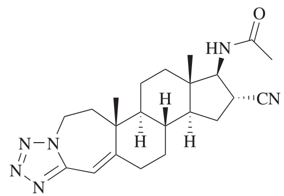
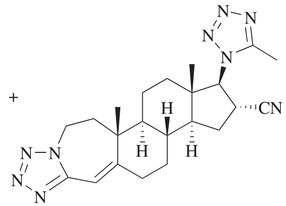
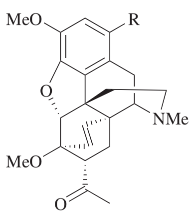
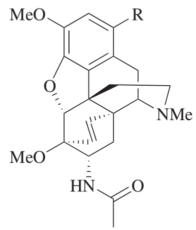
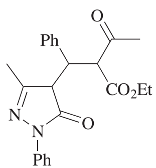
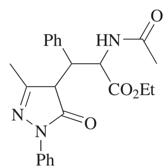
	HN_3, H_2SO_4, $CHCl_3$, rt, 30 min	 (80)	355
	HN_3, H_2SO_4, $CHCl_3$, rt, 30 min	 R: α-Me (88); β-Me (82)	355
	HN_3, H_2SO_4, $CHCl_3$, rt, 30 min	 (85)	355
	HN_3, H_2SO_4, $CHCl_3$, rt, 30 min	 (65)	355

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{22}			
	HN_3, $BF_3{\bullet}OEt_2$, $CHCl_3$, 0° to rt, 24 h	 (25) +  (20)	356
C_{23}			
	A. NaN_3, perchloric acid, 75°, 5 h B. NaN_3, HCl (concd), 60°, 6 h	 R / Conditions: H, A (50); Cl, B (23)	357
	NaN_3, H_2SO_4, $CHCl_3$, 0–50°, 5 h	 (48)	263

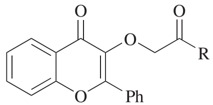
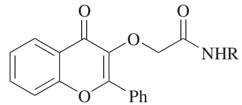
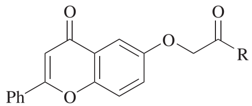
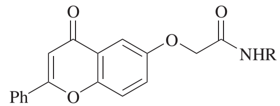
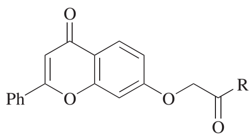
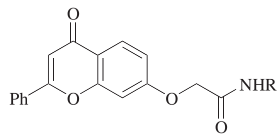
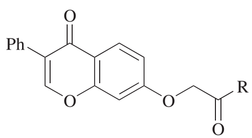
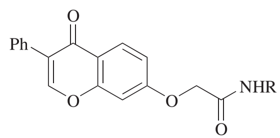
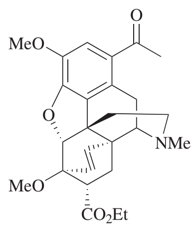
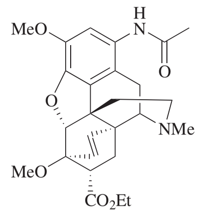
C_{23-29}				
	NaN_3, H_2SO_4, rt, 1 h		R: Ph (78); 4-FC_6H_4 (85); 4-$MeOC_6H_4$ (72); 2-$C_{10}H_7$ (71); 4-PhC_6H_4 (65)	358
	NaN_3, H_2SO_4, rt, 1 h		R: Ph (91); 4-FC_6H_4 (96); 4-$MeOC_6H_4$ (94); 2-$C_{10}H_7$ (89); 4-PhC_6H_4 (61)	358
	NaN_3, H_2SO_4, rt, 1 h		R: Ph (87); 4-FC_6H_4 (85); 4-$MeOC_6H_4$ (67); 2-$C_{10}H_7$ (77); 4-PhC_6H_4 (85)	358
	NaN_3, H_2SO_4, rt, 1 h		R: Ph (89); 4-FC_6H_4 (93); 4-$MeOC_6H_4$ (91); 2-$C_{10}H_7$ (88); 4-PhC_6H_4 (90)	358

TABLE 3. SCHMIDT REACTIONS OF ACYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{26}			
	NaN_3, HCl (concd), rt, 12 h	 (35)	359

[a] Silica sulfuric acid is silica-bound sulfuric acid generated by treating silica gel with chlorosulfonic acid.

[b] The reaction was performed in the presence of 1 equivalent of dimethyl phosphite.

[c] The reaction was performed in the presence of 1 equivalent of diethyl phosphite.

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3

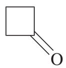
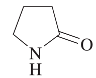
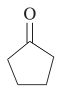
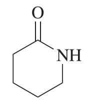
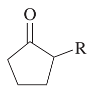
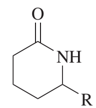
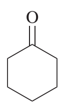
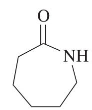
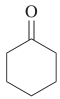
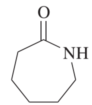
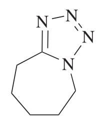
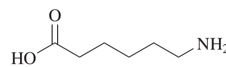
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	HN_3, H_2SO_4, $CHCl_3$, rt, 2 h	 (20)	360
C_5 	NaN_3, silica sulfuric acid,[a] 60°, 25 min	 (95)	282
C_{5-8} 	HN_3, H_2SO_4, $CHCl_3$, 5°, 1 h	 **I** R: H (80), Me (75), Et (63), *n*-Pr (61), *i*-Pr (46)	53
	NaN_3, PPA, 50°, 9–14 h	**I** R: H (83), Me (87), *n*-Pr (82)	54
C_6 	NaN_3, HCl	 **I** (63)	1
	NaN_3, AcOH, HBr (cat)	**I** (56)	1

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	$TMSN_3$, Promoter (x eq), DCE, rt	 **I** Promoter / x / Time (h): $FeCl_3$ 1.0 0.5 (82) $FeCl_3$ 0.1 12 (78) $InBr_3$ 0.5 3 (40) $InCl_3$ 0.5 3 (30) $ZrCl_4$ 0.5 3 (15)	286
	NaN_3, $FeCl_3$ (1 eq), DCE, rt, 3 h	**I** (70)	286
	NaN_3, MsOH, DME, –30° to rt, 3 h	**I** (96)	56
	NaN_3, PPA, 50°, 8 h	**I** (89)	54
	NaN_3, silica sulfuric acid,[a] 60°, 35 min	**I** (92)	282
	NaN_3, P_2O_5–SiO_2, MW, 7 min	**I** (70)	289
	NaN_3, $Fe(HSO_4)_3$, grinding, 50°, 20 min	**I** (88)	288
	NaN_3, $SiCl_4$, MeCN, rt, 20 h	 (95)	70
	1. NaN_3, H_2SO_4 2. HCl	 (90)	195

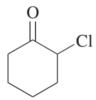
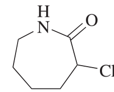
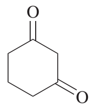
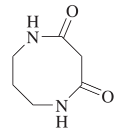
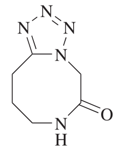
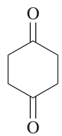
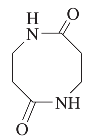
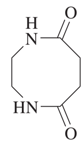
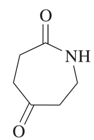
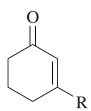
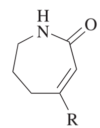
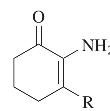
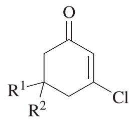
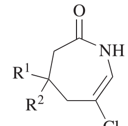
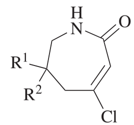
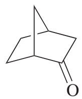
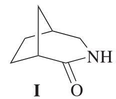
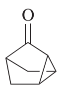
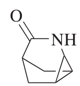
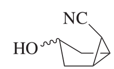
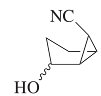
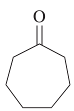
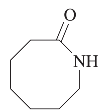
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	HN_3, H_2SO_4, $CHCl_3$, 40–45°, 1 h	 (31)	53
	HN_3, H_2SO_4, $CHCl_3$, rt, 24 h	 (—) +  (—)	361
	HN_3, HCl, $CHCl_3$	 **I** +  **II** **I** + **II** (20–27)	362
	Azide, $FeCl_3$, DCE, rt	 Azide / Time $TMSN_3$ 55 min (68) NaN_3 3.5 h (68)	286
C_{6-7} 	NaN_3, PPA, 40°, 6 h	 **I** +  **II** R / **I** / **II** H (13) (—) Me (—) (—)	363

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-8} 	NaN_3, PPA, 120°, 2 h	 **I** +  **II** R¹ / R² / **I** / **II**: H / H / (11) / (15)	364
		Me / H / (17) / (35)	365
		Me / Me / (32) / (36)	365
C_7 	NaN_3, H_2SO_4, PhH, 15°	 **I** (10)	366
	HN_3, H_2SO_4, P_2O_5, $CHCl_3$, 0° to rt, 4 h	**I** (43)	367
	NaN_3, HCl, 5°, 5 h	**I** (16)	367
	NaN_3, PPA, 60°, 2 d	**I** (34)	368
	NaN_3, H_2SO_4, $CHCl_3$, 0° to rt, 12 h	 **I** +  **II** +  **III** +  **IV** **I** (11), **II** (13), **III + IV** (33)	369
	NaN_3, PPA, 50°, 9 h	 **I** (89)	54
	NaN_3, silica sulfuric acid,[a] 60°, 35 min	**I** (92)	282

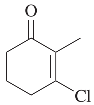
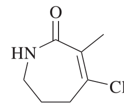
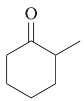
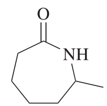
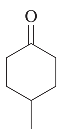
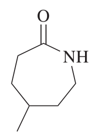
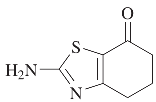
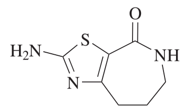
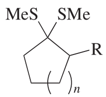
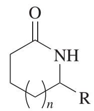
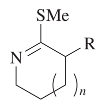
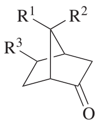
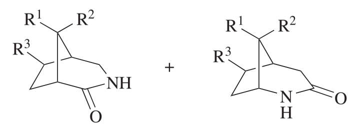
	NaN_3, P_2O_5–SiO_2, MW, 7 min	**I** (72)	289
	NaN_3, $Fe(HSO_4)_3$, grinding, 50°	**I** (90)	288
	Azide, $FeCl_3$, DCE, rt	**I** Azide / Time: $TMSN_3$, 45 min (80); NaN_3, 3 h (72)	286
	NaN_3, PPA, 120°, 2 h	 (54)	370
	NaN_3, silica sulfuric acid,[a] 60°, 30 min	 **I** (95)	282
	NaN_3, P_2O_5–SiO_2, MW, 7 min	**I** (75)	289
	NaN_3, silica sulfuric acid,[a] 60°, 25 min	 **I** (95)	282
	NaN_3, P_2O_5–SiO_2, MW, 7 min	**I** (70)	289
	NaN_3, $Fe(HSO_4)_3$, grinding, 50°, 20 min	**I** (90)	288

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	NaN_3, H_2SO_4, $CHCl_3$, rt, 24 h	 (88)	371
C_{7-10}			
	1. IN_3, CH_2Cl_2, –78 to –10°, 2 h 2. TFA, $CHCl_3$, rt, 2 h	 *n* R 1 H (73) 2 H (76) 2 Me (60) 3 H (59) 4 H (65)	83
	$TMSN_3$, $SnCl_4$, I_2, CH_2Cl_2, –78° to rt, 2.5 h	 *n* R 1 H (95) 2 H (46) 2 Me (31) 3 H (51) 4 H (38)	83
C_{7-14}			
	NaN_3, H_2SO_4, $CHCl_3$, rt, 1–36 h	 **I** **II**	68

R^1	R^2	R^3	**I + II**	**I:II**
H	H	H	(35)	100:0
H	MeO	H	(48)	73:27
H	Cl	H	(28)	85:15
H	Br	H	(37)	81:19
H	TsO	H	(52)	35:65

		Cl	H	H	(29)	83:17	
		Br	H	H	(41)	100:0	
		TsO	H	H	(40)	36:64	
		MeO_2C	H	H	(31)	66:34	
		MeO_2C	H	Br	(52)	52:48	

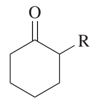
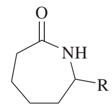
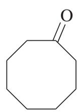
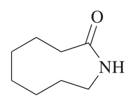
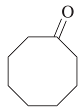
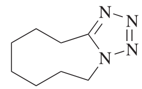
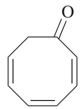
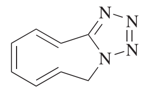
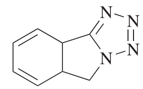
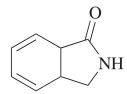
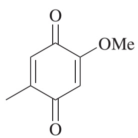
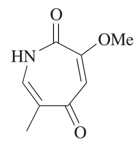
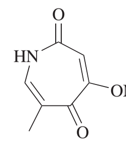
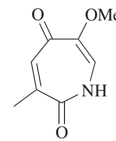
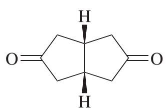
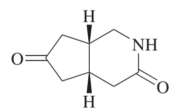
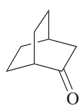
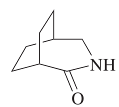
C_{7-18} 	NaN_3, H_2SO_4 or PPA, 0–50°, 1–10 h		**R**		
			Me	(96)	54
			NC–	(76)	54
			Et	(93)	53
			n-Pr	(97)	53
			EtO_2C	(80)	53
			i-Bu	(77)	372
			n-C_6H_{13}	(16)	372
			Bn	(49)	368
			4-$MeC_6H_4CH_2$	(45)	368
			2-$MeOC_6H_4CH_2$	(42)	368
			4-$MeOC_6H_4CH_2$	(40)	368
			n-$C_{12}H_{25}$	(25)	372
C_8 	NaN_3, silica sulfuric acid,[a] 60°, 25 min	 **I**	(92)		282
	NaN_3, P_2O_5–SiO_2, MW, 7 min	**I** (70)			289
	NaN_3, $Fe(HSO_4)_3$, grinding, 50°, 25 min	**I** (92)			288

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	NaN_3, H_2SO_4, 0° to rt, 12 h	 (—)	373
	NaN_3, TFA, 0° to rt, 6 h	 (—) +  (—)	373
	NaN_3, HCl, 0° to rt, 5 h	 (66)	373
	NaN_3, H_2SO_4, 0–70°, 70 h	 (22) +  (16) +  (13)	374
	NaN_3, HCl, rt, 3 h	 (52)	116
	HN_3, AcOH, 0° to rt, 3 h	 (56)	375

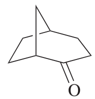
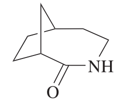
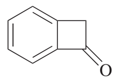
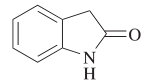
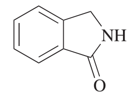
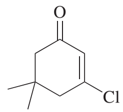
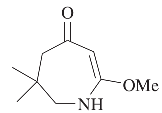
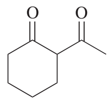
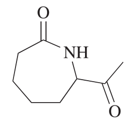
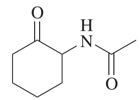
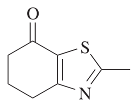
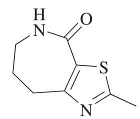
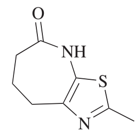
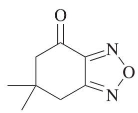
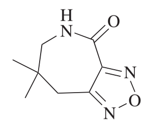
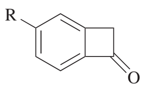
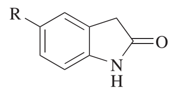
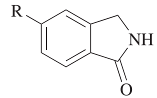
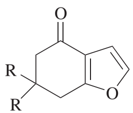
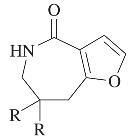
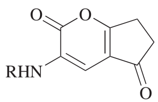
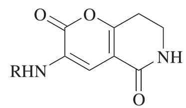
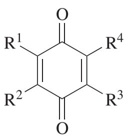
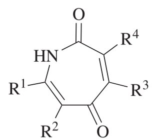
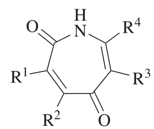
	HN_3, H_2SO_4, P_2O_5, $CHCl_3$, 0° to rt, 20 h	 (40)	376
	NaN_3, CCl_3CO_2H,[b] 65°	 I +  II **I + II** (—), **I**:**II** = 1:9	59
	NaN_3, PPA, MeOH, reflux, 4 h	 (36)	377
	NaN_3, PPA, 40°, 6 h	 (32) +  (6)	378
	NaN_3, H_2SO_4, 0°, 10 h	 (68) +  (—)	55
	NaN_3, H_2SO_4, $CHCl_3$, rt, 24 h	 (55)	371

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{8-9} 	NaN_3, H_2SO_4, PhH, 60°	 **I** +  **II** R | **I + II** | **I:II** H | (—) | 7:3 MeO | (—) | 1:9	59
C_{8-10} 	NaN_3, H_2SO_4, 0°, 10 h	 R H (79) Me (79)	379
C_{8-15} 	$TMSN_3$, H_2SO_4, CH_2Cl_2, rt, 3 h	 R H (67) Bz (71)	380
C_{8-21} 	NaN_3, H_2SO_4	 **I** +  **II** (—)	

R^1	R^2	R^3	R^4	**I**	Refs.
H	Me	H	Me	(80)	71
H	Me	Me	Me	(80)	71
H	*i*-Pr	H	Me	(75)	71
Me	Me	Me	Me	(80)	71
H	Me	H	*i*-Pr	(—)	381
H	H	Bn	Bn	(—)	381
Me	H	Bn	Bn	(—)	381

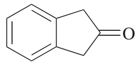
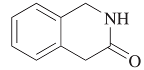
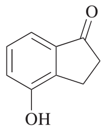
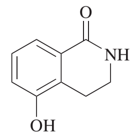
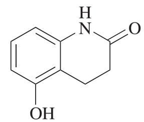
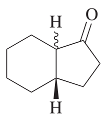
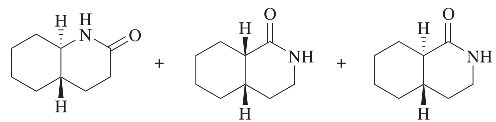
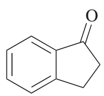
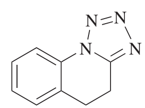
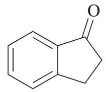
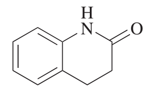
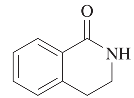
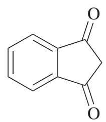
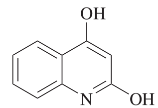
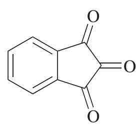
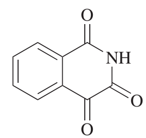
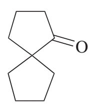
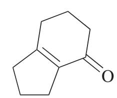
C_9 	NaN_3, H_2SO_4, $CHCl_3$, 40°, 3 h	 (87)	382
	NaN_3, TFA, 70°, 18 h	 **I** (76)	383
	$TMSN_3$, MsOH, MsCl, <5°	**I** +  **II** **I** + **II** (92), **I**:**II** = 1:2.5	384
	NaN_3, H_2SO_4, $CHCl_3$, rt, 1 h	 **I** **II** **III** **I** + **II** + **III** (—), **I**:**II**:**III** = 3.5:2.6:1	385
	NaN_3, $SiCl_4$, MeCN, rt, 13 h	 (93)	70

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	NaN_3, H_2SO_4	 **I** +  **II**	386

Solvent	Temp	Time	**I** + **II**	**I**:**II**
Et_2O	rt	4 h	(0)	—
Et_2O	reflux	1 h	(0)	—
Et_2O	reflux	4 h	(0)	—
PhH	60°	4 h	(100)	68:32
PhH	60°	10 min	(100)	71:29
PhH	rt	4 h	(100)	68:32

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	NaN_3, PPA, 50°, 10 h	**I** (90)	54
	NaN_3, PPA, 50–60°	**I** + **II** (60), **I**:**II** = 76:24	387
	NaN_3, H_2SO_4, $CHCl_3$, 0–30°, 3 h	 (—)	388
	Azide, $FeCl_3$, DCE, rt		286
	NaN_3, PPA, 60°, 7 h	 (33)	389

Azide	Time	
$TMSN_3$	40 min	(82)
NaN_3	3 h	(72)

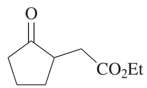
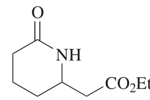
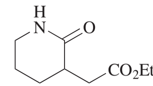
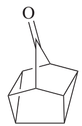
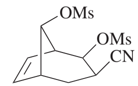
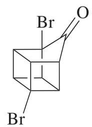
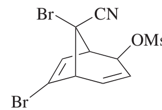
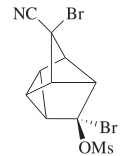
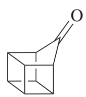
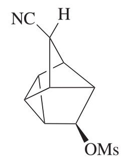
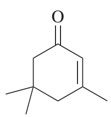
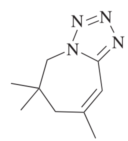
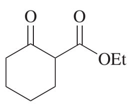
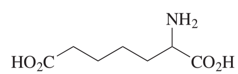
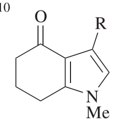
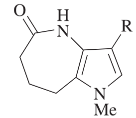
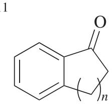
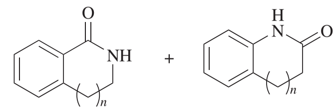
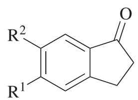
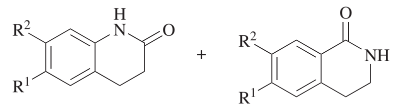
	1. HN_3, HCl (g), $CHCl_3$, 5°, 3 h 2. HCl (concd), reflux, 3 h	 **I** +  **II** **I + II** (50)	284
	NaN_3, MsOH, CH_2Cl_2, 0°, 20 min	 (20)	390
	NaN_3, MsOH, CH_2Cl_2, 0°, 10 min	 (62) +  (12)	81
	NaN_3, MsOH, CH_2Cl_2, 0°, 10 min	 (60)	391
	NaN_3, $SiCl_4$, MeCN, rt, 5 h	 (95)	70
	NaN_3, HCl, H_2O	 (20)	1

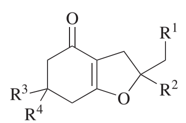
TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-10} 	NaN_3, H_2SO_4, $CHCl_3$, rt, 30 min	 R: H (40); Me (31)	392
C_{9-11} 	NaN_3, HCl (concd)	 I + II	393
	A: NaN_3, H_2SO_4, PhH, 60° B: NaN_3, CCl_3CO_2H,[b] 65°	 I + II; **I + II** (—)	59

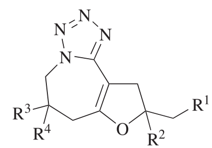
n	I	II
1	(—)	(—)
2	(—)	(—)
3	(7)	(87)

R^1	R^2	Conditions	I:II
H	H	A	7:3
H	H	B	1:4
H	HO	A	1:4
H	HO	B	1:9
HO	H	A	9:1
HO	H	B	1:4
H_2N	H	A	1:1
H_2N	H	B	1:9
H	H_2N	A	9:1
H	H_2N	B	1:4
Cl	H	A	3:2
Cl	H	B	1:9
H	Cl	A	4:1

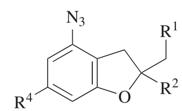
H	Cl	B	1:9
O_2N	H	A	9:1
O_2N	H	B	1:9
H	O_2N	A	4:1
H	O_2N	B	1:4
MeO	H	A	1:9
MeO	H	B	1:9
H	MeO	A	7:3
H	MeO	B	1:4
AcHN	H	A	9:1
AcHN	H	B	1:9
H	AcHN	A	9:1
H	AcHN	B	—
AcO	H	A	—
AcO	H	B	1:4
H	AcO	A	—
H	AcO	B	1:9



NaN_3, $SiCl_4$, MeCN, rt



I +



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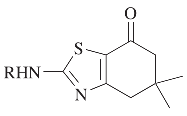
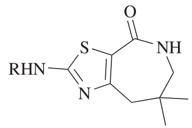
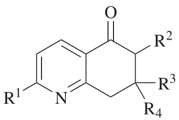
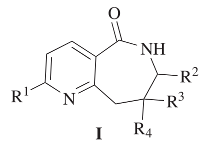
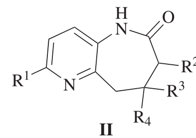
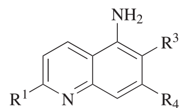
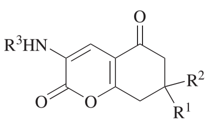
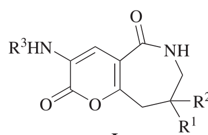
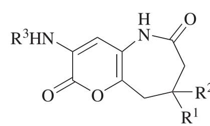
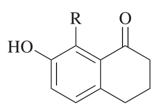
R^1	R^2	R^3	R^4	**I**	**II**
Br	H	H	H	(68)	(—)
Br	H	Me	H	(56)	(—)
Br	Me	H	H	(89)	(—)
Br	H	Me	Me	(65)	(—)
I	H	H	H	(42)	(18)
I	H	H	Me	(44)	(14)
I	Me	H	H	(42)	(19)
I	H	Me	Me	(50)	(—)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-11} 	NaN_3, H_2SO_4, $CHCl_3$, rt, 24 h	 R: H (—); Ac (—)	371
C_{9-15} 	NaN_3, H_2SO_4	 **I** +  **II** +  **III**	395
C_{9-18} 	A: NaN_3, H_2SO_4, $CHCl_3$, –15 to 0°, 5 h B: NaN_3, H_2SO_4, $CHCl_3$, rt, 2 h C: $TMSN_3$, H_2SO_4, CH_2Cl_2, 35°, 2 h D: $TMSN_3$, H_2SO_4, CH_2Cl_2, –15 to 0°, 5 h	 **I** +  **II**	380

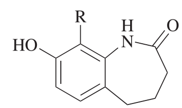
R^1	R^2	R^3	R^4	**I**	**II**	**III**
H	H	H	H	(16)	(11)	(36)
Me	H	H	H	(7)	(17)	(33)
MeO	H	H	H	(12)	(46)	(15)
H	H	H	H_2NCO	(19)	(0)	(0)
H	H	Me	Me	(6)	(12)	(57)
H	Ph	H	H	(0)	(0)	(0)

R^1	R^2	R^3	Conditions	**I + II**	**I:II**
H	H	H	A	(78)	10:1
H	H	H	B	(85)	3.3:1
H	H	H	C	(81)	4.5:1
H	Me	H	A	(94)	38:1
H	Me	H	B	(96)	3.2:1
H	Me	H	C	(99)	4.2:1
H	Me	H	D	(96)	20:1
Me	Me	H	A	(85)	17.5:1
Me	Me	H	C	(83)	2.3:1
H	H	Bz	B	(99)	3.9:1
H	H	Bz	D	(98)	21:1
H	Me	Bz	B	(97)	4.3:1
H	Me	Bz	D	(92)	10:1
Me	Me	Bz	A	(99)	9:1
Me	Me	Bz	B	(98)	3.1:1
Me	Me	Bz	D	(98)	18:1

C_{10}

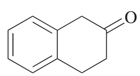


NaN_3, MsOH, 8°, 1 h

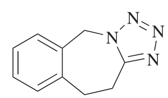


R	
H	(76)
O_2N	(84)

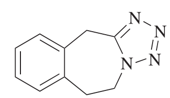
287



HN_3, BF_3•OEt_2, PhH, rt, 24 h



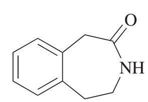
(21) +



(9)

396

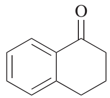
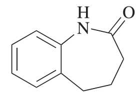
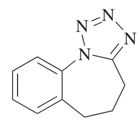
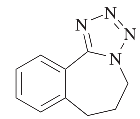
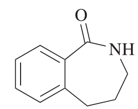
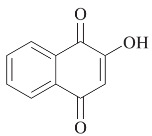
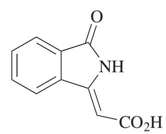
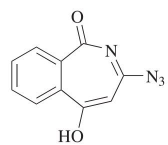
Azide, $FeCl_3$, DCE, rt



Azide	Time	
$TMSN_3$	46 min	(70)
NaN_3	2.5 h	(67)

286

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	NaN_3, CCl_3CO_2H,[b] 60°	 **I** (85)	1
	Azide, $FeCl_3$, DCE, rt	**I** Azide / Time: $TMSN_3$, 40 min (80); NaN_3, 2.5 h (75)	286
	HN_3, BF_3•OEt_2, PhH, rt, 24 h	**I** (5) +  **II** (33) +  **III** (2)	396
	NaN_3, HCl, 0° to rt, 4 h	**I** (42) + **III** (23) +  (13)	397
	NaN_3 (1.3 eq), H_2SO_4, 5° to rt, 2 h	 (80)	398
	NaN_3 (10 eq), H_2SO_4, 0°, 15 min	 (69)	398

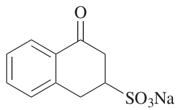
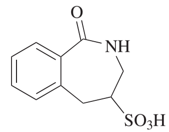
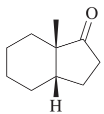
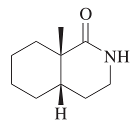
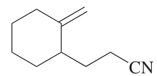
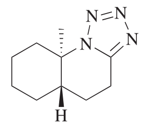
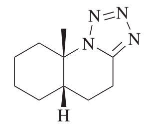
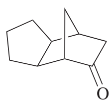
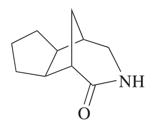
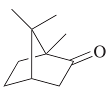
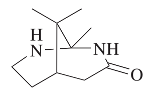
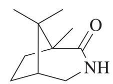
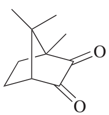
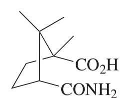
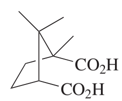
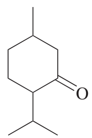
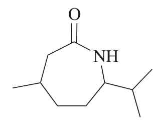
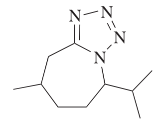
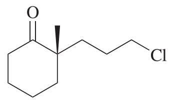
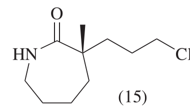
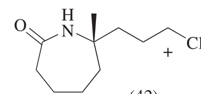
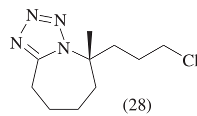
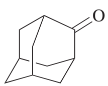
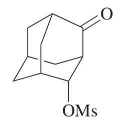
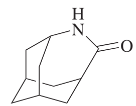
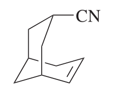
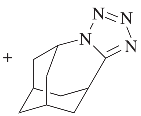
	HN_3	 (—)	399
	HN_3, H_2SO_4, PhH, 0°, 20 min	 (—) +  (—) +  (—) +  (—)	400
	NaN_3, H_2SO_4, 0°	 (—)	366
	NaN_3, H_2SO_4, $CHCl_3$, 30–50°, 7 h	 **I** (40) +  (5)	401
	NaN_3, H_2SO_4, $CHCl_3$	**I** (30)[c]	77
	NaN_3, H_2SO_4, $CHCl_3$, 0°, 3 h	 (57) +  (14)	402

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	NaN_3, H_2SO_4, rt, 50 h	 (70) +  (16)	55
	NaN_3, TFA, H_2O	 (15) +  (42) +  (28)	29
	NaN_3	 **I** +  **II** +  **III** +  **IV**	

Conditions	**I**	**II**	**III**	**IV**	Refs.
MsOH, rt, 50 h	(88)	(11)	(0)	(0)	403
MsOH, AcOH, rt, 50 h	(3)	(33)	(61)	(0)	403
TFA, rt, 3 h	(0)	(60)	(40)	(0)	403
MsOH, $CHCl_3$, rt, 20 h	(36)	(34)	(10)	(8)	403
MsOH, AcOH, 24 h	(0)	(70)	(30)	(0)	403
AcOH, *p*-TsOH	(0)	(31)	(0)	(0)	404

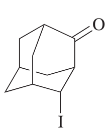
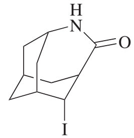
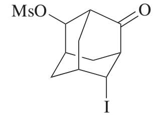
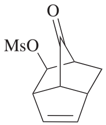
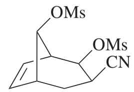
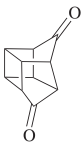
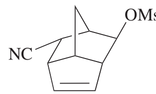
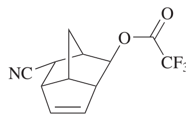
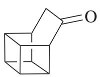
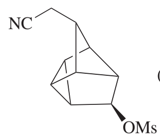
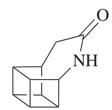
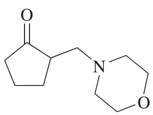
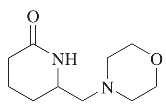
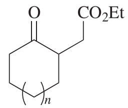
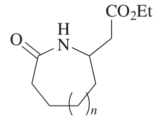
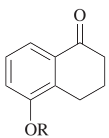
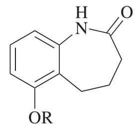
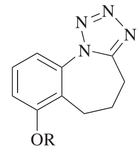
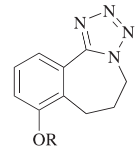
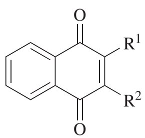
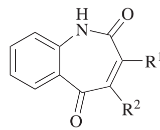
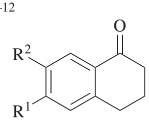
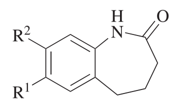
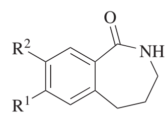
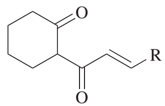
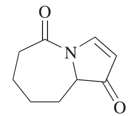
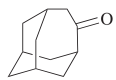
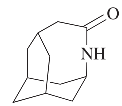
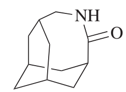
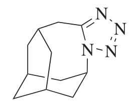
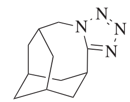
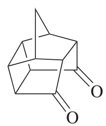
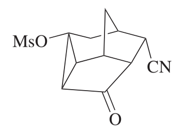
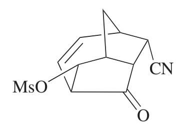
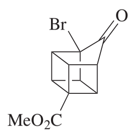
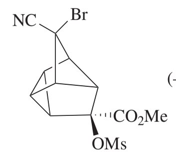
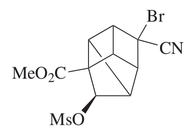
	NaN_3, MsOH, rt, 1 h	 (15) +  (6)	405
	NaN_3, MsOH	 (40)	390
	NaN_3, MsOH, 0°, 1 h	 (45)	406
	NaN_3, TFA, 0°, 1 h	 (—)	406
	NaN_3, MsOH, CH_2Cl_2, 0°, 15 min	 (60) +  (32)	407
	NaN_3, H_2SO_4, 0° to rt, 5 h	 (20)	408

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10-11}			
	NaN_3, H_2SO_4, 0°, 10 h	 *n* 1 (74) 2 (80)	409
	NaN_3, CCl_3CO_2H,[b] reflux, 6 h	 **I** +  **II** +  **III** R / **I** / **II + III** H (59) (11) Me (55) (6)	410
	NaN_3, H_2SO_4, rt	 R^1 R^2 H Cl (22) Cl Cl (49) Cl Br (12) H Me (50)	411
C_{10-12}			
	A: NaN_3, H_2SO_4, PhH, 60° B: NaN_3, CCl_3CO_2H,[b] 65°	 **I** +  **II** **I + II** (—)	59

R^1	R^2	Conditions	**I**:**II**
H	H	A	4:1
H	H	B	7:3
H_2N	H	A	4:1
H_2N	H	B	4:1
H	H_2N	A	9:1
H	H_2N	B	3:2
HO	H	A	3:2
HO	H	B	2:3
H	HO	A	4:1
H	HO	B	7:3
Cl	H	A	9:1
Cl	H	B	3:2
H	Cl	A	4:1
H	Cl	B	7:3
O_2N	H	A	9:1
O_2N	H	B	4:1
H	O_2N	A	9:1
H	O_2N	B	9:1
MeO	H	A	1:1
MeO	H	B	1:1
H	MeO	A	4:1
H	MeO	B	7:3
AcHN	H	A	9:1
AcHN	H	B	2:3
H	AcHN	A	9:1
H	AcHN	B	7:3
AcO	H	A	—
AcO	H	B	7:3
H	AcO	A	—
H	AcO	B	7:3

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10-16} 	NaN_3 (2 eq), H_2SO_4	 + RNH_2 (—) R: Me (76); Ph (76); 4-$O_2NC_6H_4$ (82); 4-$MeOC_6H_4$ (70)	412
C_{11} 	NaN_3, MsOH, rt, 24 h	 **I** +  **II** +  **III** +  **IV** **I** + **II** (7), **I**:**II** = 1:1 **III** + **IV** (48), **III**:**IV** = 1:1	413
	NaN_3, MsOH, CH_2Cl_2, 0°, 2 h	 (15) +  (10)	414
	NaN_3, MsOH, 0°, 10 min	 (—) +  (—)	81

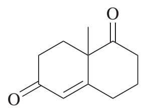
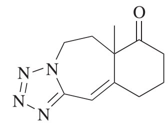
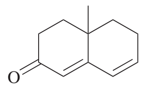
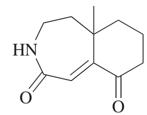
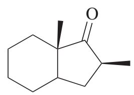
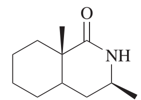
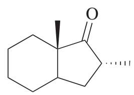
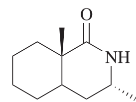
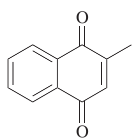
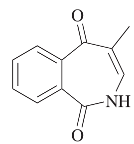
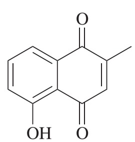
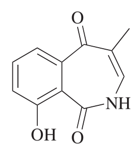
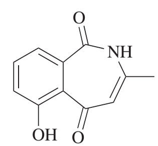
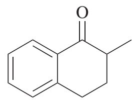
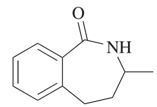
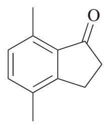
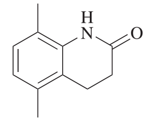
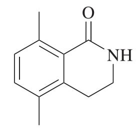
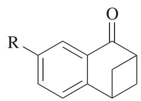
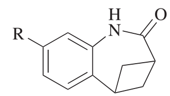
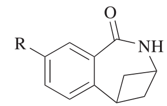
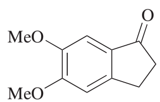
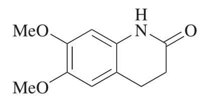
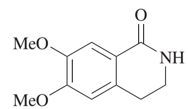
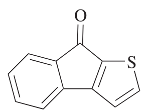
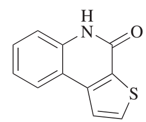
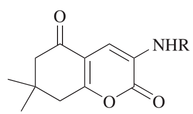
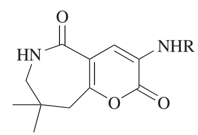
	NaN_3 (2 eq), HCl (concd), rt, 1 h	 (35)	415
	NaN_3, PPA, rt, 4 h	 (20)	416
	NaN_3, H_2SO_4, PhH, 0°, 30 min	 (27)	119
	NaN_3, H_2SO_4, PhH, 0°, 30 min	 (31)	119
	NaN_3, H_2SO_4, 0°, 1 h	 (85)	71
	NaN_3, H_2SO_4, 0°, 1 h	 (56) +  (10)	417

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	NaN_3, HCl, 0° to rt, 4 h	 (34)	397
	NaN_3, PPA, 60°	 (24) +  (41)	387
	NaN_3, H_2SO_4, PhH, 60°, 12 h	 **I** +  **II** R / **I** / **II** H (68) (23) H_2N (56) (24) O_2N (64) (16)	418
	$TMSN_3$, MsOH, MsCl, <0°	 **I** +  **II** **I** + **II** (90), **I**:**II** = 1:1	384
	HN_3, CCl_3CO_2H, H_2SO_4, 55°	 (—)	419
	NaN_3, H_2SO_4, $CHCl_3$, 0° to rt, 4 h	 R H (71) PhCO (91)	420

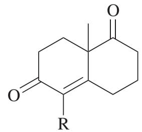
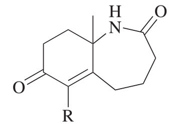
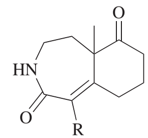
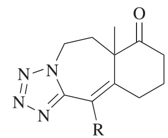
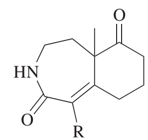
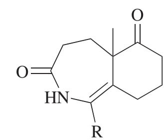
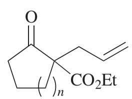
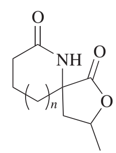
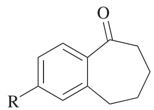
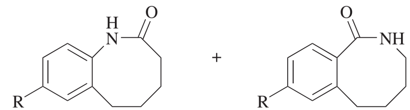
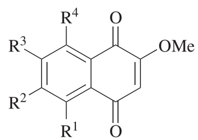
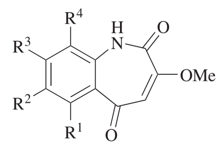
C_{11-12} 	NaN_3 (2 eq), H_2SO_4, 5°, 1 h	 R: H (46), Me (35)	415
	NaN_3 (1 eq), HCl (concd), rt, 45 min	 R: H (47), Me (25)	415
	NaN_3 (2 eq), HCl (concd), rt, 1 h	 (35)	415
	NaN_3 (3 eq), CCl_3CO_2H,[b] 60°, 2.5 h	 **I** +  **II** R / **I** / **II**: H (0) (20); Me (6) (0)	415
	NaN_3, H_2SO_4, $CHCl_3$, rt, 1 h	 *n*: 1 (65); 2 (60)	415a

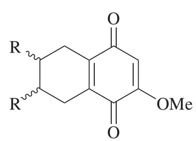
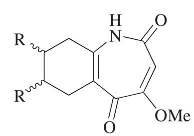
TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11-12}			
	A: NaN_3, H_2SO_4, PhH, 60° B: NaN_3, CCl_3CO_2H,[b] 65° C: NaN_3, HCl, DME, rt D: NaN_3, concd HCl	 **I** + **II**	

R	Conditions	**I + II**	**I:II**	Refs.
H	A	(—)	4:1	59
H	B	(—)	4:1	59
H	C	(83)	1:0	421
H	D	(89)	1:0	422
MeO	A	(—)	4:1	59
MeO	B	(—)	4:1	59

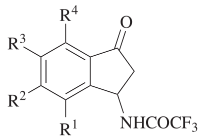
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11-13}			
	NaN_3, H_2SO_4, 0° to rt, 24 h		423

R^1	R^2	R^3	R^4
H	H	H	H
H	H	H	Me
Me	H	H	H
H	Me	H	Me
H	Me	Me	H
Me	H	H	Me
Me	H	Me	H
Me	Me	H	H

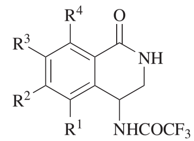
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	NaN_3, H_2SO_4, rt, 16 h		424

R	
H	(19)
Cl	(16)
Me	(6)

C$_{11-14}$

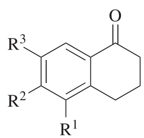


NaN$_3$, TFA, reflux, 5 h

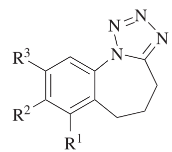


R^1	R^2	R^3	R^4	
H	H	H	H	(62)
H	F	H	H	(67)
H	H	F	H	(56)
Br	H	H	H	(69)
Cl	Cl	H	H	(73)
Me	H	H	H	(69)
H	Me	H	H	(66)
H	H	Me	H	(54)
Me	H	Me	H	(71)
H	H	Et	H	(59)
H	H	*i*-Pr	H	(64)

425



NaN$_3$, BF$_3$•OEt$_2$, PhH, rt, 24 h

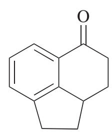


(50–70)

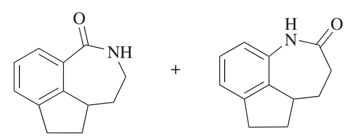
R^1	R^2	R^3
H	H	MeO
H	MeO	MeO
H	MeO	EtO
H	EtO	MeO
H	EtO	EtO

396

C$_{12}$



NaN$_3$, PPA, 80°, 5 h

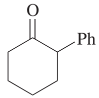
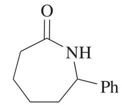
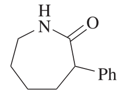
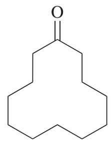
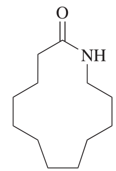
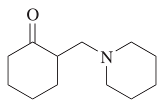
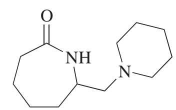
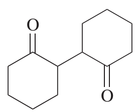
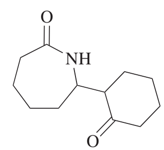


I + **II**

I + II (54), **I**:**II** = 1:1.5

426

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}			
	A: NaN_3, PPA, rt, 18 h B: NaN_3, PPA, rt to 55° C: NaN_3, H_2SO_4, $CHCl_3$, 0°, 3 h D: NaN_3, PPA, 0°, 3 h E: NaN_3, H_2SO_4, Et_2O, rt, 3 h F: NaN_3, H_2SO_4, PhH, rt, 3 h	 **I** +  **II** Conditions / **I + II** / **I:II** A (40) 1:10 B (30) 1:3 C (60) 1:2 D (40) 0:100 E (15) 1.3:1 F (15) 100:0	 368 368 296 296 296 296
	A: NaN_3, silica sulfuric acid,[a] 60°, 30 min B: NaN_3, P_2O_5, MW, 7 min C: NaN_3, $Fe(HSO_4)_3$, grinding, 50°, 30 min	 **I** Conditions A (95) B (75) C (94)	 282 289 288
	Azide, $FeCl_3$, DCE, rt	**I** Azide / Time $TMSN_3$ 65 min (81) NaN_3 4 h (65)	286
	NaN_3, HCl (concd), rt	 (63)	333
	NaN_3, PPA, 15° to rt, 15 h	 (29)	427

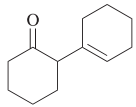
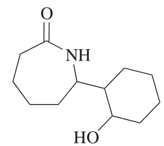
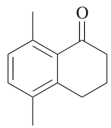
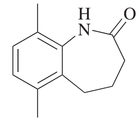
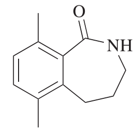
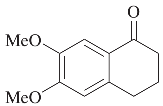
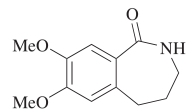
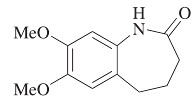
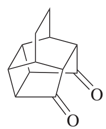
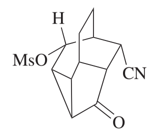
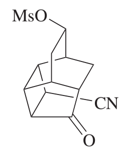
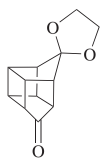
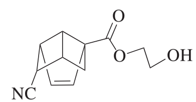
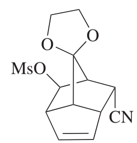
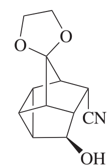
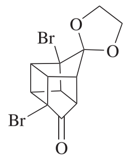
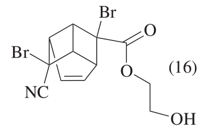
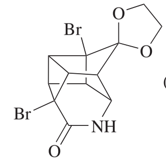
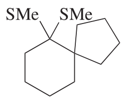
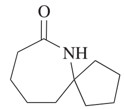
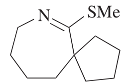
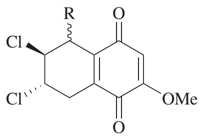
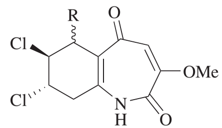
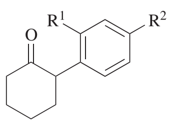
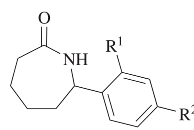
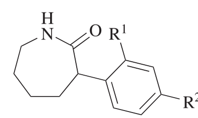
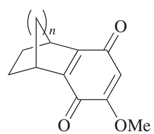
	NaN_3, PPA, 15° to rt, 15 h	 (60)	428
	NaN_3, PPA, 60°	 (43) +  (19)	387
	NaN_3, HCl (concd), 0° to rt, 12 h	 (69) +  (26)	429
	NaN_3, MsOH, CH_2Cl_2, 0°, 30 min	 (45) +  (15)	430
	NaN_3, MsOH, 0°, 1 h	 (16) +  (10) +  (5)	431

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

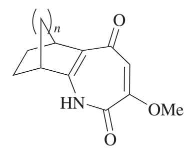
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}			
	NaN_3, MsOH, 0°, 1 h	 (16) +  (20)	431
	1. IN_3, CH_2Cl_2, –78 to –10°, 2 h 2. TFA, $CHCl_3$, rt, 2 h	 (47)	83
	$TMSN_3$, $SnCl_4$, I_2, CH_2Cl_2, –78°, 2.5 h	 (41)	83
$C_{12–13}$			
	NaN_3, TFA, 0° to rt, 2.5 h	 R: Me (31); Et (41)	424
	A: NaN_3, PPA, 0°, 6 h B: NaN_3, H_2SO_4, PhH, rt, 6 h C: NaN_3, H_2SO_4, Et_2O, 0°, 6 h	 **I** +  **II**	296

Conditions	R^1	R^2	**I**	**II**
A	H	H	(60)	(—)
B	H	H	(—)	(40)
C	H	H	(—)	(30)
A	H	O_2N	(16)	(64)
B	H	O_2N	(25)	(45)
C	H	O_2N	(—)	(65)
A	O_2N	H	(17)	(68)
B	O_2N	H	(28)	(47)
C	O_2N	H	(39)	(31)
A	O_2N	O_2N	(—)	(55)
B	O_2N	O_2N	(—)	(80)
C	O_2N	O_2N	(—)	(42)
A	H	Me	(10)	(—)
B	H	Me	(40)	(5)
C	H	Me	(15)	(15)
A	H	MeO	(10)	(—)
B	H	MeO	(5)	(—)
C	H	MeO	(11)	(4)

C_{12-13}

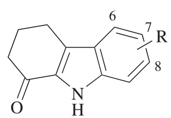


NaN_3, H_2SO_4, 0°, 2 min

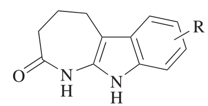


n	
1	(1.4)
2	(31)

424



NaN_3, PPA, 100°, 8 h



R	
H	(45)
6-Cl	(57)
6-Me	(49)
7-Me	(44)
8-Me	(58)

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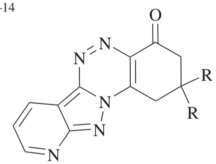
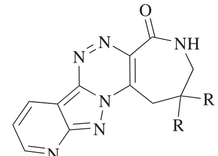
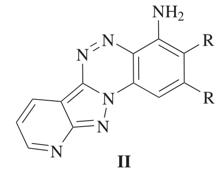
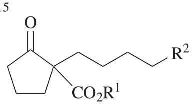
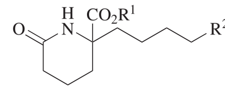
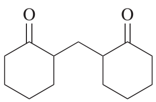
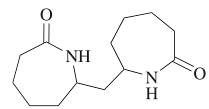
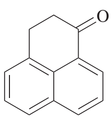
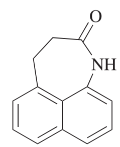
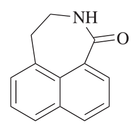
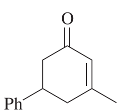
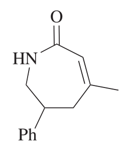
TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12-14} 	NaN_3, H_2SO_4, $CHCl_3$, rt, 3 h	 **I** +  **II** R / **I** / **II** H / (16) / (13) Me / (6) / (17)	433
C_{12-15} 	NaN_3, H_2SO_4, $CHCl_3$	 R^1 / R^2 Me / NC– / (48) Et / EtO_2C / (87)	434
C_{13} 	A: NaN_3, HCl, 0°, 30 min B: NaN_3, PPA, rt, 24 h	 Conditions A (57) B (80)	435
	NaN_3, H_2SO_4, 0°	 (37) +  (—)	436
	NaN_3, PPA, 0–55°, 7 h	 (30)	368

C_{13}

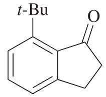
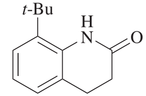
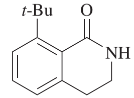
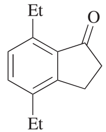
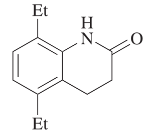
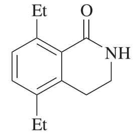
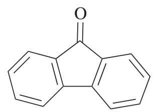
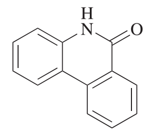
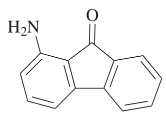
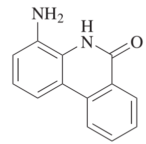
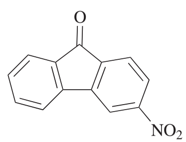
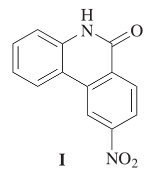
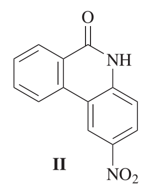
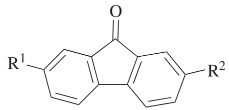
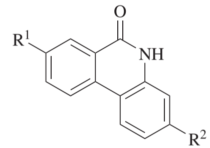
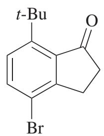
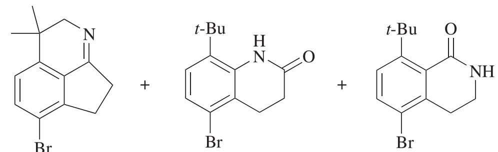
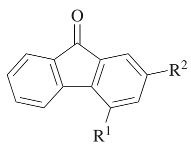
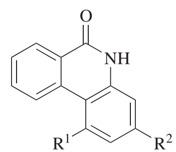
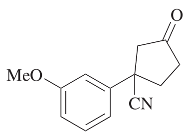
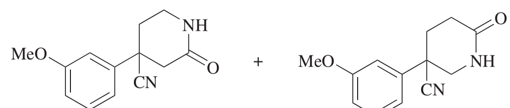
	NaN_3, PPA	 (5) +  (20)	437
	NaN_3, PPA, 60°	 (10) +  (25)	387
	A: NaN_3, PPA, 70°, 22 h B: NaN_3, CCl_3CO_2H,[b] 60° C: NaN_3, H_2SO_4	 Conditions: A (92); B (55); C (99)	54 1 1
	NaN_3, H_2SO_4	 (80)	438
	NaN_3, H_2SO_4, $CHCl_3$	 **I** +  **II** **I + II** (98), **I**:**II** = 7:3	439

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}			
	NaN_3, H_2SO_4, 0° to rt, 24 h	 R^1 / R^2 Cl / H_2N (61) Cl / O_2N (80) Br / H_2N (55) Br / O_2N (100)	440
	NaN_3, PPA, 50°, 9 h	 (20) + **I** + **II** **I** + **II** (47), **I**:**II** = 85:15	387
	NaN_3, H_2SO_4, 0° to rt, 48 h	 R^1 / R^2 H_2N / H (99) O_2N / H (96) Cl / O_2N (71)	440
	NaN_3, CCl_3CO_2H[b]	 **I** + **II** **I** + **II** (—), **I**:**II** = 2:3	441
	NaN_3, 80% H_2SO_4, PhH	**I** + **II** (—), **I**:**II** = 100:0	441

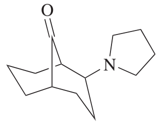
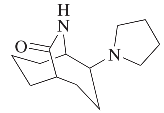
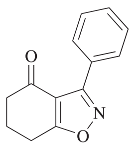
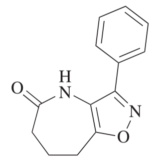
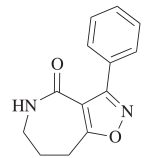
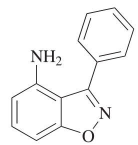
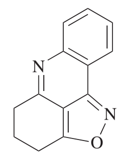
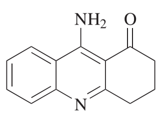
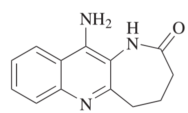
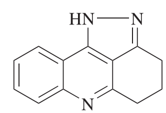
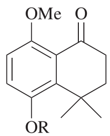
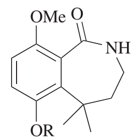
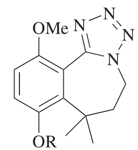
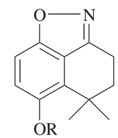
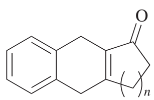
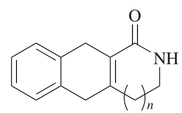
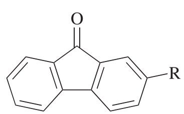
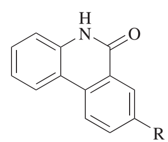
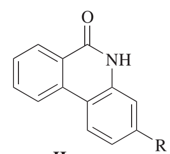
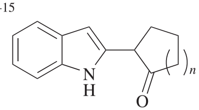
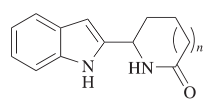
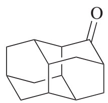
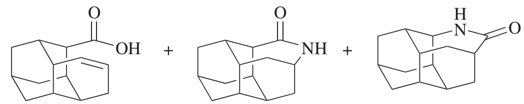
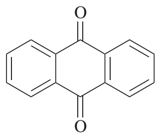
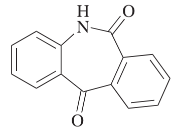
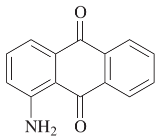
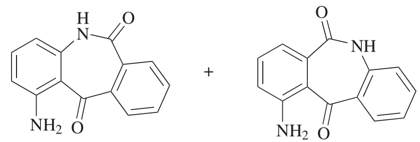
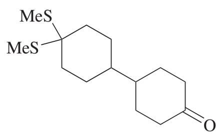
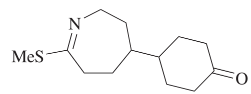
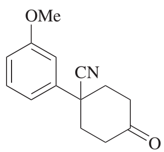
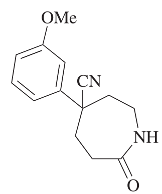
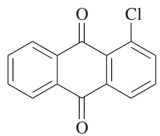
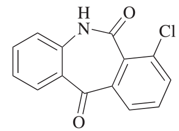
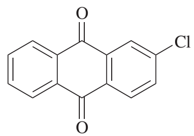
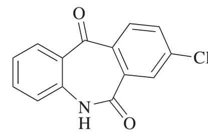
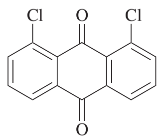
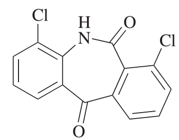
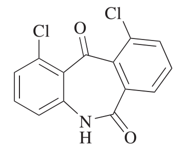
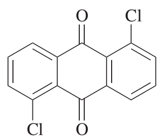
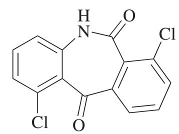
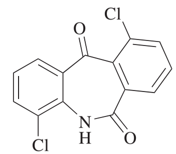
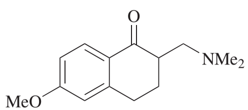
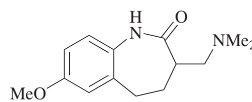
	NaN_3, 98% H_2SO_4, PhH	**I** + **II** (—), **I**:**II** = 2:3	441
	NaN_3, 98% H_2SO_4, $CHCl_3$	**I** + **II** (—), **I**:**II** = 100:0	441
	NaN_3, PPA	**I** + **II** (—), **I**:**II** = 1:1	441
	NaN_3, H_2SO_4, $CHCl_3$, 50°, 1 h	 (56)	442
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 3 h	 (31) +  (4) +  (30) +  (2)	443
	NaN_3, H_2SO_4, $CHCl_3$, rt, 8 h	 (60) +  (16)	444

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13-14}			
	NaN_3, H_2SO_4, $CHCl_3$, 70°, 8 h	 **I** +  **II** +  **III** R / **I** / **II** / **III** H / (36) / (28) / (0) Me / (51) / (18) / (8)	445
	NaN_3, PPA, 100°, 3 h	 *n* / 1 / (65) 2 / (58)	446
	NaN_3, H_2SO_4, $CHCl_3$, rt, 1 h	 **I** +  **II** R / **I + II** / **I:II** O_2N / (—) / 1:1 MeO / (—) / 19:1	439
C_{13-15}			
	NaN_3, H_2SO_4, $CHCl_3$, rt	 *n* / 1 / (62) 2 / (57) 3 / (48)	341

C_{14} 	NaN_3, MsOH, rt, 2.5 h	 (41) **I** **I + II** (50) **II**	447
	NaN_3, H_2SO_4	 (77)	450
	NaN_3, H_2SO_4, rt, 4 h	 **I** **II** **I + II** (80), **I**:**II** = 35:65	448
	$TMSN_3$, $SnCl_4$, I_2, CH_2Cl_2, –78° to rt, 2.5 h	 (90)	83
	NaN_3, CCl_3CO_2H,[b] 60°, 4 h	 (88)	449

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (10) + isomers (4)	450
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (8) + isomers (8)	450
	NaN_3, H_2SO_4, 50°, 4 h	 **I** +  **II** **I** + **II** (90)	451
	NaN_3, H_2SO_4, 50°, 4 h	 **I** +  **II** **I** + **II** (95)	451
	NaN_3, H_2SO_4, rt, 16 h	 (55)	62

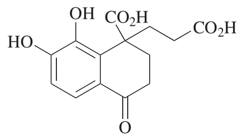
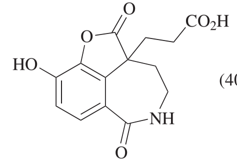
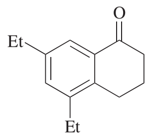
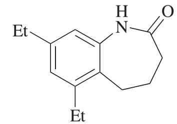
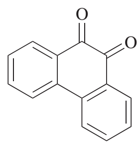
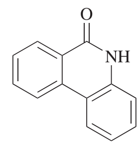
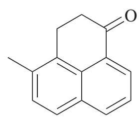
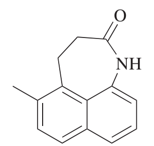
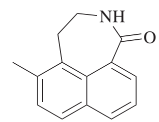
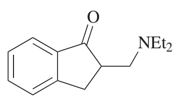
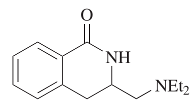
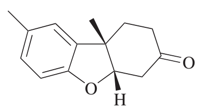
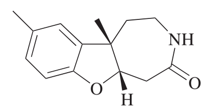
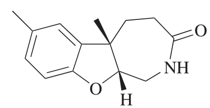
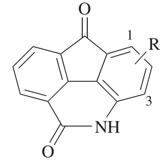
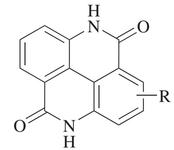
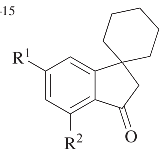
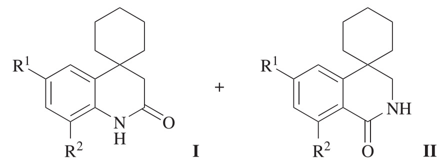
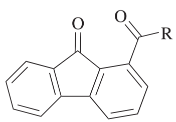
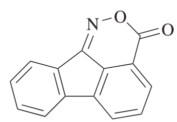
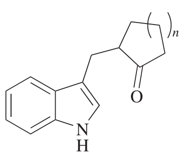
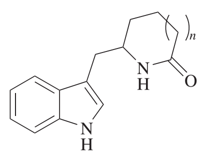
	NaN_3, PPA, 60°, 6 h	 (40)	452
	NaN_3, H_2SO_4	 (—)	12
	NaN_3, H_2SO_4, 0° to rt, 3 h	 (92)	453
	NaN_3, H_2SO_4, AcOH, 50°, 1 h	 (50) +  (6)	454
	NaN_3, HCl (concd)	 (—)	333
	NaN_3, PPA, 40°, 1 h	 (38) +  (56)	455

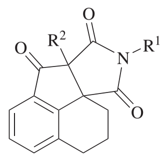
TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	NaN_3, H_2SO_4, 50°, 4 h	 R: H (86); 1-O_2N (—); 3-O_2N (—)	456
$C_{14–15}$ 	A: NaN_3, H_2SO_4, PhH, 60° B: NaN_3, CCl_3CO_2H,[b] 65°		

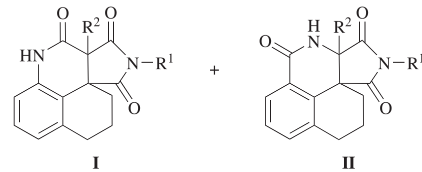
R^1	R^2	Conditions	**I + II**	**I:II**	Refs.
H	H	A	(83)	7:3	457
H	H	B	(—)	1:4	59
MeO	H	A	(78)	1:9	457
MeO	H	B	(—)	1:9	59
H	MeO	A	(66)	1:9	457
H	MeO	B	(—)	1:9	59

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	NaN_3, H_2SO_4	 R: HO (—); MeO (—)	458
	NaN_3, H_2SO_4, 0 to 50°, 5 h	 *n*: 1 (70); 2 (74)	459

C_{14-16}



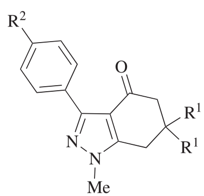
A: NaN_3, H_2SO_4, rt
B: NaN_3, PPA, 80°, 15 h



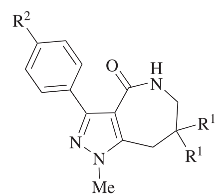
R^1	R^2	Conditions	I	II
H	H	A	(91)	(0)
H	H	B	(45)	(30)
Me	H	A	(87)	(0)
Me	H	B	(47)	(48)
Me	Me	A	(74)	(0)
Me	Me	B	(43)	(28)

460

C_{14-17}



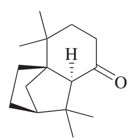
HN_3, H_2SO_4, PPA, rt, 0.5 h



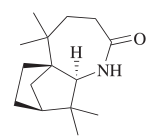
R^1	R^2	
H	H	(62)
H	Cl	(31)
Me	H	(61)
H	MeO	(26)
Me	Cl	(20)
Me	O_2N	(21)
Me	MeO	(27)

461

C_{15}

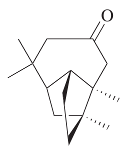
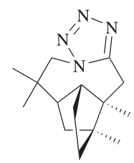
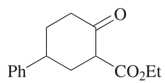
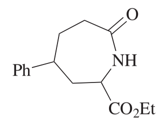
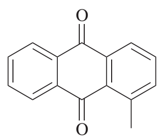
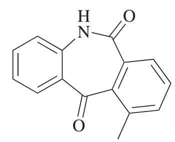
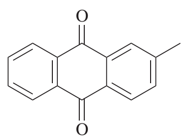
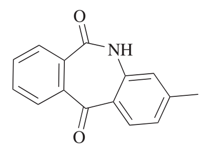
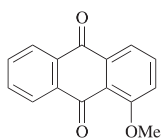
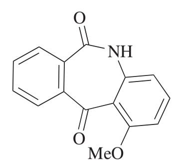


NaN_3, H_2SO_4, $CHCl_3$,
0°, 45 min


(32)

462

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	NaN_3, H_2SO_4, $CHCl_3$, 0°, 45 min	 (42)	462
	A: NaN_3, PPA, rt, 3 h B: NaN_3, H_2SO_4, $CHCl_3$, rt, 48 h	 Conditions: A (74); B (26)	463
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (19) + isomers (23)	450
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (20) + isomers (18)	450
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (63)	450

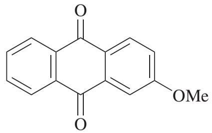
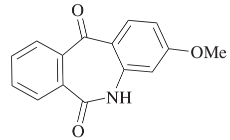
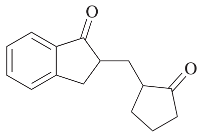
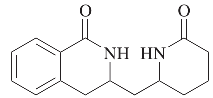
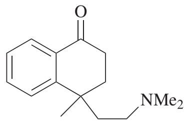
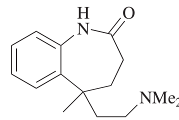
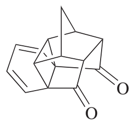
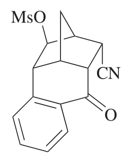
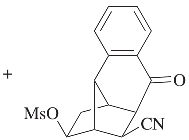
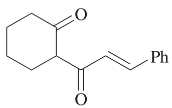
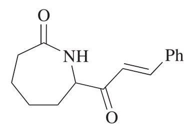
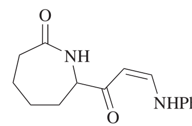
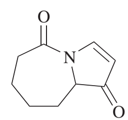
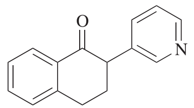
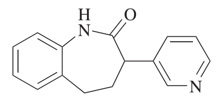
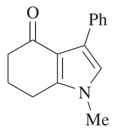
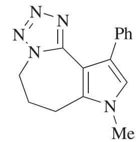
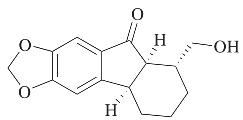
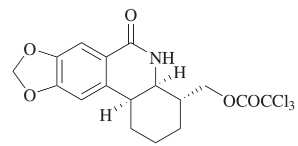
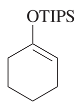
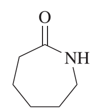
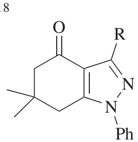
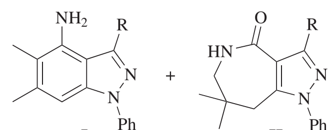
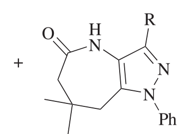
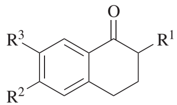
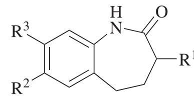
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (22) + isomers (5)	450
	NaN_3, H_2SO_4, $CHCl_3$, 0°, 1 h	 (58)	464
	NaN_3, PPA, 60°, 24 h	 (93)	58
	NaN_3, MsOH, 0°, 45 min	 (—) +  (—)	465
	NaN_3 (1 eq), H_2SO_4	 (50) +  (6) +  (5)	412

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	NaN_3, H_2SO_4, AcOH, 50°, 0.5 h; rt, 1 h	 (34)	466
	NaN_3, H_2SO_4, $CHCl_3$, rt, 30 min	 (34)	392
	NaN_3, CCl_3CO_2H,[b] 60°, 60 h	 (55)	467
	1. $TMSN_3$, Dowex, CH_2Cl_2, rt, 48 h 2. $h\nu$, c-C_6H_{12}, 0°, 3.5 h	 (83)	468
C_{15-18}			
	NaN_3, PPA, 60°, 12 h	 **I** + **II** +  **III** **I + II + III** (—) R / **I**:**II**:**III** H / 0:100:0 Me / 18:61:21 *i*-Pr / 17:67:16	469



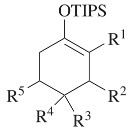
NaN$_3$, AcOH, 50°, 2 h



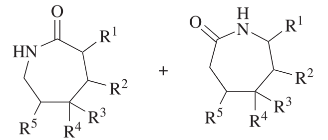
R^1	R^2	R^3	
3-C_5H_4N	H	H	(66)
Ph	Cl	H	(33)
Ph	MeO	MeO	(44)

470

C_{15-19}



1. TMSN$_3$, PPTS, CH$_2$Cl$_2$, rt, 2 d
2. *h*ν, *c*-C$_6$H$_{12}$, 0°, 1 h

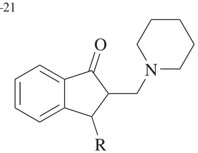


I + **II**

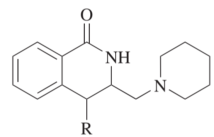
R^1	R^2	R^3	R^4	R^5	**I**	**II**
H	H	H	H	H	(69)	(0)
Me	H	H	H	H	(20)	(12)
H	H	H	H	Me	(36)	(36)
H	H	Me	H	H	(68)	(0)
H	H	Me	Me	H	(60)	(0)
H	H	–O(CH$_2$)$_2$O–		H	(77)	(0)
H	H	*t*-Bu	H	H	(63)	(0)

74

C_{15-21}



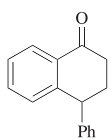
NaN$_3$, HCl



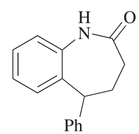
R	
H	(—)
Ph	(—)

333

C_{16}



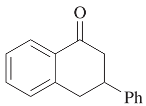
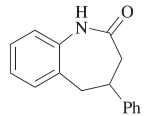
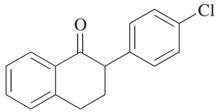
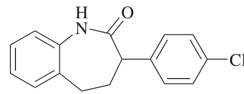
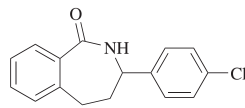
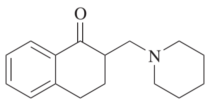
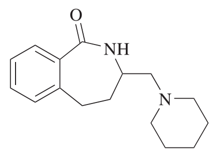
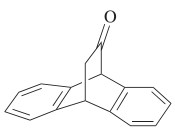
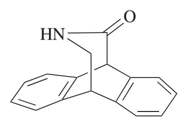
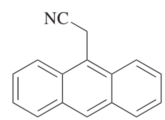
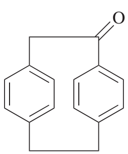
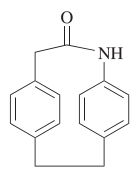
NaN$_3$, AcOH, 50°, 2 h

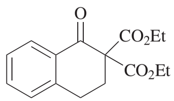
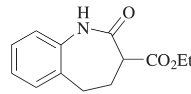
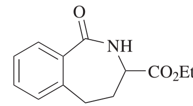
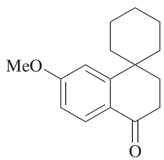
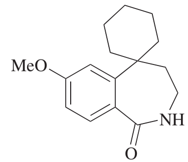
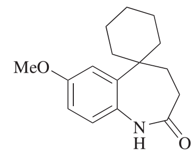
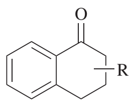
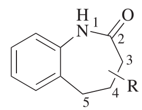
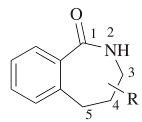
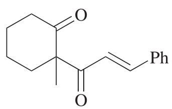
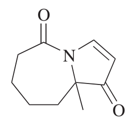
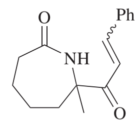
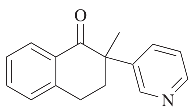
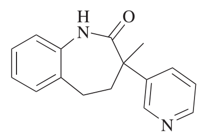


(84)

470

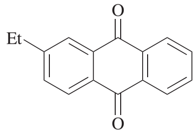
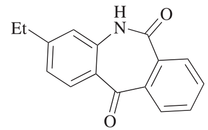
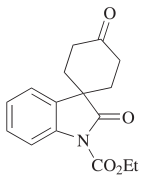
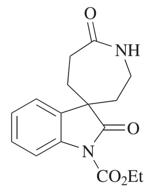
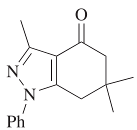
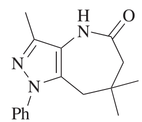
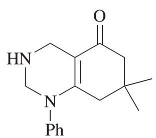
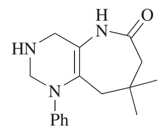
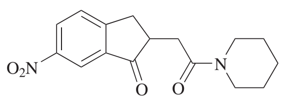
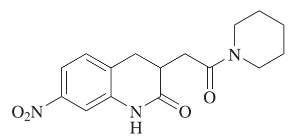
TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

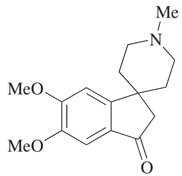
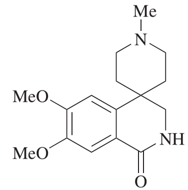
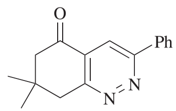
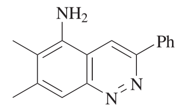
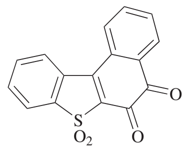
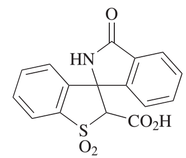
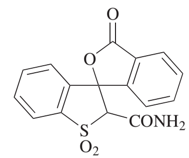
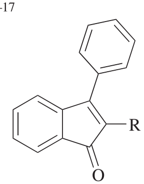
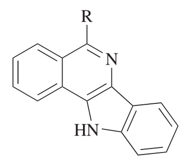
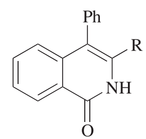
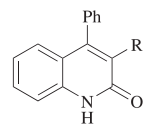
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16} 	NaN_3, H_2SO_4, AcOH, 50°, 45 min	 (61)	471
	NaN_3, AcOH, rt to 50°, 3 h	 (42) +  (—)	472
	NaN_3, HCl (concd)	 (—)	333
	NaN_3, CCl_3CO_2H,[b] 60°	 (10) +  (35)	473
	NaN_3, H_2SO_4, dioxane, 15–45°, 45 min	 (52)	474

	NaN_3, MsOH, $CHCl_3$, reflux, 36 h	 (50) +  (27)	397
	NaN_3, H_2SO_4, PhH, 60°, 8 h	 (28) +  (38)	457
	NaN_3, H_2SO_4, AcOH, rt to 50°, 4 h	 **I** +  **II**	475
	NaN_3 (2 eq), H_2SO_4	 (75) +  (*E*) + (*Z*) (traces)	412
	NaN_3, AcOH, 50°, 2 h	 (66)	470

R	**I + II**
3-Ph	(—)
4-Ph	(65)
5-Ph	(63)
3-(4-ClC_6H_4)	(47)

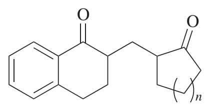
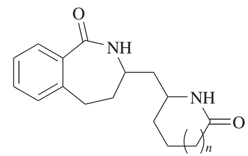
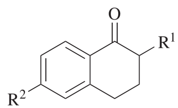
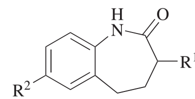
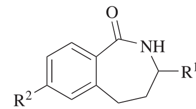
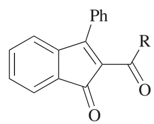
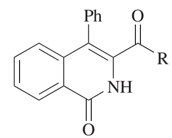
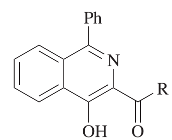
TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}			
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (22)	450
	NaN_3, H_2SO_4, $CHCl_3$, –10° to rt	 (90)	476
	NaN_3, PPA, 100°, 5 h	 (54)	477
	NaN_3, H_2SO_4, $CHCl_3$, 0° to rt, 5 h	 (70)	478
	NaN_3, H_2SO_4, PhH, 40°, 15 min	 (63)	479

	NaN_3, H_2SO_4, 60°, 45 min	 (79)	480
	NaN_3, H_2SO_4, rt, 2 h	 (75)	481
	NaN_3, H_2SO_4, 45°, 30 min	 (80) +  (8)	482
C_{16-17}			
	HN_3	 R: Me (—); Et (—)	61
	NaN_3, AcOH, 50°, 1 h	 **I** +  **II**	483

R	**I + II**	**I:II**
Me	(60)	1:3
NC–	(60)	3:1
Et	(70)	0:100

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16-17}			
	NaN_3, H_2SO_4, rt to 55°, 4.5 h	 *n*: 1 (82); 2 (63)	464
	NaN_3, H_2SO_4, AcOH, 50°, 2 h	 **I** +  **II**	470
		R^1 / R^2 / **I** / **II**: H / n-C_6H_{13} / (45) / (38); Ph / MeO / (36) / (25)	
C_{16-18}			
	NaN_3, AcOH, rt, 1 h	 R: H_2N (40); EtO (30)	484
	NaN_3, H_2SO_4, rt, 1 h	 R: H_2N (50); EtO (40)	484

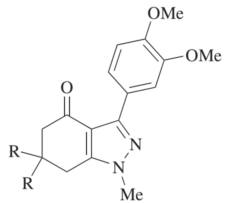
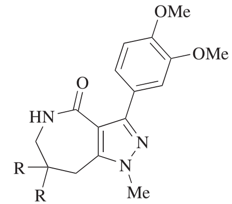
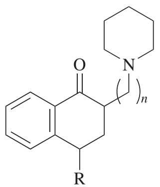
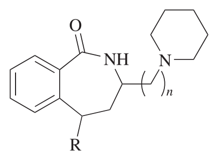
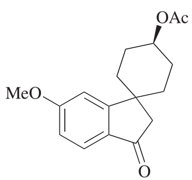
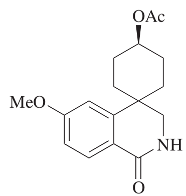
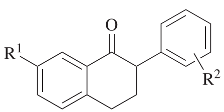
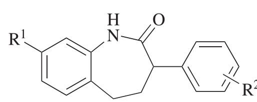
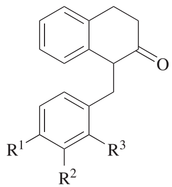
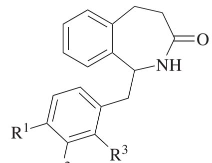
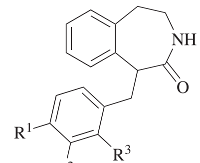
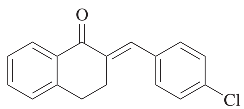
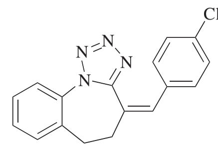
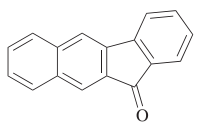
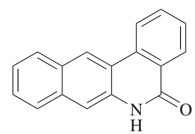
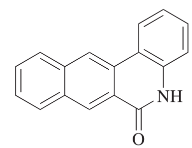
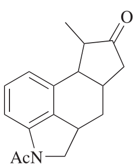
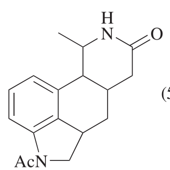
	NaN_3, H_2SO_4, PPA, $CHCl_3$, rt, 30 min		R / H (48) / Me (39)	461
C_{16-22}				
	NaN_3, HCl		*n* R / 1 H (95) / 2 H (—) / 1 Ph (73)	333
C_{17}				
	NaN_3, CCl_3CO_2H,[b] 60°, 6.5 h		(76)	485
	NaN_3, AcOH, 50°, 1 h		R^1 R^2 / H 3-CF_3 (12) / H 4-CF_3 (35) / MeO H (40)	466

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17} 	NaN_3, PPA, 40°, 5 h	 **I** +  **II** R^1 / R^2 / R^3 / **I** / **II** H / H / H / (20) / (—) Cl / H / H / (47) / (—) H / H / O_2N / (30) / (—)	461
	NaN_3, $SiCl_4$, MeCN, rt, 18 h	 (80)	70
	NaN_3, H_2SO_4, CCl_3CO_2H,[b] 100°, 4 h	 (23) +  (21)	486
	NaN_3, H_2SO_4, AcOH, 40°	 (56)	487

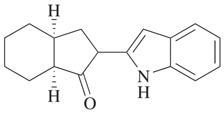
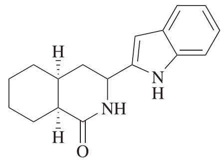
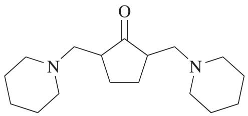
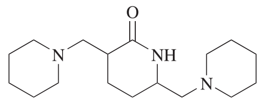
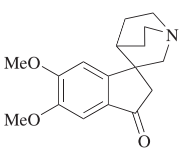
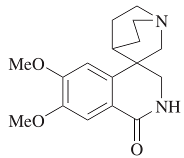
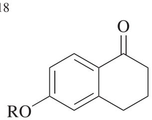
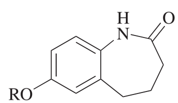
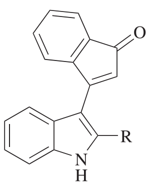
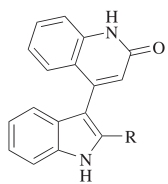
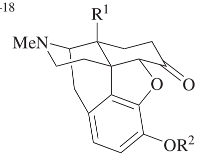
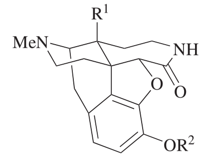
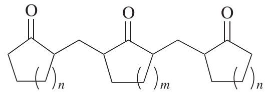
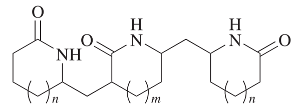
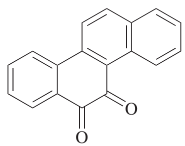
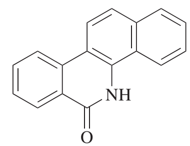
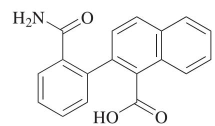
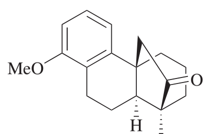
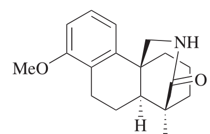
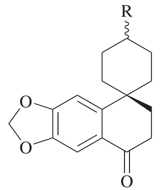
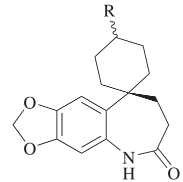
		NaN_3, HCl, H_2SO_4, $CHCl_3$, 0°, 4 h	 (60)	488
		NaN_3, H_2SO_4, 0° to rt, 5 h	 (45)	408
		NaN_3, H_2SO_4, 60°, 45 min	 (90)	480
C_{17-18}		NaN_3, H_2SO_4	 R: Bn (71); n-C_8H_{17} (62)	489
		NaN_3, H_2SO_4, $CHCl_3$, 0–50°, rt	 R: H (72); Me (69)	490

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17-18} 	NaN_3, PPA, 65°	 R^1 / R^2: H / H (40); H / Me (52); HO / Me (23)	491
C_{17-20} 	NaN_3, H_2SO_4, 0 to 55°, 5 h	 *n* / *m*: 1 / 1 (70); 1 / 2 (59); 2 / 1 (66); 2 / 2 (63)	492
C_{18} 	NaN_3, H_2SO_4	 (100)	262
	NaN_3, H_2SO_4, 50°, 1 h	 (70)	262
	NaN_3, H_2SO_4, $CHCl_3$, –10°, 1 h	 (14)	493

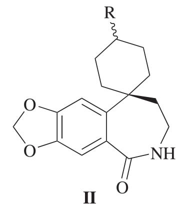


NaN$_3$, CCl$_3$CO$_2$H[b]



I

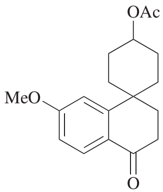
+



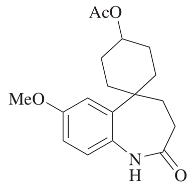
II

494

R	**I + II**	**I:II**
α-OAc	(48)	1:1
β-OAc	(59)	1:1

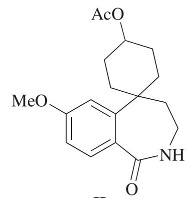


NaN$_3$, CCl$_3$CO$_2$H,[b] 60°, 4 h



I

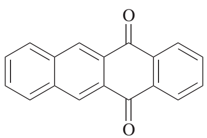
+



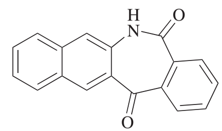
II

I + II (80), **I**:**II** = 2:3

495

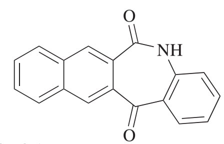


NaN$_3$, H$_2$SO$_4$, rt, 24 h



I

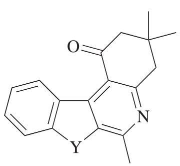
+



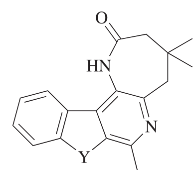
I

I + II (85), **I**:**II** = 9:1

496

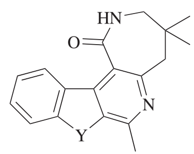


NaN$_3$, H$_2$SO$_4$, rt, 24 h



I

+

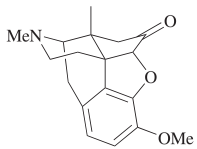
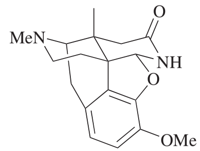
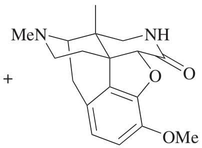
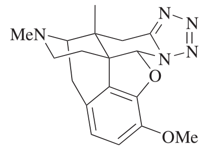
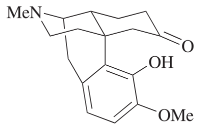
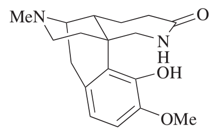
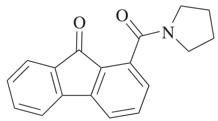
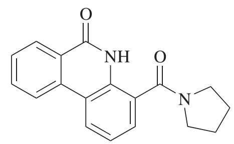
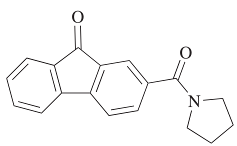
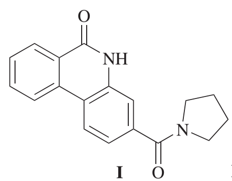
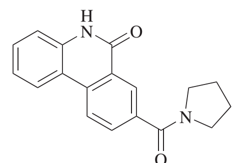


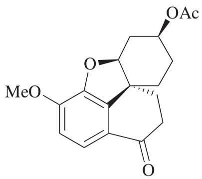
II (—)

Y	**I**
HN	(82)
S	(80)

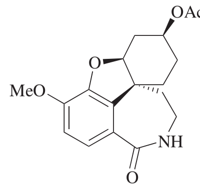
497

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

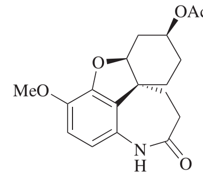
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18} 	NaN_3, P_2O_5, MsOH, 65°, 24 h	 (9) +  (3) +  (15)	498
	NaN_3, PPA, 65°	 (16)	491
	NaN_3, H_2SO_4	 (—)	499
	NaN_3, H_2SO_4, $CHCl_3$, rt, 1 h	 **I** +  **II** **I + II** (72)	500



NaN$_3$, CCl$_3$CO$_2$H[b]

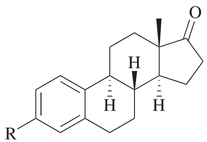


(38) +

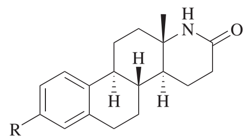


(34) 501

C$_{18-20}$

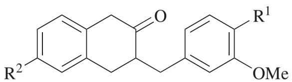


HN$_3$, H$_2$SO$_4$, PhH, rt

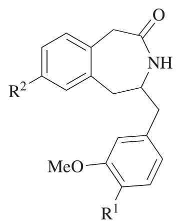


R	
HO	(—)
MeO	(—)
AcO	(—)

502

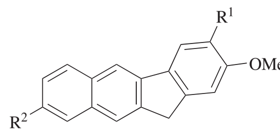


NaN$_3$, PPA, 70°, 2 h



I

+

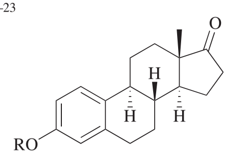
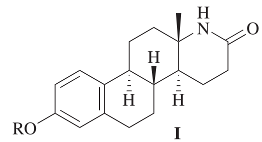
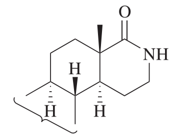
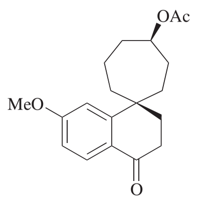
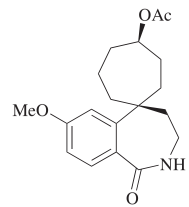
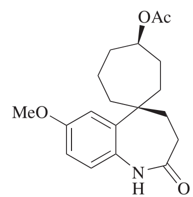
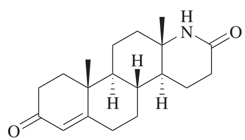
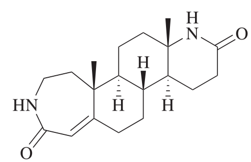


II

503

R^1	R^2	**I**	**II**
H	H	(23)	(—)
H	MeO	(45)	(—)
MeO	MeO	(44)	(—)

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18-23} 	A: NaN_3, PPA, 60°, 10 h B: HN_3, H_2SO_4, rt, 2 h	 **I** +  **II**	504
C_{19} 	NaN_3, CCl_3CO_2H,[b] 60°, 4 h	 **I** +  **II** **I + II** (79), **I:II** = 2:3	505
	NaN_3, PPA, 0°, 20 min	 (35)	506

R	Conditions	**I + II**	**I:II**
H	A	(—)	2:1
Me	A	(—)	1:0
Ac	A	(—)	1:0
c-C_5H_9	B	(—)	1:0

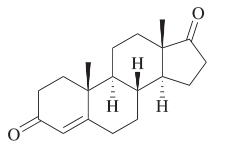
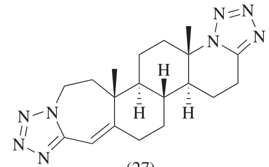
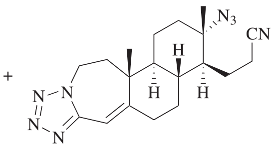
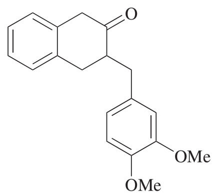
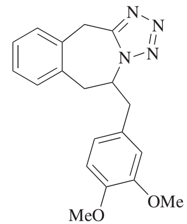
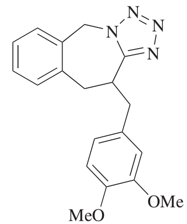
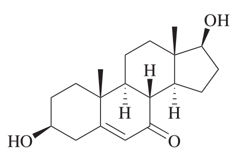
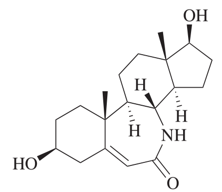
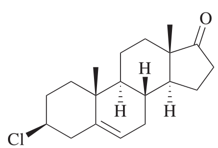
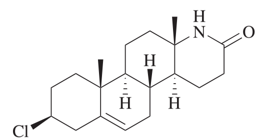
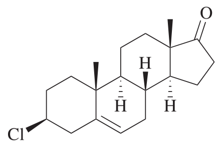
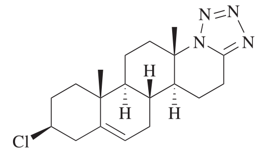
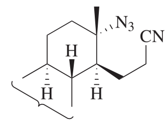
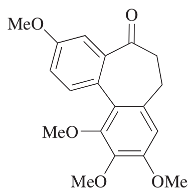
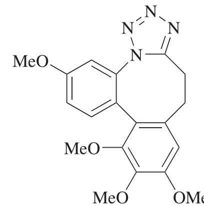
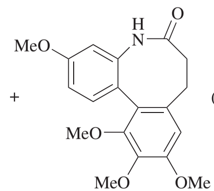
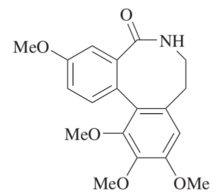
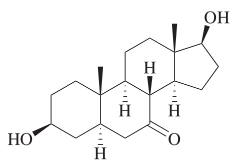
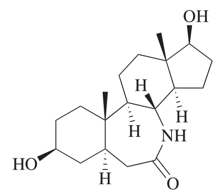
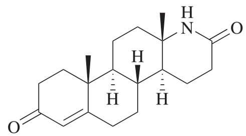
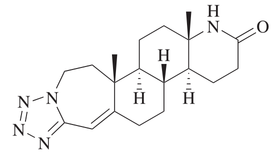
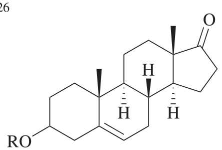
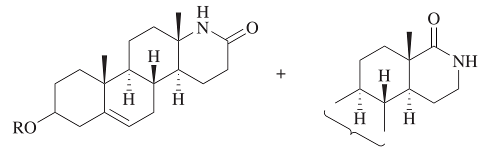
	HN_3, BF_3•OEt_2, $CHCl_3$	 (27) +  (7)	507
	NaN_3, $TiCl_4$, MeCN, reflux, 4 h	 **I** +  **II** **I** + **II** (46), **I**:**II** = 4:1	503
	NaN_3, PPA, 50°, 8 h	 (—)	508
	NaN_3, H_2SO_4, PhH, rt, 30 min	 (60)	34

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{19}			
	HN_3, BF_3•OEt_2, PhH, 0°, 5 h	 (—) +  (—)	34
	$TMSN_3$, TFA, rt, 24 h	 (68) +  (13) +  (5)	509
	NaN_3, PPA, 50°, 8 h	 (—)	508

	HN_3, BF_3•OEt_2, $CHCl_3$, 0° to rt, 24 h	 (30)	509a
$C_{19–26}$			
	NaN_3, H_2SO_4, $CHCl_3$, 10°	 **I** + **II**	510

R	**I**	**II**
H	(28)	(33)
Ac	(27)	(40)
Bz	(39)	(20)

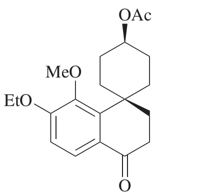
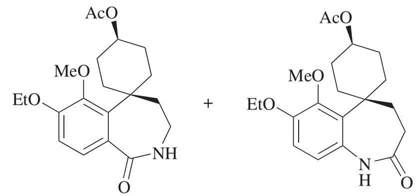
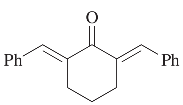
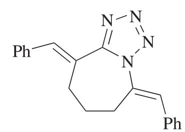
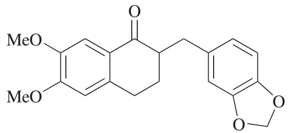
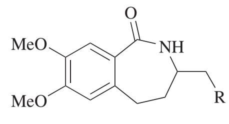
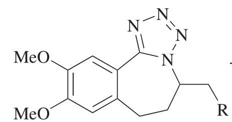
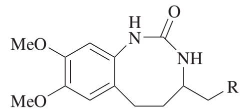
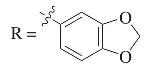
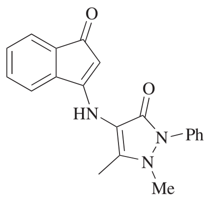
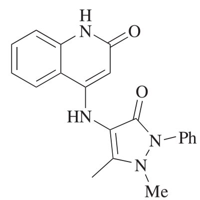
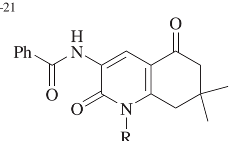
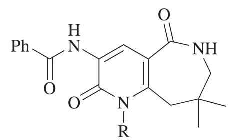
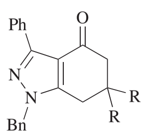
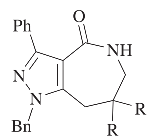
C_{20}			
	NaN_3, CCl_3CO_2H, PhH, 60°, 8 h	 **I** + **II** **I** + **II** (70), **I**:**II** = 2:3	511
	NaN_3, $SiCl_4$, MeCN, rt, 14 h	 (90)	70

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{20} 	NaN_3, CCl_3CO_2H,[b] 57°, 15 h	 (45) +  (12) +  (2) 	512
	NaN_3, H_2SO_4, $CHCl_3$, 0 to 50°, 5 h	 (73)	490
C_{20-21} 	NaN_3, H_2SO_4, $CHCl_3$, 0° to rt, 4 h	 R: HO_2CCH_2 (80); MeO_2CCH_2 (84)	420
C_{20-22} 	HN_3, H_2SO_4, $CHCl_3$, rt, 30 min	 R: H (10); Me (10)	461

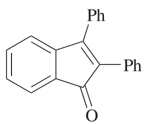
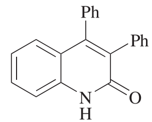
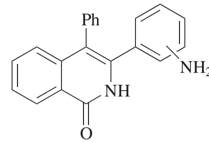
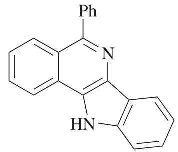
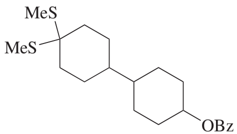
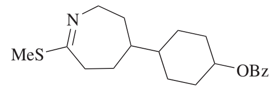
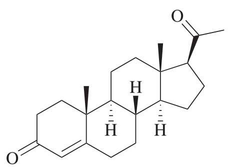
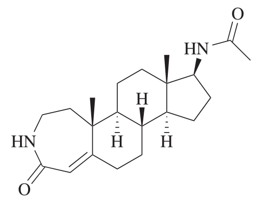
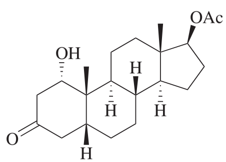
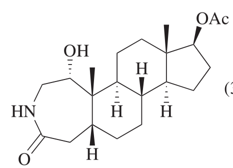
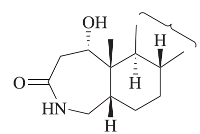
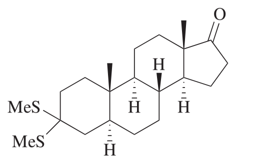
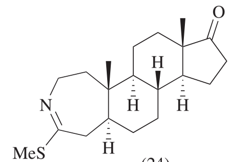
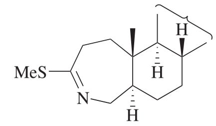
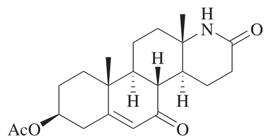
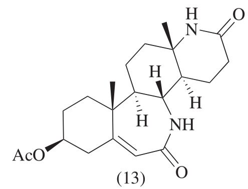
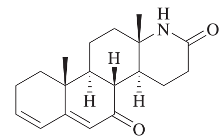
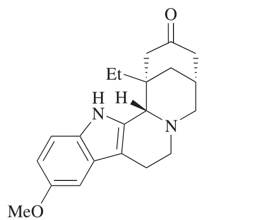
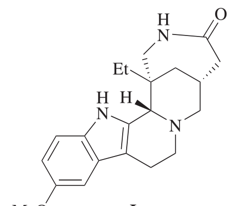
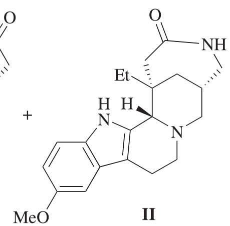
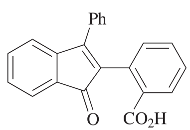
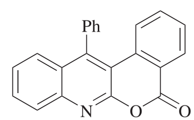
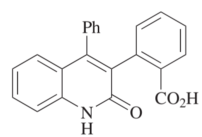
C_{21}			
	NaN_3, AcOH, H_2SO_4	 (40) +  (10) +  (20)	61
	$TMSN_3$, $SnCl_4$, I_2, CH_2Cl_2, –78° to rt, 2.5 h	 (58)	83
	NaN_3, PPA, 50°, 10 h	 (29)	354
	HN_3, H_2SO_4, $CHCl_3$, 0°, 20 min	 (38) +  (18)	513

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{21}			
	$TMSN_3$, $SnCl_4$, I_2, CH_2Cl_2, –78° to rt, 2.5 h	 (24) +  (24)	83
	NaN_3, PPA, 60°, 10 h	 (13) +  (30)	514
	NaN_3, H_2SO_4, $CHCl_3$	 **I** +  **II** **I + II** (85), **I:II** = —	515
C_{22}			
	NaN_3, AcOH, 80°, 1 h	 **I** (50) +  **II** (23)	516

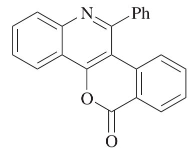
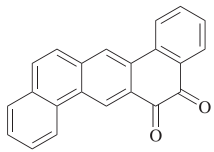
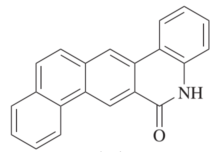
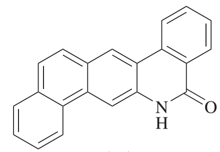
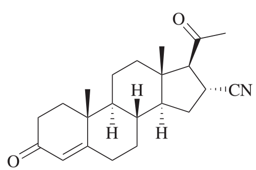
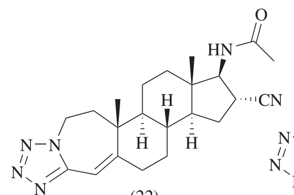
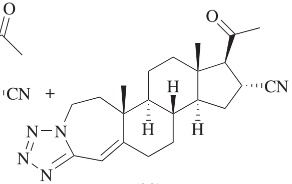
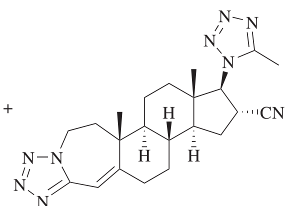
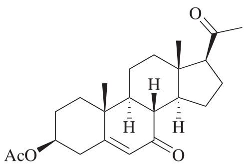
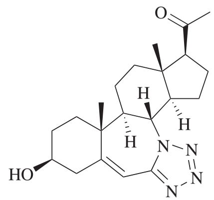
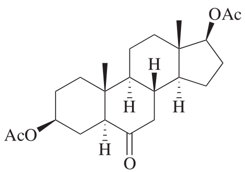
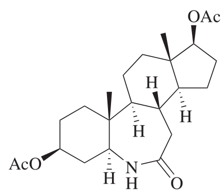
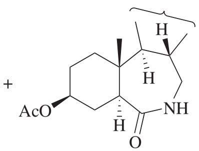
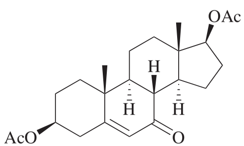
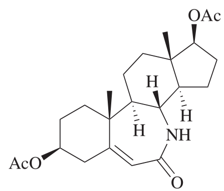
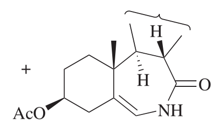
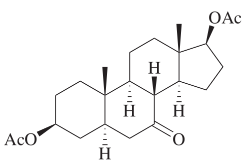
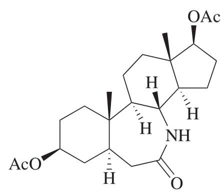
	NaN_3, AcOH, H_2SO_4, 40°, 45 min	**I** (25) + **II** (19) +  (15)	516
	NaN_3, H_2SO_4	 (—) +  (—)	453
	HN_3, BF_3•OEt_2, $CHCl_3$, 0° to rt, 24 h	 (22) +  (20) +  (15)	356

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{23}			
	HN_3, $BF_3 \cdot OEt_2$, $CHCl_3$, rt, 20 h	 (50)	517
	NaN_3, H_2SO_4, PhH, 20°, 2 h	 (26) +  (22)	508
	NaN_3, PPA, 50°, 8 h	 (26) +  (22)	508
	NaN_3, PPA, 50°, 8 h	 (—)	508

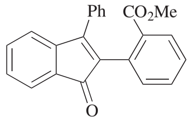
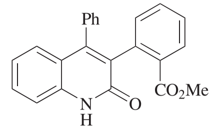
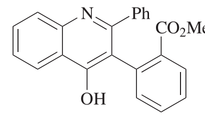
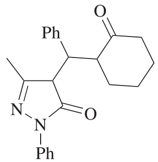
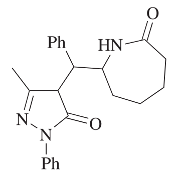
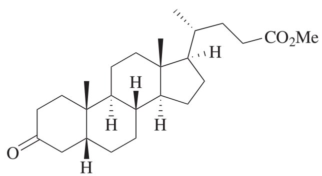
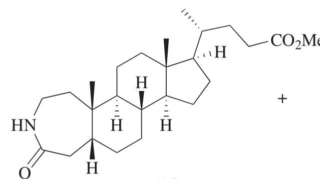
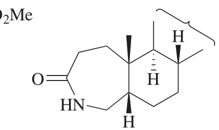
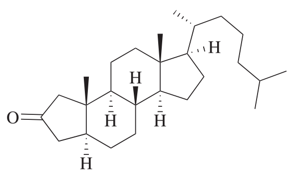
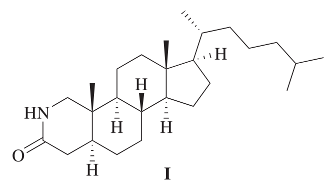
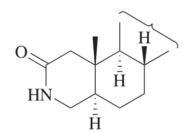
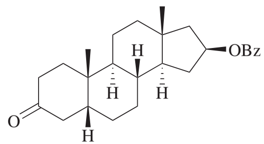
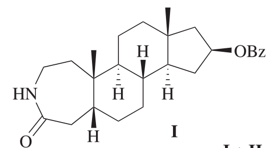
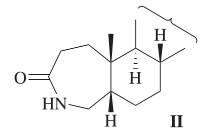
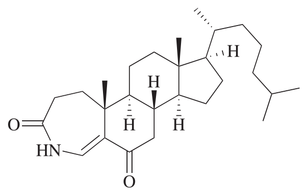
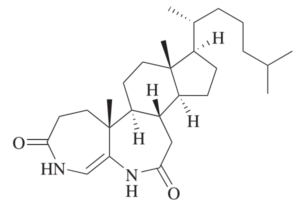
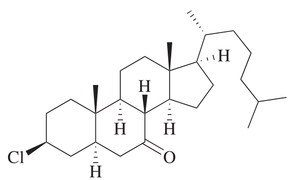
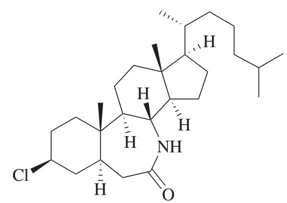
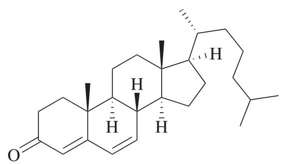
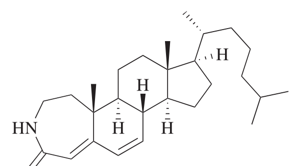
	NaN_3, AcOH, H_2SO_4, 40°, 45 min	 (8) +  (69)	516
	NaN_3, H_2SO_4, $CHCl_3$, 0–50°, 5 h	 (63)	263
C_{25}			
	NaN_3, H_2SO_4, $CHCl_3$, 0°, 30 min	 (15) +  (40)	518
C_{26}			
	NaN_3, PPA, 60°, 10 h	 **I** +  **II** **I + II** (77), **I:II** = —	519

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{26}			
	HN_3, H_2SO_4, $CHCl_3$, 0°, 20 min	 **I** +  **II** **I** + **II** (97), **I**:**II** = —	520
	NaN_3, PPA, 60°, 1 h	 (48)	521
C_{27}			
	NaN_3, H_2SO_4, PhH, rt, 1 h	 (50)	522
	NaN_3, H_2SO_4, PhH, rt, 1 h	 **I** (20)	523
	NaN_3, PPA, rt, 2 h	**I** (75)	416

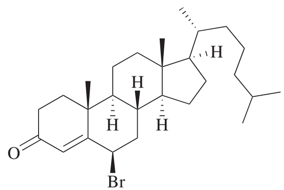
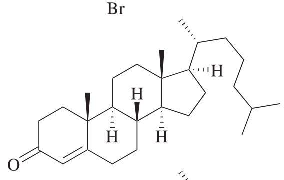
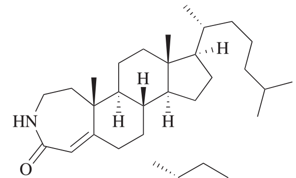
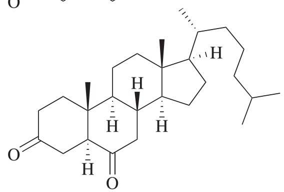
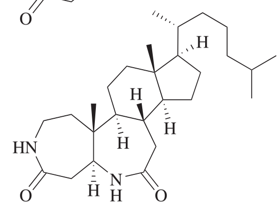
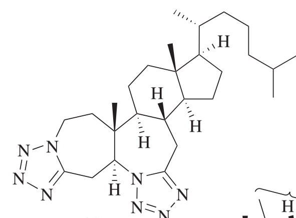
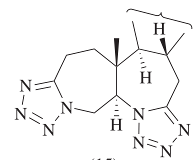
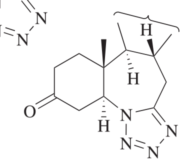
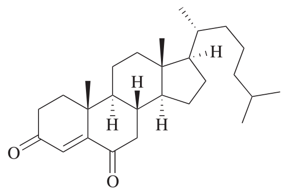
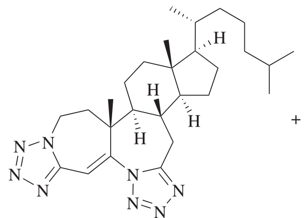
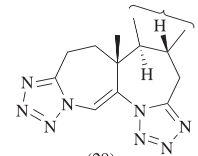
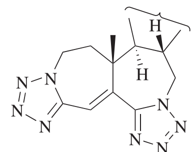
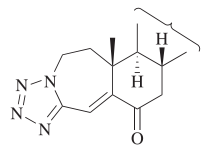
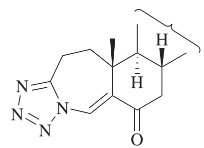
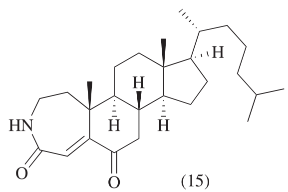
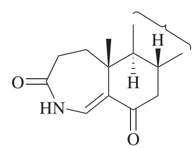
	NaN_3, H_2SO_4, PhH, rt, 1 h	**I** (20)	523
	NaN_3, PPA, 50°, 10 h	 (60)	354
	NaN_3, PPA, 65°, 12 h	 (—)	524
	HN_3, BF_3•OEt_2, PhH, rt, 5 h	 (20) +  (15) +  (10)	525

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{27} 	HN_3, BF_3•OEt_2, $CHCl_3$, 40°, 10 h	 **I** (33) +  (29) +  (11)	526
	HN_3, BF_3•OEt_2, PhH, rt, 5 h	**I** (5) +  (20) +  (10)	525
	NaN_3 (1 eq), PPA, 55°, 10 h	 (15) +  (25)	521

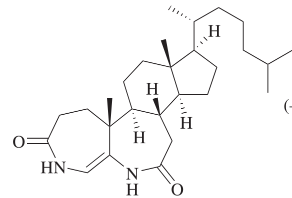
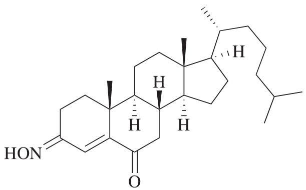
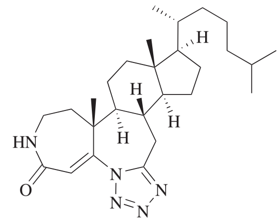
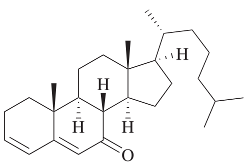
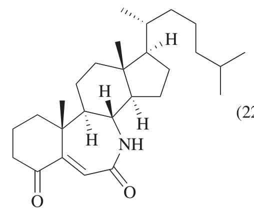
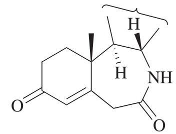
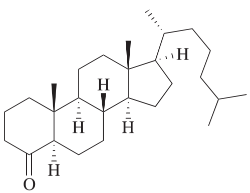
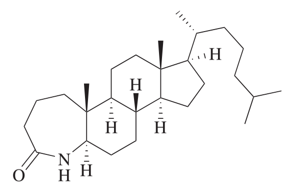
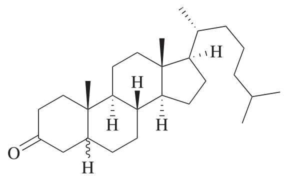
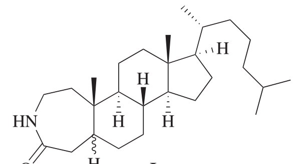
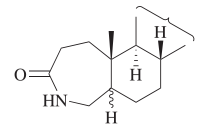
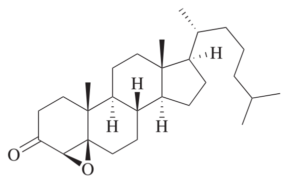
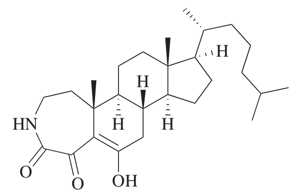
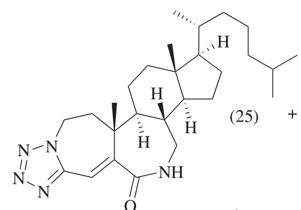
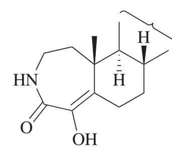
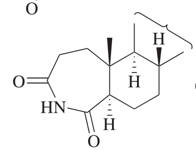
	NaN_3 (2 eq), PPA, 55°, 10 h	 (—)	521
	HN_3, BF_3•OEt_2, $CHCl_3$, 0° to rt, 24 h	 (73)	527
	NaN_3, PPA, rt, 2 h	 (22) +  (12)	416
	NaN_3, PPA, 50°, 6 h	 (25)	528

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{27} 	NaN_3, PPA, 65°, 12 h	 **I** +  **II** H / **I + II** / **I:II** α / (67) / 1:1 β / (86) / 1:1	529
	NaN_3, PPA, 50°, 6 h	 (40)	528
	HN_3, BF_3•OEt_2, PhH, rt, 3 d	 (25) +  (—) +  (10)	530

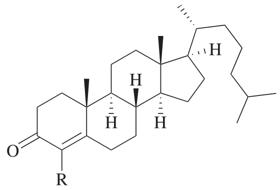
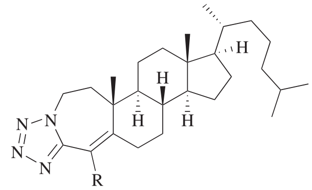
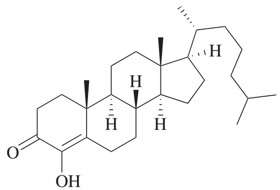
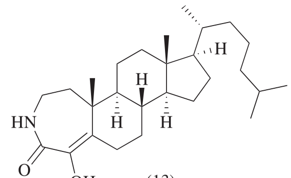
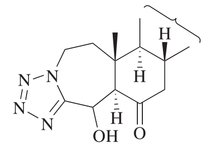
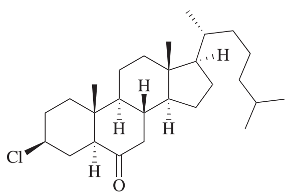
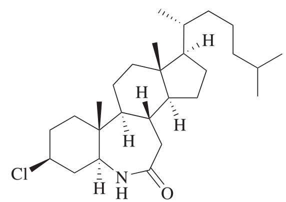
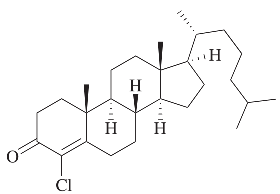
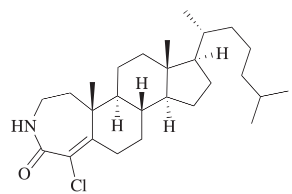
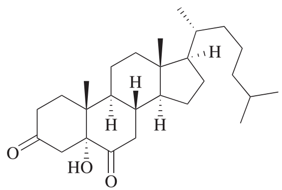
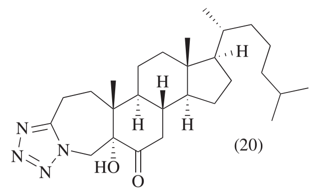
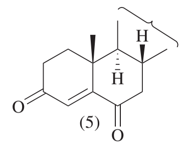
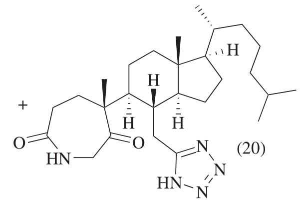
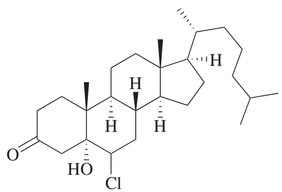
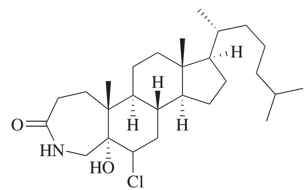
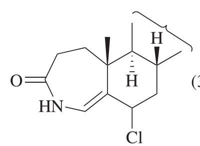
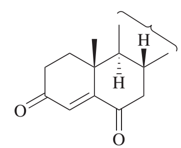
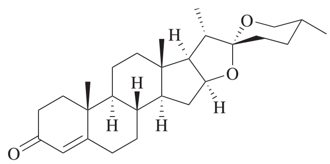
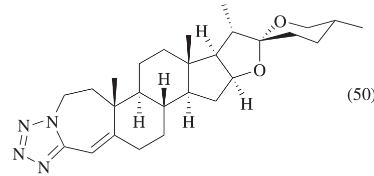
	HN_3, BF_3•OEt_2, PhH, rt, 3 d	 R: Cl (75); Br (70)	530
	HN_3, BF_3•OEt_2, PhH, rt, 3 d	 (13) +  (10)	530[d]
	NaN_3, H_2SO_4, PhH, rt, 1 h	 (50)	531
	NaN_3, PPA, 50°, 6 h	 (50)	528

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{27}			
	HN_3, BF_3•OEt_2, PhH, rt, 5 h	 (20) +  (5) +  (20)	525
	HN_3, BF_3•OEt_2, PhH, rt, 24 h	 (30) +  (30) +  (25)	532[d]

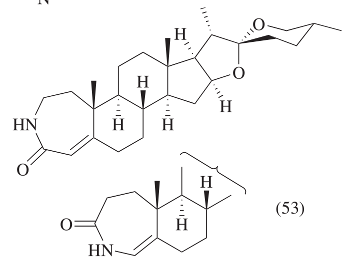


HN_3, BF_3•OEt_2, $CHCl_3$, 0° to rt, 20 h

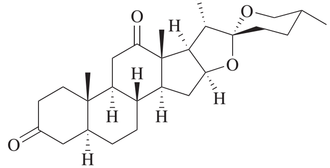


(50) 533

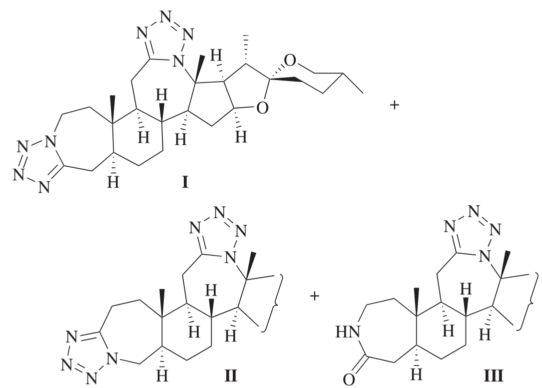
NaN_3, H_2SO_4



(27) + (53) 534

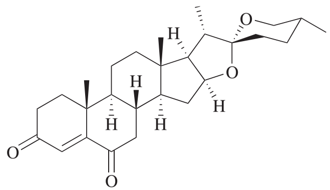
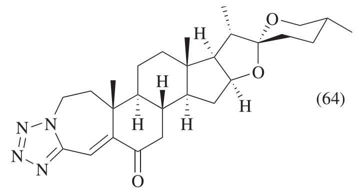
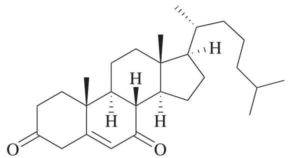
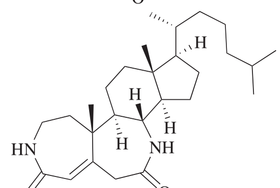
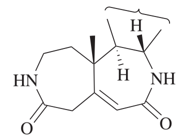
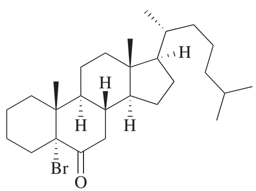
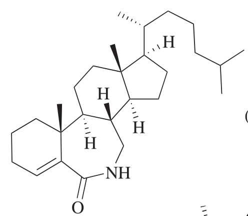
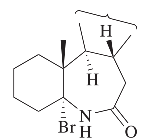
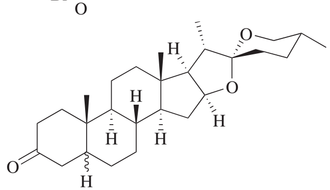
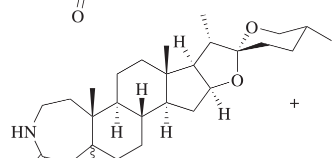
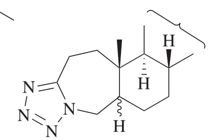


HN_3, BF_3•OEt_2, $CHCl_3$, 0° to rt, 24 h



I + **II** + **III** (20), **I**:**II**:**III** = 3:2:1 535

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{27} 	HN_3, BF_3•OEt_2, $CHCl_3$, 0° to rt, 24 h	 (64)	526
	NaN_3, PPA, 60°, 10 h	 **I** **I** or **II** (40)[e]  **II**	536
	HN_3, BF_3•OEt_2, $CHCl_3$, 0° to rt, 24 h	**I** or **II** (18)[e]	536
	NaN_3, H_2SO_4, PhH, rt, 1 h	 (—) +  (—)	537
	HN_3, 70°	 (25) +  (23)	538

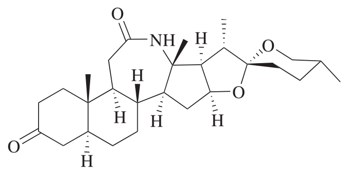
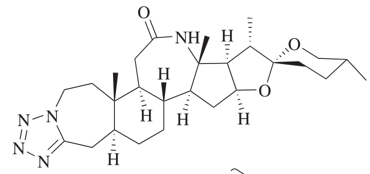
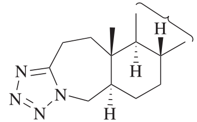
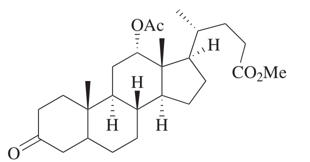
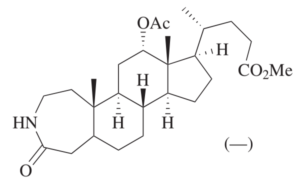
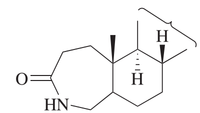
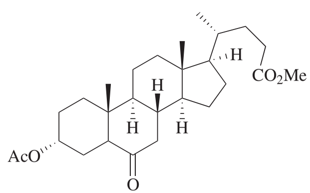
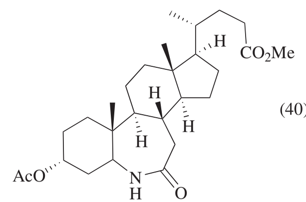
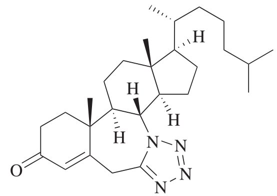
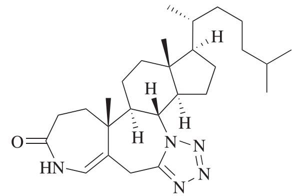
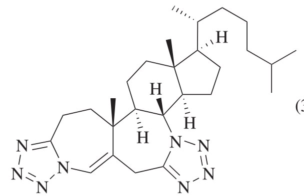
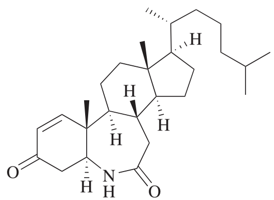
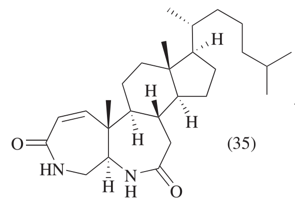
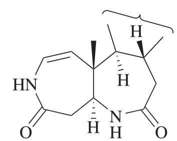
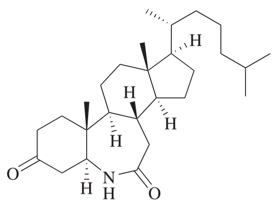
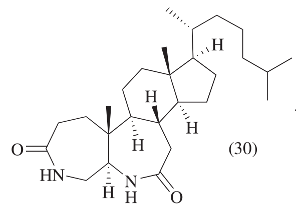
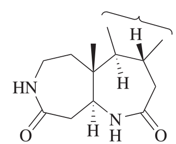
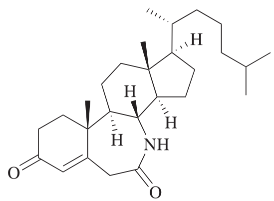
	HN_3, BF_3•OEt_2, $CHCl_3$, 0° to rt, 24 h	 (13) +  (13)	535
	HN_3, PPA	 (—) +  (—)	539[d]
	HN_3, H_2SO_4, PhH	 (40)	539[d]

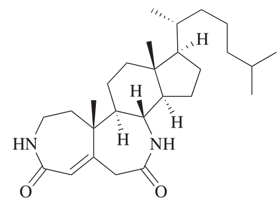
TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{27} 	NaN_3, PPA, 50°, 10 h	 (39)	540
	HN_3, BF_3•OEt_2, $CHCl_3$, 0° to rt, 28 h	 (32)	540
	NaN_3, H_2SO_4, $CHCl_3$, rt, 1 h	 (35) +  (10)	541
	NaN_3, H_2SO_4, $CHCl_3$, 0° to rt, 1.5 h	 (30) +  (35)	541

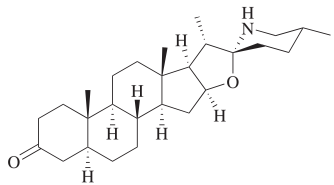
C_{27-29}



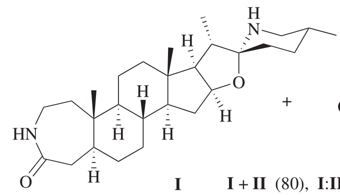
NaN_3, PPA, 60°, 12 h



(13) 542

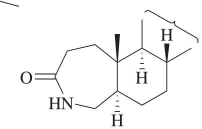


NaN_3, CCl_3CO_2H[b]



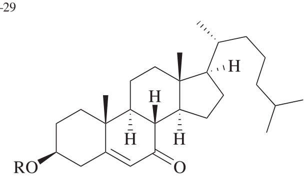
I

+

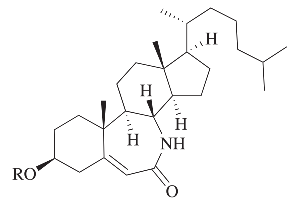


II

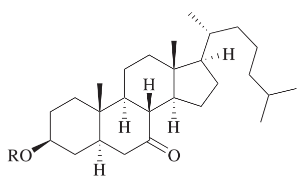
I + II (80), **I**:**II** = 3:1 543



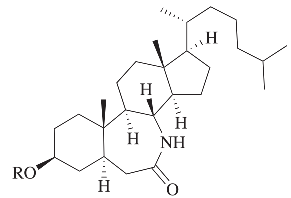
HN_3, H_2SO_4, PhH, 0°, 2 h



R		
H	(—)	544
Ac	(—)	

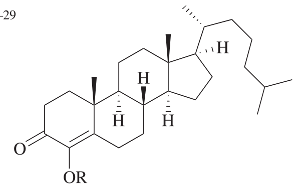
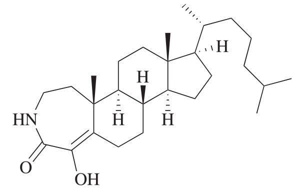
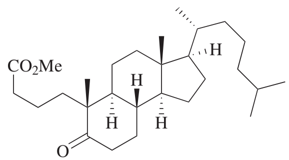
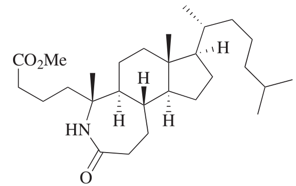
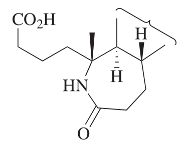
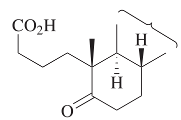
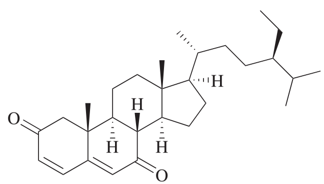
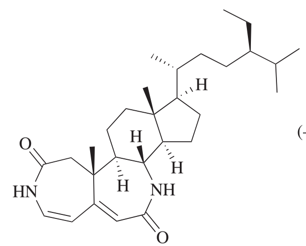


HN_3, H_2SO_4, PhH, 0°, 2 h



R		
H	(—)	544
Ac	(—)	545

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{27-29} 	NaN_3, PPA, 50°, 6 h	 R: H (58); Ac (58)	528
C_{28} 	NaN_3, PPA, 60°, 10 h	 (30) +  (17) +  (8)	546
	NaN_3, H_2SO_4	 (—)	547

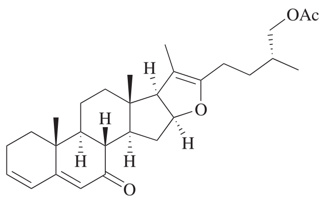
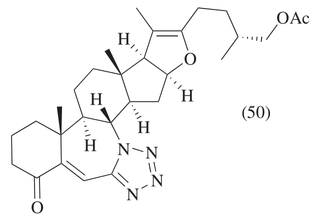
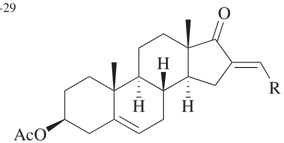
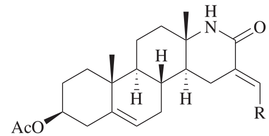
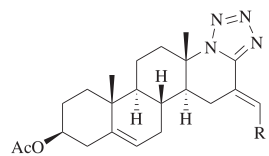
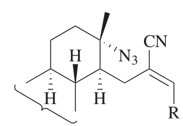
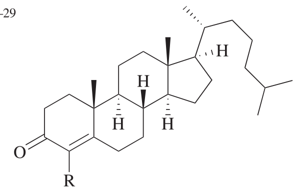
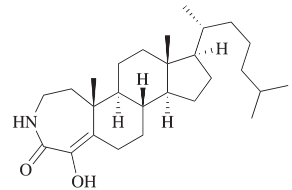
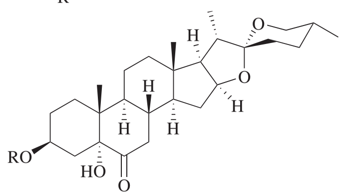
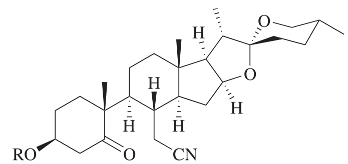
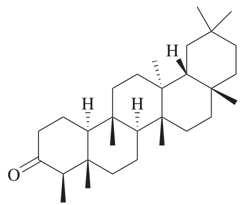
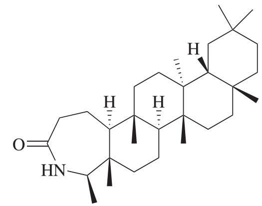
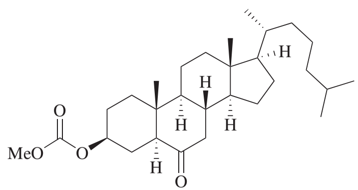
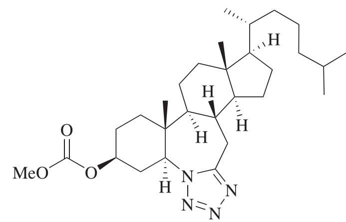
	HN_3, BF_3•OEt_2, PhH, rt, 80 h	 (50)	548
C_{28-29}			
	NaN_3, H_2SO_4, PhH, rt, 1 h	 (—) R: Ph, 4-HOC_6H_4, 4-ClC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$	549
	HN_3, BF_3•OEt_2, PhH, 0° to rt, 24 h	 **I** +  **II** **I** + **II** (—) R: Ph, 4-HOC_6H_4, 4-ClC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$	549

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{28-29} 	HN_3, BF_3•OEt_2, PhH, rt, 3 d	 R: MeO (60); AcO (50)	530
	NaN_3, H_2SO_4, PhH	 R: Me (—); Et (—)	550
C_{29} 	HN_3, H_2SO_4, $CHCl_3$, 0°, 2 h	 (64)	551
	HN_3, BF_3•OEt_2, PhH, 0° to rt, 35 h	 (—)	552

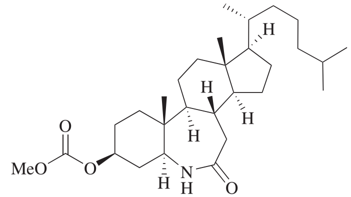
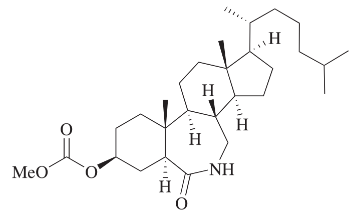
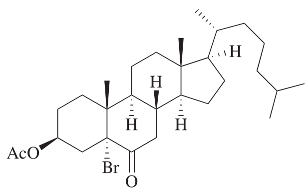
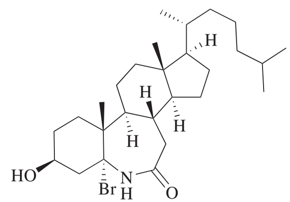
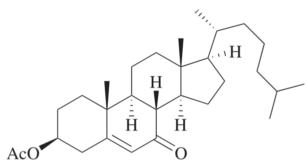
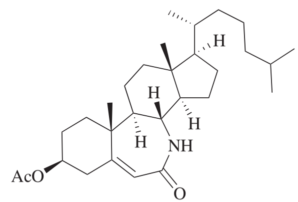
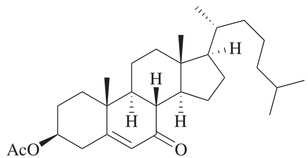
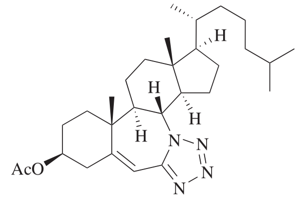
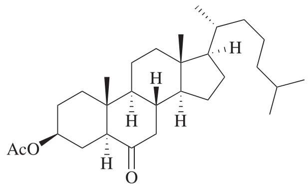
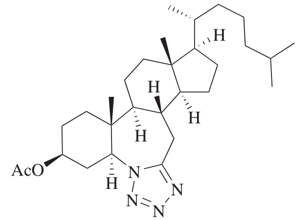
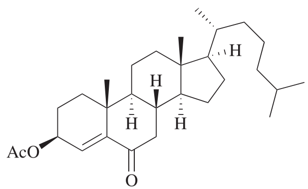
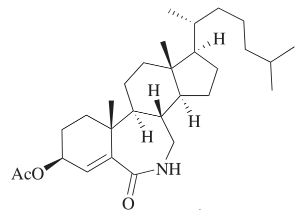
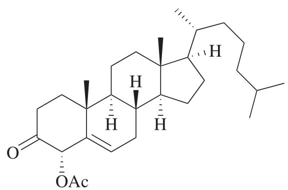
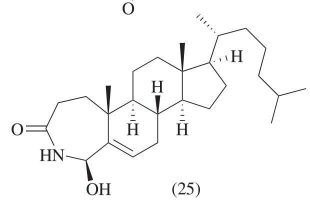
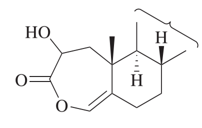
	NaN$_3$, H$_2$SO$_4$, PhH	 (—) +  (—)	552
	NaN$_3$, H$_2$SO$_4$, PhH, rt, 1 h	 (36)	537
	NaN$_3$, H$_2$SO$_4$, PhH, rt, 30 min	 (50)	553

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{29}			
	HN_3, BF_3•OEt_2, PhH, 0° to rt, 5 h	 (—)	553
	HN_3, BF_3•OEt_2, PhH, 0° to rt, 35 h	 (—)	554
	NaN_3, PPA, 60°, 8 h	 (15)	531
	HN_3, BF_3•OEt_2, PhH, rt, 24 h	 (25) +  (20)	532

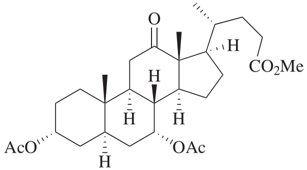
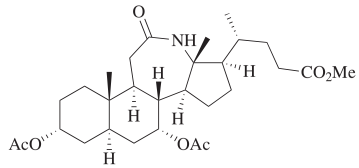
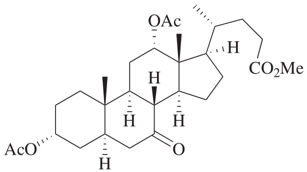
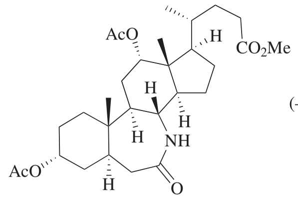
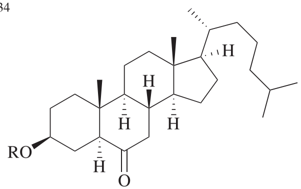
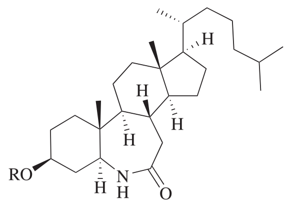
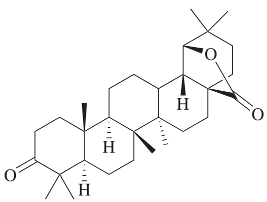
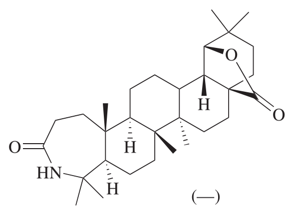
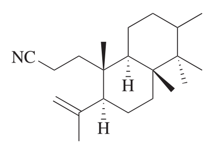
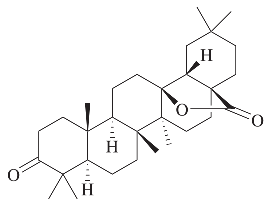
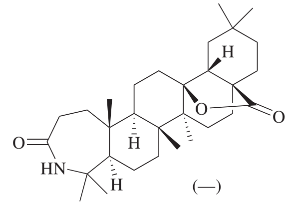
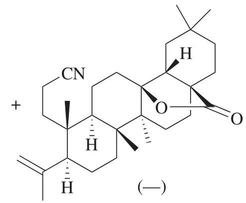
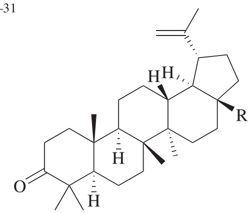
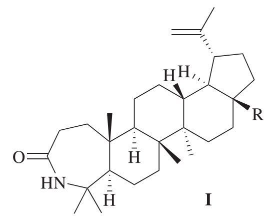
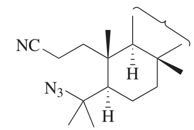
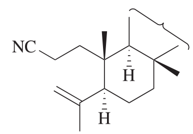
	HN_3, H_2SO_4, PhH, rt, 1 h	 (—)	539
	HN_3, PPA	 (—)	539
C_{29-34}			
	NaN_3, PPA, 100°, 10 h	 R: Ac (73); Bz (22)	544
C_{30}			
	NaN_3, PPA, 60°, 10 h	 (—) +  (—)	555[d]

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{30} 	NaN_3, PPA, 60°, 10 h	 (—) +  (—)	555
C_{30-31} 	A: HN_3, BF_3•OEt_2, PhH, rt, 16 h B: HN_3, H_2SO_4, PhH, rt, 16 h	 **I** +  **II**	556
	NaN_3, H_2SO_4, AcOH, 30–70°, 12 h	**I** +  **III**	557, 555

R	Conditions	**I**	**II**
Me	A	(—)	(45)
Me	B	(57)	(—)
MeO_2C	A	(—)	(45)
MeO_2C	B	(57)	(—)

R	**I + III**
Me	(—)
MeO_2C	(—)

C_{31}

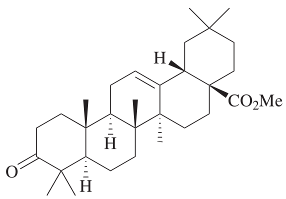
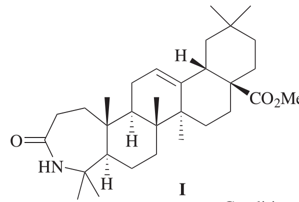
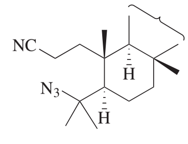
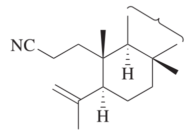
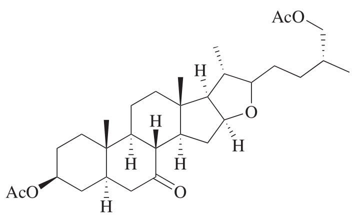
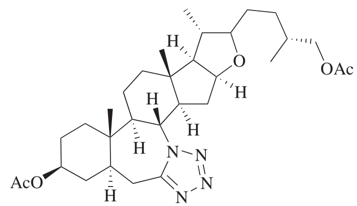
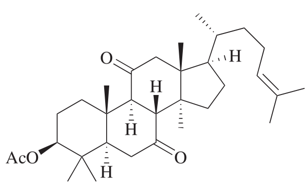
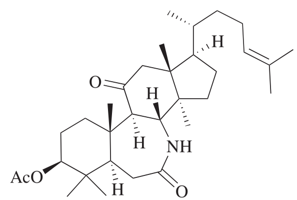
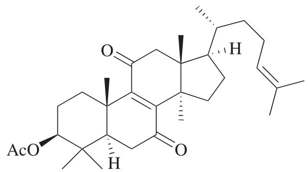
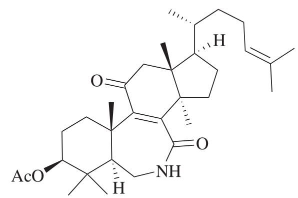
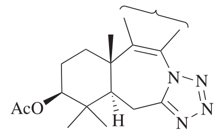
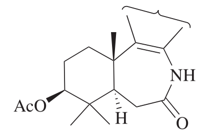
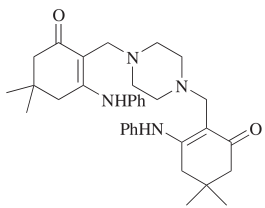
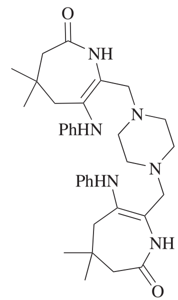
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	A: HN_3, BF_3•OEt_2, PhH, rt, 16 h B: HN_3, H_2SO_4, PhH, rt, 16 h	 **I** +  **II**	556
		Conditions / **I** / **II**: A (—) (45); B (57) (—)	
	NaN_3, H_2SO_4, AcOH, 30–70°, 12 h	**I** (—) +  (—)	557
	HN_3, BF_3•OEt_2, PhH, rt, 80 h	 (—)	548[d]
	NaN_3, H_2SO_4, 0°, 15 min	 (44)	558

TABLE 4. SCHMIDT REACTIONS OF CARBOCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{31} 	NaN_3, H_2SO_4, 0°, 30 min	 (50) +  (—) +  (—)	558
C_{34} 	NaN_3, H_2SO_4, $CHCl_3$, 0° to rt, 5 h	 (70)	478

[a] Silica sulfuric acid is silica-bound sulfuric acid generated by treating silica with chlorosulfonic acid.

[b] Molten trichloroacetic acid (mp 57°) was used as solvent.

[c] The structure was initially assigned incorrectly. It has been corrected here, see reference 401.

[d] The stereochemistry of the substrate was not specified in the reference.

[e] A single isomer of unassigned structure was obtained.

TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3

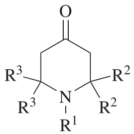
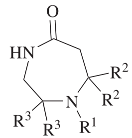
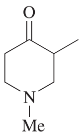
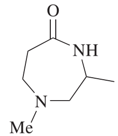
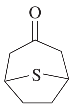
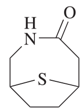
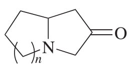
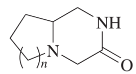
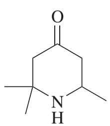
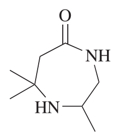
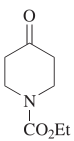
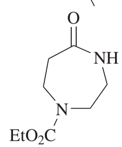
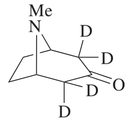
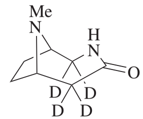
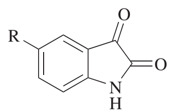
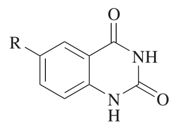
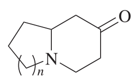
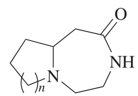
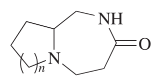
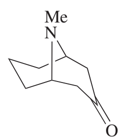
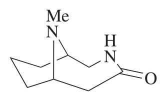
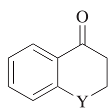
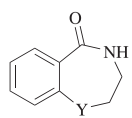
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{5-9}		NaN_3, H_2SO_4, $CHCl_3$, 0°, 45 min	 R^1 R^2 R^3: H H H (88); Me H H (53); H Me Me (51)	559
C_7		NaN_3, H_2SO_4, 0°, 1 h	 (38)	57
		HN_3, P_2O_5, H_2SO_4, $CHCl_3$, 30°, 6 h	 (73)	560
C_{7-8}		NaN_3, H_2SO_4, $CHCl_3$, 0–50°, 2 h	 *n*: 1 (44); 2 (65)	561
C_8		NaN_3, H_2SO_4, 0°, 1 h	 (64)	57
		NaN_3, H_2SO_4, 0°, 3 h	 (70)	562

TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	NaN_3, D_2SO_4, 0–50°, 3 h	 (89)	563
C_{8-9} 	$TMSN_3$, $FeCl_3$, DCE, rt, 30–35 min	 **I**; R: H (80), Me (75)	286
	NaN_3, $FeCl_3$, DCE, rt, 2.5 h	**I**; R: H (74), Me (75)	286
	NaN_3, H_2SO_4, $CHCl_3$, 0–50°, 2 h	 **I** +  **II**; *n* = 1: **I** (22), **II** (0); *n* = 2: **I** (20), **II** (—)	561
C_9 	NaN_3, H_2SO_4, $CHCl_3$, 0–50°, 4 h	 (90)	564
	HN_3, P_2O_5, $CHCl_3$, 20°, 4 h	 Y: O (67), S (68)	560

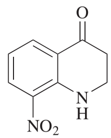
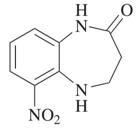
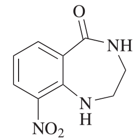
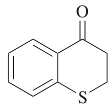
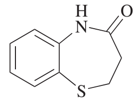
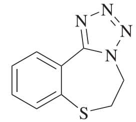
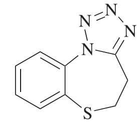
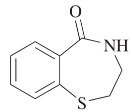
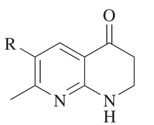
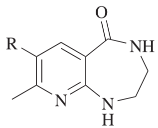
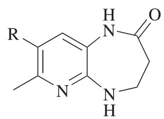
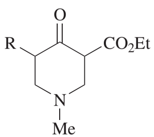
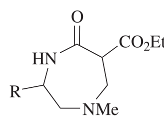
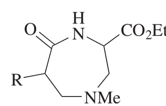
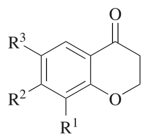
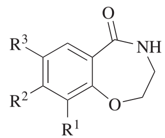
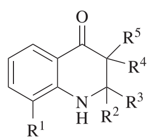
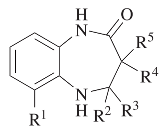
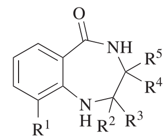
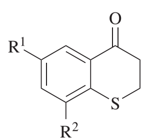
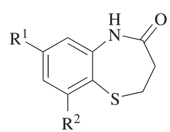
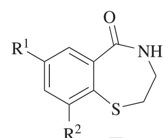
	NaN_3, MsOH	 (10) +  (86)	565
	$TMSN_3$, TFA, rt, 72 h	 **I** (—) +  (30) +  (—)	566
	NaN_3, H_2SO_4, PhH, 0° to rt, 12 h	**I** (80) +  (—)	567
	NaN_3, H_2SO_4, $CHCl_3$, rt, 1 h	 **I** +  **II** R / **I** / **II**: H (2) (79); Br (12) (73)	65
C_{9-10} 	HN_3, H_2SO_4, $CHCl_3$, 0°, 3 h	 **I** +  **II** R / **I** / **II**: H (—) (30); Me (—) (30)	568

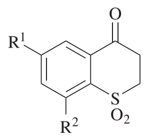
TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-10} 	NaN_3, H_2SO_4, 0° to rt, 12 h		62
C_{9-11} 	NaN_3, H_2SO_4, rt, 2 h	 **I** +  **II**	569
	NaN_3, H_2SO_4	 **I** +  **II**	570

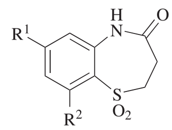
R^1	R^2	R^3	
H	H	H	(78)
H	H	Cl	(65)
H	H	Br	(70)
Cl	H	H	(75)
H	H	Me	(79)
Me	H	H	(70)
H	MeO	H	(50)
H	H	MeO	(52)

R^1	R^2	R^3	R^4	R^5	**I**	**II**
H	H	H	H	H	(30)	(0)
Me	H	H	H	H	(52)	(0)
H	H	H	Me	H	(45)	(27)
H	Me	Me	H	H	(77)	(0)
H	H	H	Me	Me	(0)	(79)

R^1	R^2	**I**	**II**
H	H	(42)	(21)
Cl	H	(78)	(0)
Br	H	(84)	(0)
Me	H	(36)	(44)
Me	Me	(21)	(33)



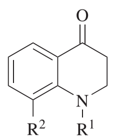
NaN_3, H_2SO_4



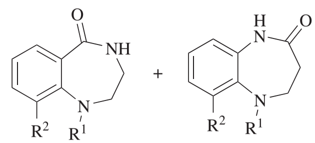
R^1	R^2	
H	H	(67)
Cl	H	(52)
Br	H	(15)
Me	H	(79)
Me	Me	(15)

570

C_{9-12}



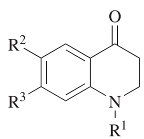
NaN_3, MsOH



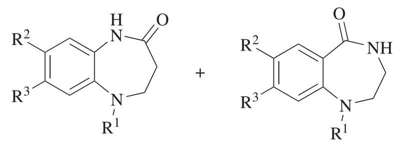
I + **II**

R^1	R^2	**I**	**II**	
H	HO	(49)	(22)	571
H	O_2N	(86)	(10)	565
H	MeO	(70)	(18)	571
Ac	MeO	(90)	(0)	571

C_{9-15}



NaN_3, H_2SO_4, $CHCl_3$, rt, 2 h



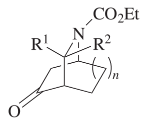
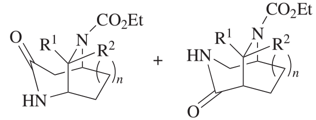
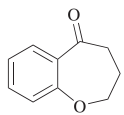
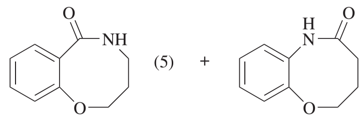
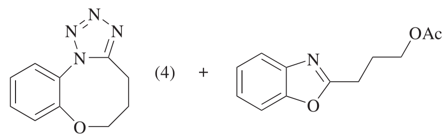
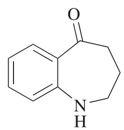
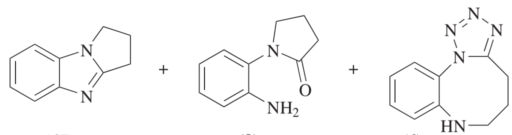
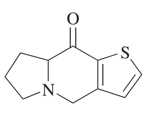
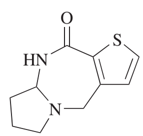
I + **II**

572

R^1	R^2	R^3	**I + II**	**I:II**
H	H	H	(88)	1:4
H	Cl	H	(92)	1:2
H	H	MeO	(95)	3:7
Me	H	H	(82)	1:3
Me	Cl	H	(91)	1:3

R^1	R^2	R^3	**I + II**	**I:II**
Me	H	MeO	(92)	1:2
Ac	H	H	(85)	19:1
Ac	Cl	H	(80)	9:1
Ac	H	MeO	(90)	9:1
Ph	H	H	(82)	1:3

TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-16} 	NaN_3, H_2SO_4, rt, 1–3 h	 **I** + **II**	67
C_{10} 	NaN_3, H_2SO_4, AcOH, 60°, 6 h	 (5) + (54) +  (4) + (13)	573
	NaN_3, H_2SO_4, AcOH, 0° to rt, 24 h	 (65) + (8) + (6)	573
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (85)	574

n	R^1	R^2	**I + II**	**I:II**
0	H	H	(38)	100:0
1	H	H	(62)	73:27
1	Me	H	(43)	70:30
1	H	Me	(72)	55:45
2	H	H	(82)	67:33
1	Ph	H	(50)	73:27
1	H	Ph	(97)	35:65

C$_{10-11}$

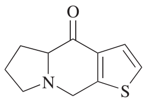
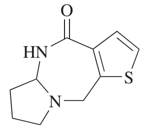
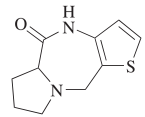
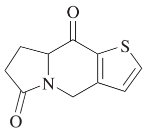
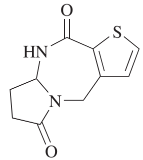
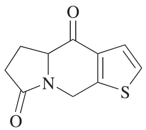
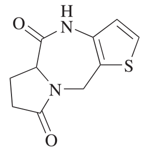
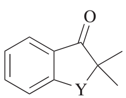
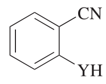
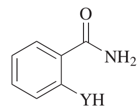
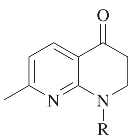
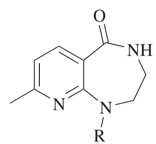
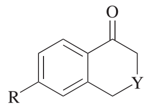
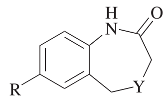
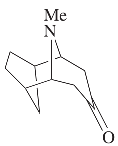
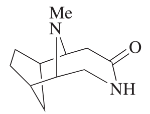
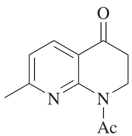
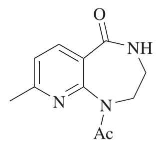
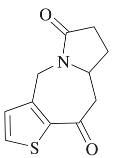
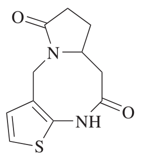
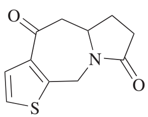
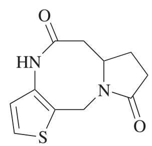
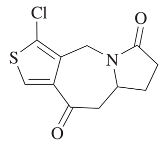
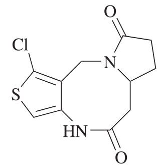
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (59) +  (32)	574
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 48 h	 (70)	574
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 12 h	 (75)	574
	NaN_3, H_2SO_4, AcOH, 0° to rt, 24 h	 **I** +  **II** Y / **I** / **II** HN (88) (6) O (51) (29)	573
	NaN_3, H_2SO_4, $CHCl_3$	 R Me (78) Et (79)	65

TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10-14} 	NaN_3, H_2SO_4, PhH, 0° to rt, 12 h	 R / Y: MeO, S (—); H, EtN (—); MeO, EtN (63)	575
C_{11} 	NaN_3, H_2SO_4	 (93)	576
	NaN_3, H_2SO_4, $CHCl_3$, rt, 1 h	 (69)	65
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 24 h	 (65)	66
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 24 h	 (70)	66

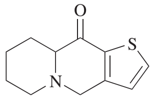


NaN$_3$, H$_2$SO$_4$, CH$_2$Cl$_2$, rt, 24 h

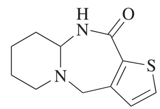


(45)

66

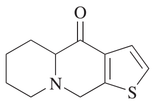


NaN$_3$, H$_2$SO$_4$, CH$_2$Cl$_2$, 0° to rt, 6 h

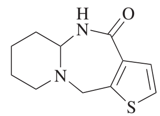


(—)

577

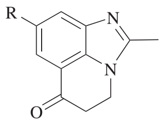


NaN$_3$, H$_2$SO$_4$, CH$_2$Cl$_2$, 0° to rt, 6 h

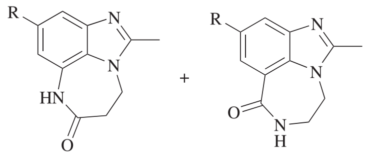


(—)

577



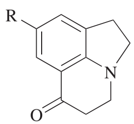
NaN$_3$, H$_2$SO$_4$, CHCl$_3$, 0° to rt, 16 h



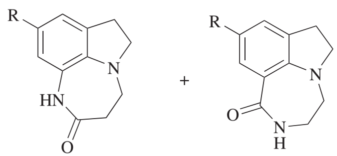
I + **II**

R	**I**	**II**
H	(46)	(50)
Cl	(14)	(78)
O$_2$N	(0)	(70)

578



NaN$_3$, PPA, 60°, 4 h

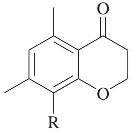
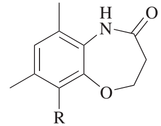
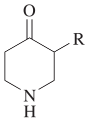
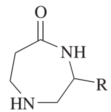
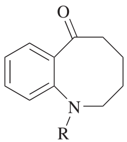
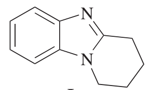
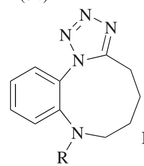
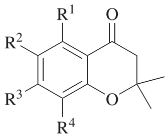
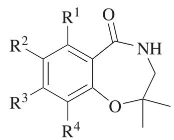
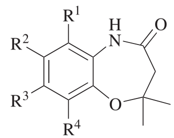


I + **II**

R	**I + II**	**I:II**
H	(74)	1:5
Cl	(68)	1:11

579

TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11-12} 	NaN_3, H_2SO_4, rt, 16 h		62
C_{11-13} 	HN_3, H_2SO_4, $CHCl_3$, 0°, 1.5 h		568
C_{11-18} 	NaN_3, H_2SO_4, AcOH, 0° to rt, 24 h	 **I** +  **II**	573
C_{11-27} 	NaN_3, H_2SO_4, AcOH, 50°, 3 h	 **I** +  **II**	580

C_{11-12}:

R	
H	(5)
Me	(5)

C_{11-13}:

R	
Ph	(71)
Bn	(74)
$BnCH_2$	(74)

C_{11-18}:

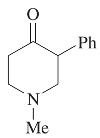
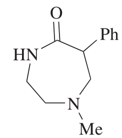
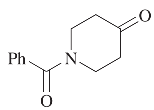
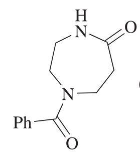
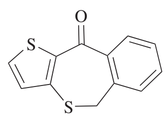
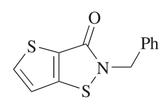
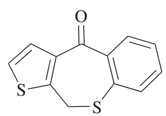
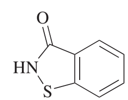
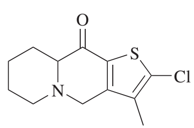
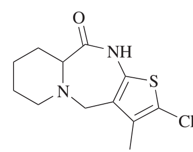
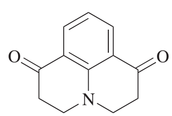
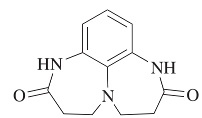
R	**I**	**II**
H	(54)	(23)
Ac	(50)	(20)
Ts	(50)	(20)

C_{11-27}:

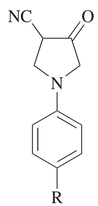
R^1	R^2	R^3	R^4	**I**	**II**
H	H	H	H	(57)	(0)
H	H	MeO	H	(47)	(0)
H	H	MsO	H	(53)	(0)
H	H	MeO	Me	(55)	(0)
Me	H	MeO	H	(0)	(49)
H	MeO	MeO	H	(54)	(0)
MeO	H	MeO	H	(0)	(54)

H	H	$NCCH_2O$	H	(45)	(0)
H	H	HO_2CCH_2O	H	(64)	(0)
H	H	H_2NCOCH_2O	H	(51)	(0)
Me	H	MsO	H	(0)	(47)
H	H	HO_2CCH_2O	Me	(75)	(0)
H	H	EtO_2CCH_2O	H	(71)	(0)
H	H	EtO_2CCH_2O	Me	(73)	(0)
H	H	$PhSO_3$	H	(35)	(0)
H	H	BnO	H	(71)	(0)
H	HO	BnO	H	(42)	(0)
H	H	$2\text{-}ClC_6H_4CH_2O$	H	(52)	(0)
H	H	$4\text{-}ClC_6H_4CH_2O$	H	(61)	(0)
H	H	PNBO	H	(91)	(0)
H	H	$4\text{-}BrC_6H_4CH_2O$	H	(48)	(0)
H	H	TsO	H	(47)	(0)
Me	H	BnO	H	(0)	(59)
Me	H	$2\text{-}ClC_6H_4CH_2O$	H	(0)	(58)
Me	H	PNBO	H	(0)	(46)
Me	H	$4\text{-}BrC_6H_4CH_2O$	H	(0)	(44)
H	H	$PhNHCOCH_2O$	H	(46)	(0)
H	H	$2\text{-}ClC_6H_4NHCOCH_2O$	H	(61)	(0)
H	H	$3\text{-}ClC_6H_4NHCOCH_2O$	H	(87)	(0)
H	H	$2\text{-}BrC_6H_4NHCOCH_2O$	H	(62)	(0)
H	H	$3\text{-}BrC_6H_4NHCOCH_2O$	H	(61)	(0)
H	H	$2,6\text{-}Cl_2C_6H_3NHCOCH_2O$	H	(48)	(0)
Me	H	$PhNHCOCH_2O$	H	(0)	(57)
H	H	$PhNHCOCH_2O$	Me	(62)	(0)
H	H	$2\text{-}MeC_6H_4NHCOCH_2O$	H	(54)	(0)
H	H	$2\text{-}Me\text{-}6\text{-}EtC_6H_3NHCOCH_2O$	H	(52)	(0)
H	$PhSO_2O$	$PhSO_2O$	H	(42)	(0)
H	TsO	TsO	H	(45)	(0)
H	$4\text{-}MeC_6H_4COHNCH_2O$	BnO	H	(39)	(0)

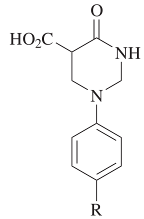
TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}		NaN_3, H_2SO_4, $CHCl_3$, 10°, 30 min	 (41)	581
		HN_3, P_2O_5, H_2SO_4, CH_2Cl_2, 20°, 4 h	 (72)	560
		NaN_3, H_2SO_4, CH_2Cl_2, rt, 3 h	 (47)	582
		NaN_3, H_2SO_4, CH_2Cl_2, rt, 3 h	 (35)	582
		NaN_3, H_2SO_4, CH_2Cl_2, 0° to rt, 6 h	 (—)	169
		NaN_3, H_2SO_4, $CHCl_3$, 0°, 15 min	 (81)	583

C_{12-13}

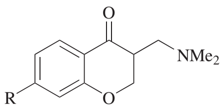


NaN_3, $CHCl_3$, concd H_2SO_4

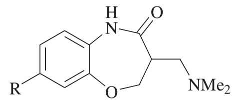


R	
Me	(82)
MeO	(84)

584

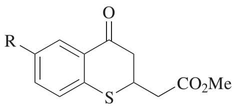


NaN_3, H_2SO_4, rt, 16 h

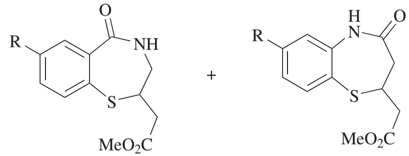


R	
H	(70)
MeO	(—)

62



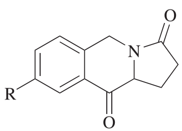
NaN_3, H_2SO_4, PhH, 0° to rt, 12 h



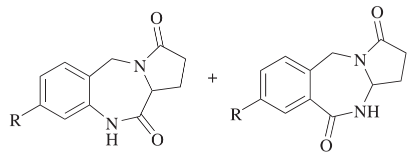
I + **II**

R	**I**	**II**
H	(36)	(24)
Cl	(—)	(—)
Me	(30)	(44)

585



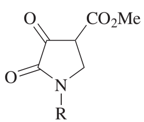
NaN_3, H_2SO_4, CH_2Cl_2, 0°, 3 h



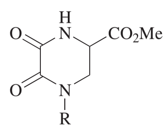
I + **II**

R	**I**	**II**
H	(100)	(0)
F	(60)	(40)
Me	(72)	(28)

169



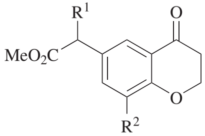
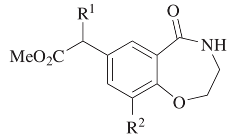
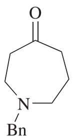
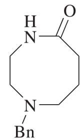
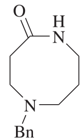
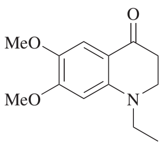
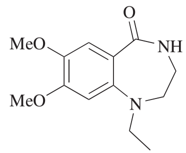
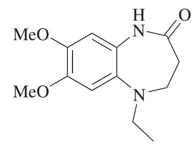
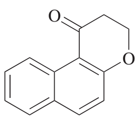
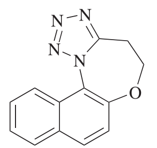
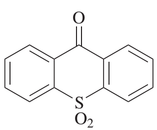
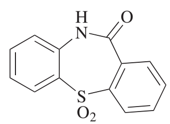
NaN_3, H_2SO_4



R	
Ph	(75)
Bn	(70)

322

TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12-14}		NaN_3, H_2SO_4, PhH, rt, 12 h	 R^1 / R^2: H / H (52); H / HO (15); H / Cl (34); Me / H (57); Et / H (46)	586
C_{13}		NaN_3, H_2SO_4, rt to 50°, 37 h	 (64) +  (—)	55
		NaN_3, H_2SO_4, $CHCl_3$	 (28) +  (54)	587
		NaN_3, $SiCl_4$, MeCN, rt, 12 h	 (40)	70
		NaN_3, CCl_3CO_2H, $CHCl_3$, rt, 12 h	 (100)	588

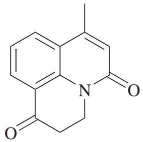
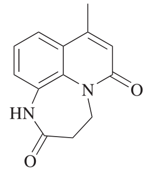
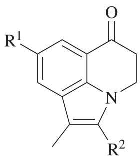
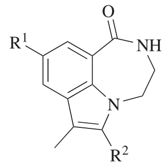
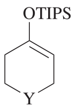
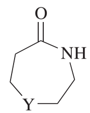
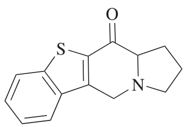
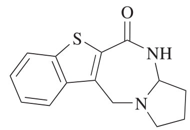
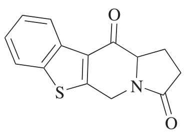
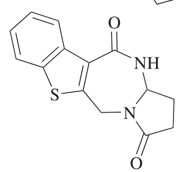
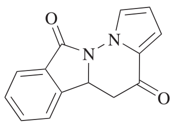
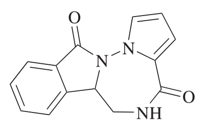
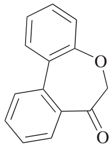
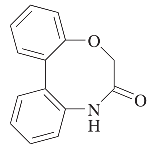
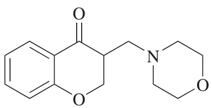
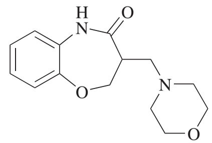
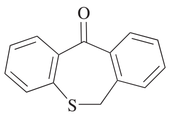
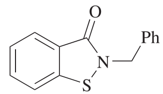
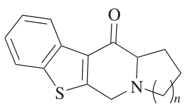
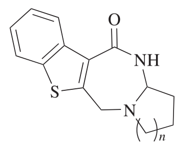
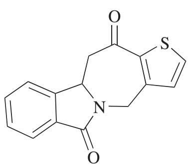
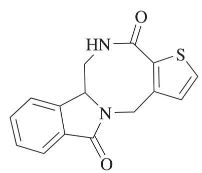
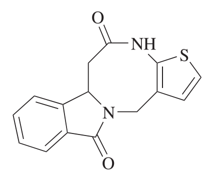
	NaN_3, H_2SO_4, $CHCl_3$, 0° to rt, 5 h	 (59)	589
C_{13-14} 	NaN_3, CCl_3CO_2H,[a] 60°	 R^1 R^2 Cl Me (—) H Et (—)	590
C_{14} 	1. $TMSN_3$, PPTS, CH_2Cl_2, rt, 2 d 2. $h\nu$, c-C_6H_{12}, 0°, 1 h	 Y O (76) S (62)	74
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 72 h	 (80)	591
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 72 h	 (51)	591
	NaN_3, H_2SO_4, CH_2Cl_2, 0° to rt, 12 h	 (68)	592

TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	NaN_3, H_2SO_4, 0° to rt, 2 h	 **I** (58)	593
	NaN_3, PPA, 50°, 4 h	**I** (38)	593
	NaN_3, H_2SO_4, rt, 16 h	 (20)	62
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 3 h	 (51)	582
$C_{14–15}$ 	NaN_3, H_2SO_4, CH_2Cl_2, rt, 72 h	 *n* 1 (65); 2 (51)	591
C_{15} 	NaN_3, H_2SO_4	 (32) +  (42)	594

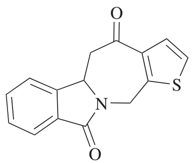
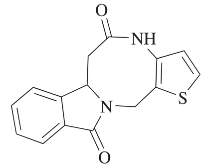
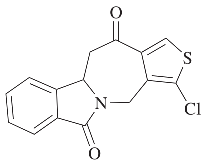
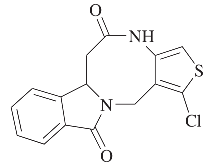
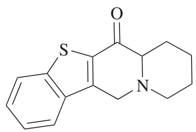
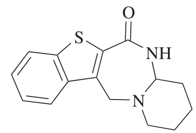
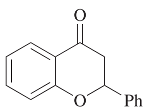
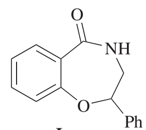
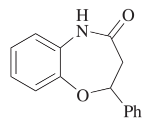
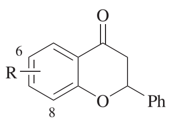
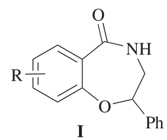
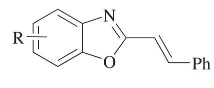
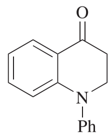
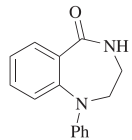
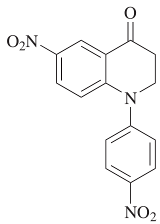
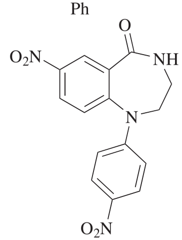
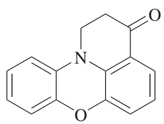
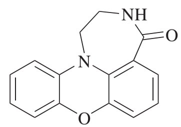
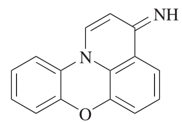
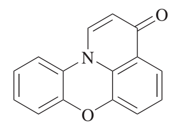
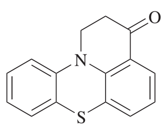
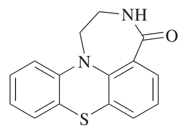
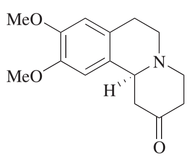
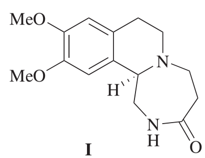
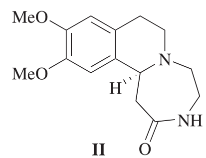
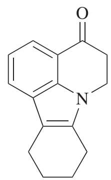
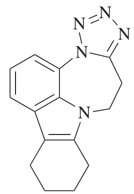
	NaN_3, H_2SO_4	 (81)	594
	NaN_3, H_2SO_4	 (76)	594
	NaN_3, H_2SO_4, CH_2Cl_2, 0° to rt, 6 h	 (—)	577
	NaN_3, H_2SO_4, AcOH, 0° to rt, 24 h	 **I** (88) +  (3)	595
	Azide, $FeCl_3$, DCE, rt	**I** — Azide: $TMSN_3$, Time: 50 min (75); Azide: NaN_3, Time: 3 h (68)	286
	NaN_3, H_2SO_4, AcOH, 40°	 **I** +  **II** — R: 6-O_2N, I (70), II (5); R: 8-O_2N, I (70), II (—)	596

TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	NaN_3, H_2SO_4, $CHCl_3$, rt, 3 h	 (—)	597
	NaN_3, H_2SO_4, $CHCl_3$, rt, 3 h	 (69)	597
	NaN_3, CCl_3CO_2H,[a] $CHCl_3$, 70°, 5 h	 (20) +  (13) +  (6)	598
	NaN_3, CCl_3CO_2H,[a] 60°, 5 h	 (—)	599
	NaN_3, H_2SO_4, CH_2Cl_2, rt, 4 h	 **I** +  **II** **I** + **II** (90)	600

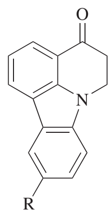


NaN$_3$, SiCl$_4$, MeCN, rt, 6 h

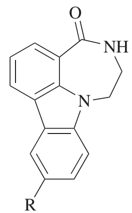


(90)

70



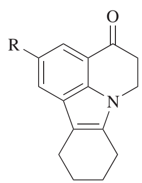
NaN$_3$, CCl$_3$CO$_2$H,[a] 60°



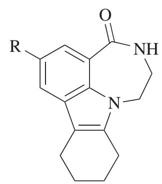
R	
H	(—)
Cl	(—)

590

C$_{15-16}$

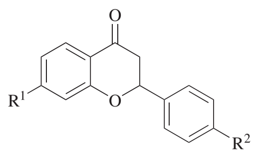


NaN$_3$, CCl$_3$CO$_2$H,[a] 60°

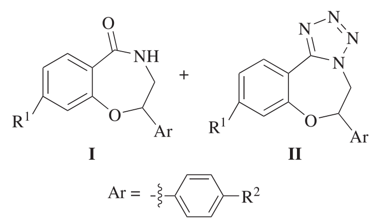


R	
H	(—)
Cl	(—)

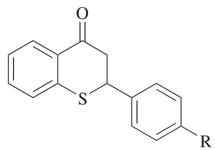
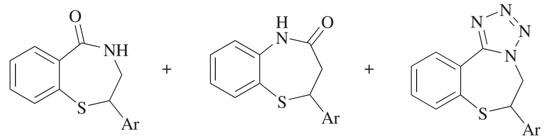
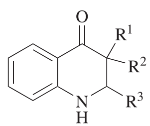
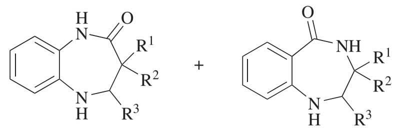
590

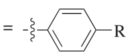


TMSN$_3$, TFA



R^1	R^2	**I**	**II**	
H	H	(25)	(3)	600a
H	F	(—)	(—)	600b
F	H	(—)	(28)	600a
H	Cl	(—)	(10)	600a
Cl	H	(—)	(6)	600a
H	O_2N	(—)	(—)	600b
H	Br	(—)	(10)	600a
Br	H	(—)	(7)	600a
MeO	H	(—)	(—)	600b

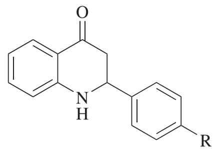
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15-16} 	$TMSN_3$, TFA, rt, 72 h	 I + II + III	566
C_{15-17} 	NaN_3, H_2SO_4, rt, 2 h	 I + II	601

Ar = 

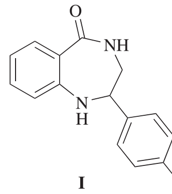
R	I	II	III
H	(40)	(20)	(22)
F	(35)	(—)	(—)
Cl	(33)	(—)	(—)
Br	(28)	(—)	(—)
MeO	(—)	(—)	(—)

R^1	R^2	R^3	I	II
H	H	Ph	(81)	(0)
H	H	4-ClC_6H_4	(79)	(0)
Me	H	Ph	(0)	(73)
Me	Me	Ph	(0)	(84)
Et	H	Ph	(0)	(76)

C_{15-21}

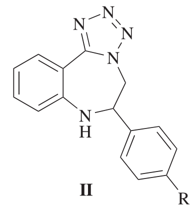


A: NaN_3, H_2SO_4, AcOH, 50°, 4 h
B: $TMSN_3$, TFA, rt, 5 d
C: NaN_3, $SnCl_4$, CH_2Cl_2, rt, 5 d
D: NaN_3, TFA, rt, 5 d



I

+

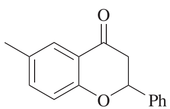


II

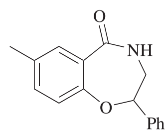
73

R	Conditions	**I**	**II**	R	Conditions	**I**	**II**
H	A	(35)	(30)	Me	C	(4)	(65)
H	B	(28)	(30)	Me	D	(5)	(40)
H	C	(5)	(60)	Ph	A	(30)	(30)
H	D	(5)	(38)	Ph	B	(35)	(30)
Me	A	(40)	(38)	Ph	C	(5)	(62)
Me	B	(35)	(35)	Ph	D	(5)	(40)

C_{16}

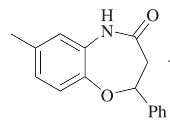


NaN_3, AcOH, 40°



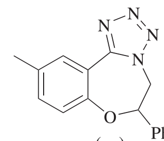
(—)

+



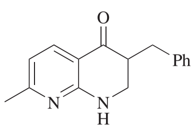
(—)

+

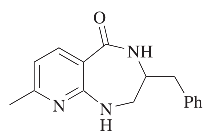


(—)

596



NaN_3, H_2SO_4, $CHCl_3$



(64)

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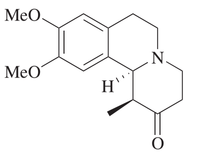
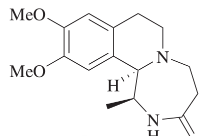
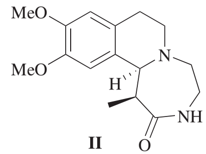
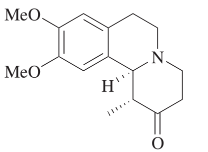
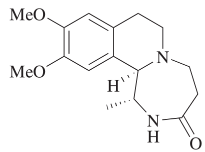
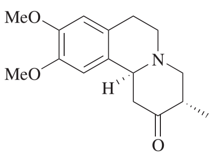
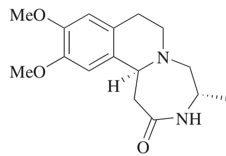
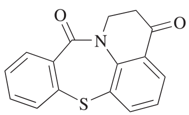
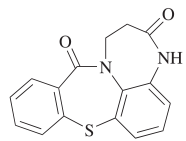
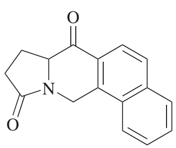
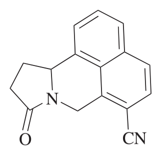
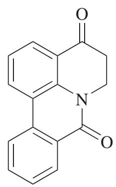
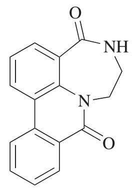
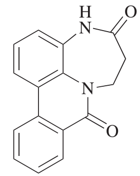
TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}		NaN_3, H_2SO_4, CH_2Cl_2, rt, 4 h	 **I** +  **II** **I + II** (69), **I**:**II** = —	600
		NaN_3, H_2SO_4, CH_2Cl_2, rt, 4 h	 (67)	600
		NaN_3, H_2SO_4, CH_2Cl_2, rt, 4 h	 (82)	600
		A: NaN_3, H_3PO_4, 65°, 5 h B: NaN_3, CCl_3CO_2H,[a] 80°, 20 h C: NaN_3, PPA, 65°, 5 h D: NaN_3, H_2SO_4, rt, 3 h	 Conditions: A (77), B (60), C (39), D (28)	603
		NaN_3, H_2SO_4, $CHCl_3$, 0° to rt, 3 h	 (32)	604

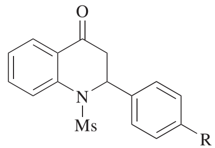
C$_{16-17}$



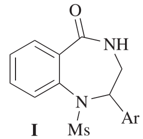
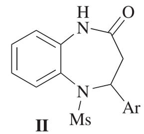
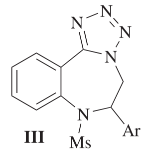
NaN$_3$, CCl$_3$CO$_2$H,[a] 60°

 (—) +  (—)

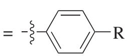
590



TMSN$_3$, TFA, rt, 72 h

 +  + 

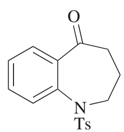
I, II, III

Ar = 

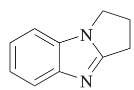
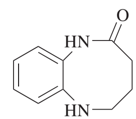
R	I	II	III
H	(35)	(25)	(20)
F	(30)	(10)	(20)
Cl	(35)	(20)	(30)
Br	(40)	(25)	(20)
MeO	(0)	(30)	(35)

605

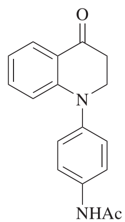
C$_{17}$



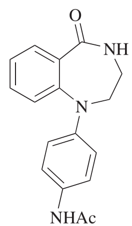
NaN$_3$, H$_2$SO$_4$, rt, 2.5 h

 (41) +  (—)

606

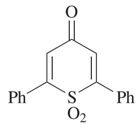
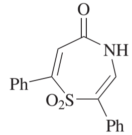
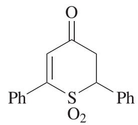
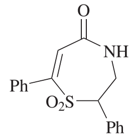
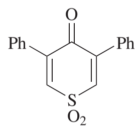
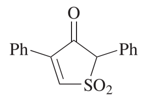
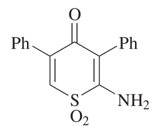
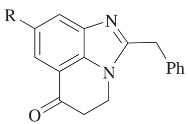
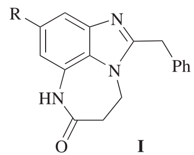
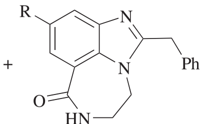
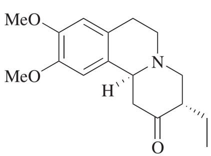
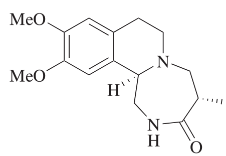
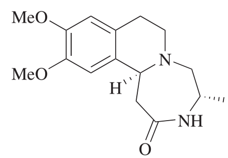


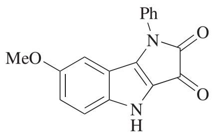
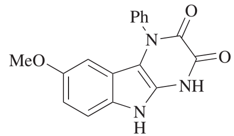
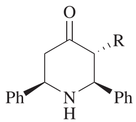
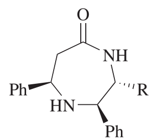
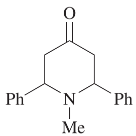
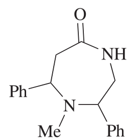
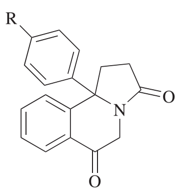
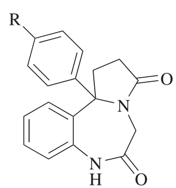
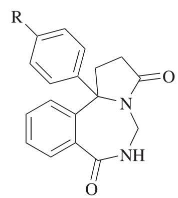
NaN$_3$, H$_2$SO$_4$, CHCl$_3$, rt, 3 h

 (74)

597

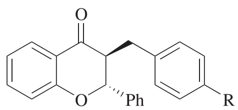
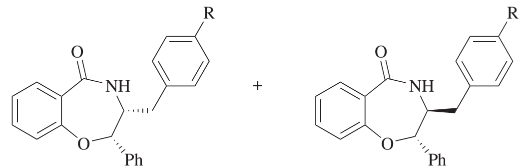
TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17} 	NaN_3, H_2SO_4, 0° to rt	 (58)	607
	NaN_3, H_2SO_4, 0° to rt	 (64)	607
	NaN_3, H_2SO_4, 0° to rt	 (30) +  (3)	607
	NaN_3, H_2SO_4, $CHCl_3$, 0° to rt, 16 h	 **I** +  **II** R / **I** / **II**: Cl (10) (76); O_2N (1) (74)	578
	NaN_3, H_2SO_4, $CHCl_3$, 0°	 (2) +  (90)	608

	Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
		NaN_3, H_2SO_4, $CHCl_3$	 (65)	322
C_{17-20}		NaN_3, H_2SO_4, $CHCl_3$, rt, 1.5 h	 (—) R: H, Me, Et, *i*-Pr	609
C_{18}		HN_3, H_2SO_4, $CHCl_3$, 0°, 1.5 h	 (95)	568
		NaN_3, H_2SO_4, $CHCl_3$, 50°, 1.5 h	 **I** +  **II**	610

R	**I**	**II**
H	(41)	(4)
Cl	(55)	(4)

TABLE 5. SCHMIDT REACTIONS OF HETEROCYCLIC KETONES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{22-23}			
	NaN_3, $AcOH/H_2SO_4$ (5:1), 55°, 12 h	 **I** + **II**	611

R	**I + II**	**I:II**
H	(80)	9:1
Cl	(72)	1:0
MeO	(63)	9:1

[a] Molten trichloroacetic acid (mp 57º) was used as solvent.

TABLE 6. SCHMIDT REACTIONS OF ALCOHOLS AND ALKENES WITH HN_3

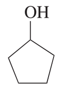
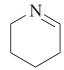
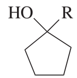
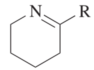
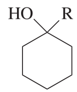
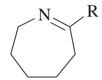
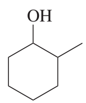
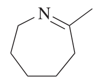
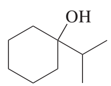
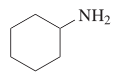
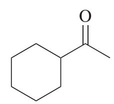
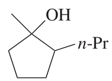
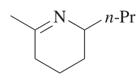
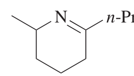
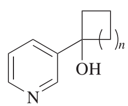
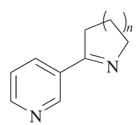
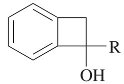
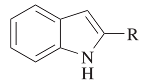
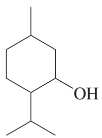
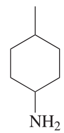
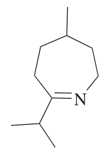
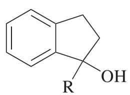
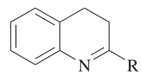
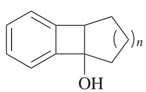
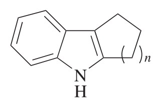
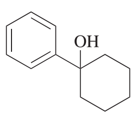
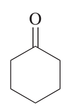
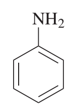
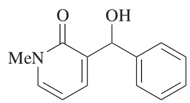
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	HN_3, H_2SO_4, $CHCl_3$, rt, 2 h	 (60)	612
$C_{6–9}$ 	1. HN_3, BF_3•OEt_2 2. H_2SO_4, $CHCl_3$	 R: Me (—); *n*-Pr (93); *n*-Bu (—)	39
$C_{6–12}$ 	NaN_3, H_2SO_4, rt, 2 h	 R: H (—)	613
		Me (22)	614
		Et (—)	614
		c-C_6H_{11} (—)	614
C_7 	HN_3, H_2SO_4, $CHCl_3$, rt, 2 h	 (30)	612
C_9 	NaN_3, H_2SO_4, rt, 2 h	 (—) +  (6)	614
	1. HN_3, BF_3•OEt_2 2. H_2SO_4, $CHCl_3$	 (—) +  (—)	39
$C_{9–10}$ 	HN_3, H_2SO_4, CH_2Cl_2	 *n*: 1 (65); 2 (75)	615

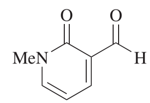
TABLE 6. SCHMIDT REACTIONS OF ALCOHOLS AND ALKENES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-15} 	1. HN_3, BF_3•OEt_2, PhH 2. H_2SO_4, $CHCl_3$, 0°	 R: Me (90); allyl (95); Ph (95); Bn (85)	616
C_{10} 	HN_3, H_2SO_4, $CHCl_3$, rt, 2 h	 (14) +  (7)	612
C_{10-16} 	HN_3, H_2SO_4, PhH	 R: Me (35); Bn (30)	41
C_{11-12} 	1. HN_3, BF_3•OEt_2, PhH, 0°, 10 min 2. H_2SO_4, PhH	 **I** *n*: 1 (85); 2 (90)	616
	HN_3, H_2SO_4, PhH	**I** *n*: 1 (85); 2 (90)	616
C_{12} 	NaN_3, H_2SO_4, rt, 2 h	 (42) +  (71)	614

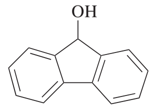
C_{13}



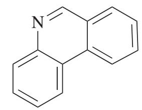
NaN_3, H_2SO_4, $CHCl_3$



(70) 329

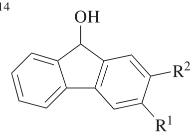


NaN_3, H_2SO_4, $CHCl_3$, 0–50°, 12 h

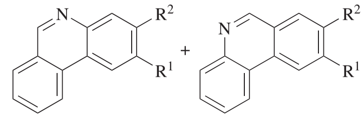


(—) 617

C_{13-14}

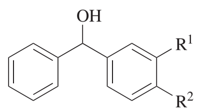


NaN_3, H_2SO_4, $CHCl_3$, rt, 12 h

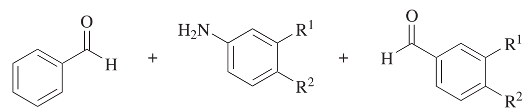


I + **II**

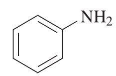
R^1	R^2	**I**	**II**	
O_2N	H	(2)	(90)	
H	O_2N	(5)	(83)	170
H_2N	H	(0)	(33)	
MeO	H	(11)	(21)	
H	MeO	(—)	(—)	
Me	H	(40)	(40)	
H	Me	(54)	(14)	



1. HN_3, Cl_3CCO_2H, $CHCl_3$
2. concd H_2SO_4, 0–55°



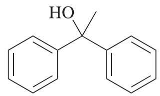
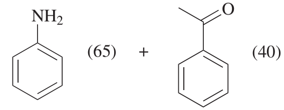
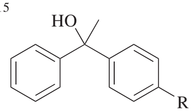
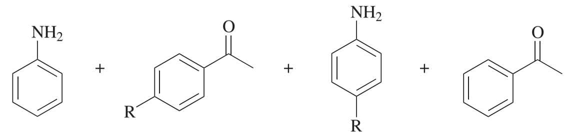
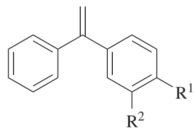
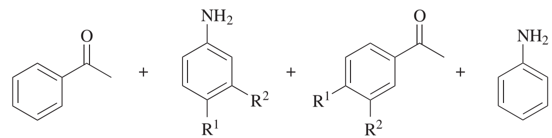
I + **II** (—) + **III**



IV (—)

R^1	R^2	**I + III**[a]	**I:III**	
H	H	(—)	—	617
H	Cl	(41)	1.0:1.3	618
Cl	H	(53)	1.0:3.7	618
H	Br	(73)	1.7:1.0	618
H	Me	(80)	3.4:1.0	618
H	MeO	(46)	6.3:1.0	618

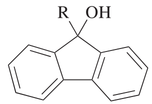
TABLE 6. SCHMIDT REACTIONS OF ALCOHOLS AND ALKENES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	NaN_3, H_2SO_4, rt	 (65) + (40)	619
C_{14-15} 	HN_3, CCl_3CO_2H, PhH	 **I** + **II** (—) + **III** + **IV** (—)	620
C_{14-16} 	NaN_3, H_2SO_4, $CHCl_3$, 0° to rt	 **I** + **II** (—) + **III** + **IV** (—)	

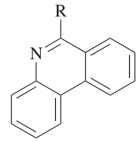
R	**I** + **III**[b]	**I**:**III**
Cl	(25)	3:1
Br	(48)	3:1
Me	(43)	1:4
MeO	(37)	0:1

R^1	R^2	**I**	**III**	Refs.
F	H	(46)	(26)	621
Br	H	(16)	(30)	621
H	Me	(34)	(15)	621
Me	Me	(37)	(7)	621
Et	H	(45)	(10)	621
EtO	H	(—)[c]	(—)[c]	42

C_{14-17}

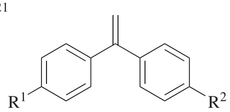


NaN_3, H_2SO_4, $CHCl_3$, rt, 1.5 h

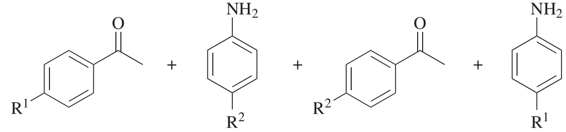


R		Refs.
Me	(47)	170
Et	(87)	622
i-Pr	(85)	622
t-Bu	(64)	622

C_{14-21}



NaN_3, H_2SO_4, $CHCl_3$, 0° to rt

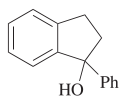


I + **II** (—) + **III** + **IV** (—)

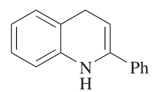
623

R^1	R^2	**I**	**III**
H	H	(55)	(—)
H	Cl	(18)	(29)
H	MeO	(49)	(8)
H	Me	(40)	(8)
MeO	Me	(8)	(39)
H	Ph	(39)	(17)
MeO	Ph	(11)	(36)
Me	Ph	(6)	(21)

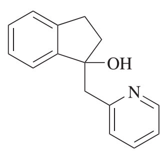
C_{15}



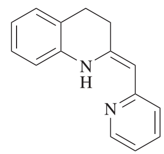
HN_3, H_2SO_4, $CHCl_3$, rt, 2 h



(91) 41

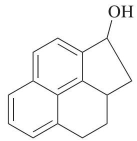
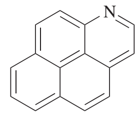
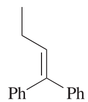
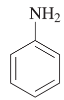
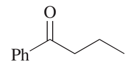
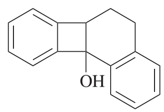
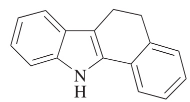
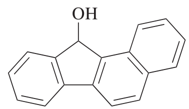
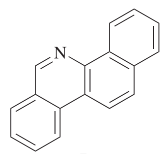
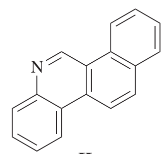
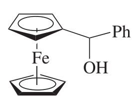
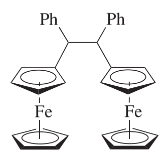
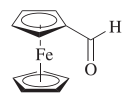
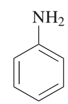


HN_3, H_2SO_4, $CHCl_3$, rt, 2 h



(93) 41

TABLE 6. SCHMIDT REACTIONS OF ALCOHOLS AND ALKENES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	1. NaN_3, MsOH, rt, 18 h 2. 10% Pd/C	 (—)	624
C_{16} 	NaN_3, H_2SO_4, rt	 (57) +  (64)	619
	1. HN_3, BF_3•OEt_2, PhH 2. H_2SO_4, PhH	 **I** (92)	616
	HN_3, H_2SO_4, PhH	**I** (92)	616
C_{17} 	1. NaN_3, CCl_3CO_2H, $CHCl_3$, rt, 2 h 2. H_2SO_4, $CHCl_3$	 **I** +  **II** **I** + **II** (—), **I**:**II** = 2.9:1	388
	1. HN_3, CCl_3CO_2H, PhH 2. AcOH, rt, 18 h	 (—) +  (—) +  (—)	625

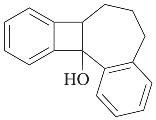
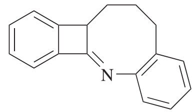
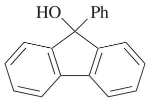
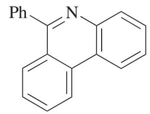
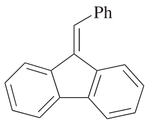
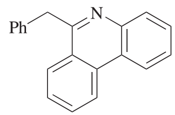
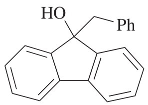
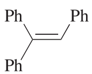
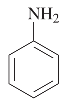
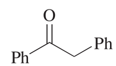
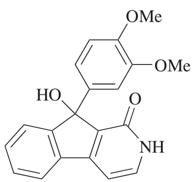
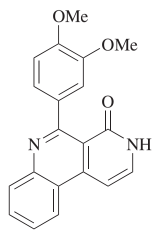
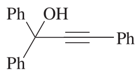
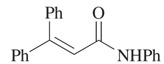
		1. HN_3, BF_3•OEt_2, PhH 2. H_2SO_4, $CHCl_3$	 (96)	616
C_{19}		NaN_3, H_2SO_4, $CHCl_3$, rt, 1.5 h	 (94)	170
C_{20}		NaN_3, H_2SO_4, $CHCl_3$, rt, 1.5 h	 (49) **I**	170
		NaN_3, H_2SO_4, $CHCl_3$, rt, 1.5 h	**I** (40)	170
		NaN_3, H_2SO_4, rt	 (30) +  (25)	619
		NaN_3, PPA, 25–45°, 12 h	 (87)	329

TABLE 6. SCHMIDT REACTIONS OF ALCOHOLS AND ALKENES WITH HN_3 (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{21}			
	HN_3, H_2SO_4, $CHCl_3$, 0°, 1.5 h	 (15)	353

[a] The products were isolated as mixtures of the corresponding carboxylic acids after oxidation.

[b] The products were isolated as mixtures of the corresponding amine hydrochlorides.

[c] The ratio of **I**:**III** was 6.2:1.

TABLE 7. SCHMIDT REACTIONS OF NITRO COMPOUNDS WITH HN_3

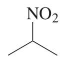
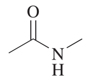
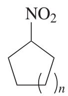
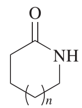
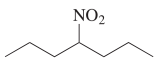
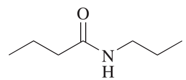
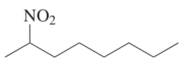
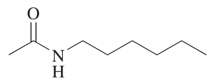
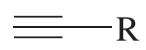
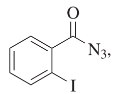
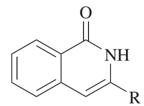
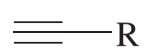
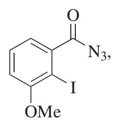
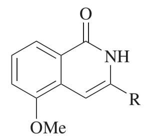
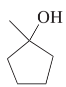
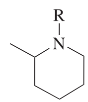
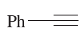
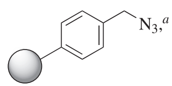
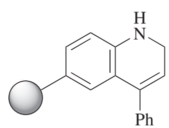
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	1. NaN_3, NaOH, H_2O, heat 2. H_2SO_4, $CHCl_3$, rt	 (44)	84
$C_{5–6}$ 	1. NaN_3, NaOH, H_2O, heat 2. H_2SO_4, $CHCl_3$, rt	 *n* 1 (67); 2 (81)	84
C_7 	1. NaN_3, NaOH, H_2O, heat 2. H_2SO_4, $CHCl_3$, rt	 (62)	84
C_8 	1. NaN_3, NaOH, H_2O, reflux 2. H_2SO_4, $CHCl_3$, rt	 (47)	84

Table 8. Schmidt Reactions of Carbocations with Alkyl and Acyl Azides

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-8} 	 Pd/C, PPh_3, CuI, Et_3N, EtOH, 80°, 12 h	 R: $HO(CH_2)_2$ (82); $HOCMe_2$ (82); $HO(CH_2)_3$ (85); $MeCH(OH)CH_2$ (60); $Cl(CH_2)_3$ (56); $HO(CH_2)_4$ (55); $NC(CH_2)_3$ (73); n-C_6H_{13} (44)	626
C_{4-9} 	 Pd/C, PPh_3, CuI, Et_3N, EtOH, 80°, 12 h	 R: $HO(CH_2)_2$ (78); $HO(CH_2)_3$ (84); $NC(CH_2)_3$ (65); n-C_6H_{13} (85); Ph (43); 4-MeC_6H_4 (40)	626
C_6 	1. RN_3, TfOH, CH_2Cl_2 2. $NaBH_4$, MeOH	 R: n-Bu (95); Bn (86)	24
C_8 	 TfOH, CH_2Cl_2, 0° to rt	 (>95)	627

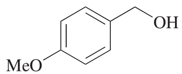
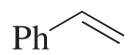
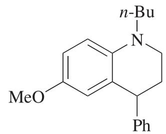
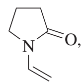
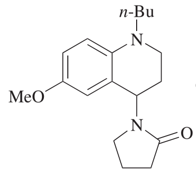
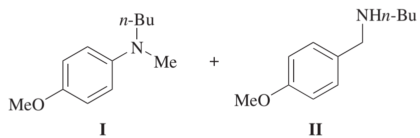
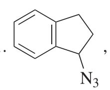
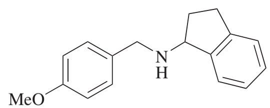
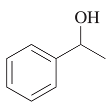
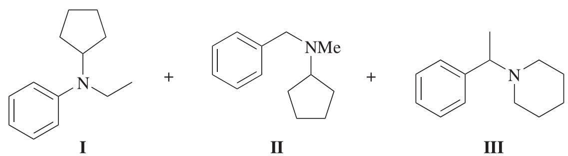
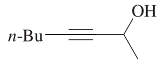
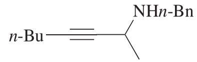
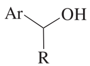
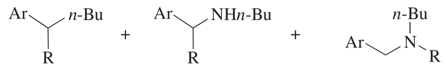
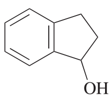
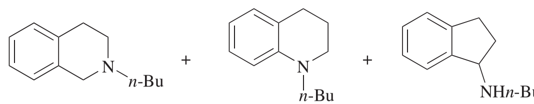
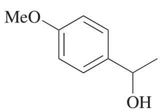
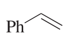
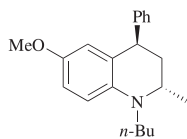
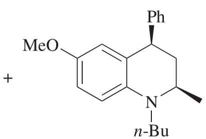
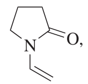
	, n-BuN_3, TfOH, CH_2Cl_2, rt, 12 h	 (66)	628
	, n-BuN_3, TfOH, CH_2Cl_2, rt, 12 h	 (77)	628
	1. n-BuN_3, $SnCl_4$, CH_2Cl_2 2. $NaBH_4$, MeOH	 **I** + **II** (97), **I**:**II** = 1:2	17
	1. , $SnCl_4$, CH_2Cl_2 2. $NaBH_4$, MeOH	 (69)	17
	1. c-$C_5H_9N_3$, $SnCl_4$, CH_2Cl_2 2. $NaBH_4$, MeOH	 **I** + **II** + **III** (57), **I**:**II**:**III** = 2.5:1:2	24

TABLE 8. SCHMIDT REACTIONS OF CARBOCATIONS WITH ALKYL AND ACYL AZIDES (*Continued*)

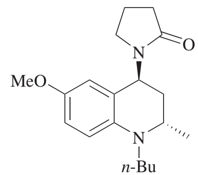
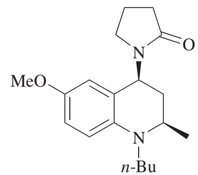
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	1. n-BuN_3, TfOH, CH_2Cl_2 2. $NaBH_4$, MeOH	 (48)	24
$C_{8–13}$ 	1. n-BuN_3, $SnCl_4$ or TfOH, CH_2Cl_2 2. $NaBH_4$, MeOH	 **I** **II** **III**	24

Aryl	R	**I + II + III**	**I:II:III**
Ph	Me	(81)	4.5:1:1
4-MeC_6H_4	H	(61)	1:6:0
4-$MeOC_6H_4$	H	(97)	1:2:0
3,4-$(OCH_2O)C_6H_3$	H	(100)	1:2:0
3,4-$(MeO)_2C_6H_3$	H	(98)	1:1.5:0
4-$MeOC_6H_4$	Me	(97)	12.5:2.5:1
4-$MeOC_6H_4$	i-Pr	(91)	3.5:0:1
4-PhC_6H_4	H	(77)	1:3:0

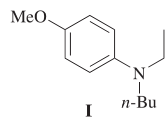
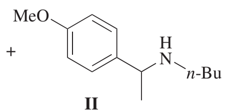
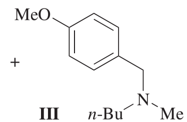
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	1. n-BuN_3, TfOH, PhH 2. $NaBH_4$	 **I** **II** **III** **I + II + III** (73), **I:II:III** = 28:8:1	24
	, n-BuN_3, $SnCl_4$, PhH, reflux, 12 h	 (10) +  (39)	628



n-BuN$_3$, TfOH, CH$_2$Cl$_2$, rt, 12 h

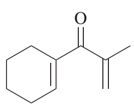
 (9) +  (27) 628

1. n-BuN$_3$, SnCl$_4$, CH$_2$Cl$_2$
2. NaBH$_4$, MeOH

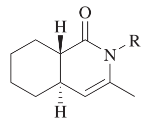
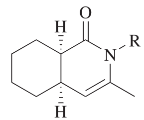
 **I** +  **II** +  **III** 17

I + II + III (95), **I:II:III** = 12:2.5:1

C$_{10}$



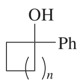
RN$_3$, BF$_3$•OEt$_2$, NaHCO$_3$, CH$_2$Cl$_2$, 0°, 0.5 h

 **I** +  **II**

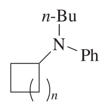
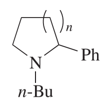
R	I + II	I:II
Bn	(80)	2:1
Ph(CH$_2$)$_3$	(70)	3:1
(*E*)-PhCH=CHCH$_2$	(73)	2.5:1

629

C$_{10-12}$



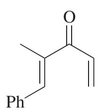
1. n-BuN$_3$, TfOH, CH$_2$Cl$_2$
2. NaBH$_4$, MeOH

 **I** +  **II**

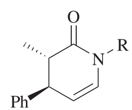
n	I + II	I:II
1	(97)	1:5.1
2	(66)	1.1:1
3	(82)	2.4:1

24

C$_{12}$



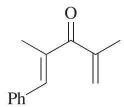
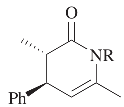
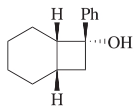
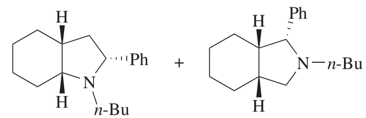
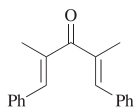
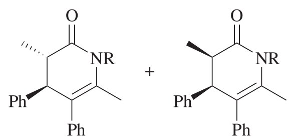
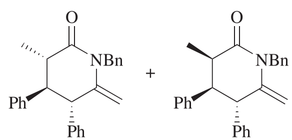
RN$_3$, BF$_3$•OEt$_2$, NaHCO$_3$, CH$_2$Cl$_2$, 0°, 1 h



R	
Bn	(62)
Ph(CH$_2$)$_3$	(40)
(*E*)-PhCH=CHCH$_2$	(43)

629

TABLE 8. SCHMIDT REACTIONS OF CARBOCATIONS WITH ALKYL AND ACYL AZIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	RN_3, BF_3•OEt_2, $NaHCO_3$, CH_2Cl_2, –78°, 0.5 h	 R: Bn (75); $Ph(CH_2)_3$ (80); (*E*)-PhCH=$CHCH_2$ (72)	629
C_{14} 	1. *n*-BuN_3, $SnCl_4$ or TfOH, CH_2Cl_2 2. $NaBH_4$, MeOH	 **I** + **II** **I + II** (91), **I**:**II** = 1:1	24
C_{19} 	RN_3, BF_3•OEt_2, $NaHCO_3$, CH_2Cl_2, –78°, 10 min	 **I** + **II** R / **I + II** / **I:II**: Bn (82) 2:1; $Ph(CH_2)_3$ (78) 2.3:1; (*E*)-PhCH=$CHCH_2$ (85) 2:1	629
	BnN_3, BF_3•OEt_2, CH_2Cl_2, –78°, 30 min; 0°, 15 min	 **I** + **II** **I + II** (72), **I**:**II** = 1:1	629

[a] The azide was derived from Merrifield resin.

TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES

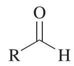
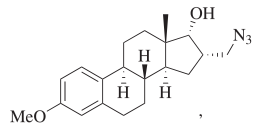
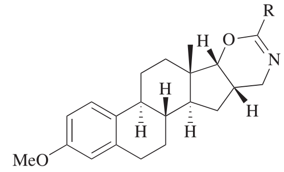
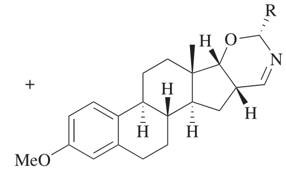
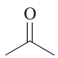
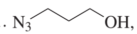
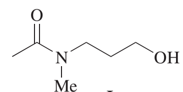
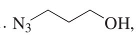
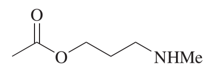
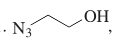
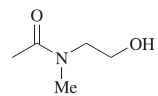
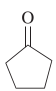
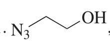
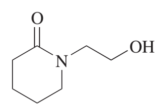
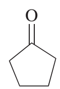
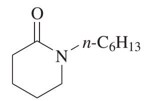
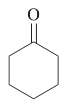
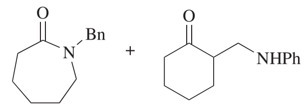
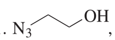
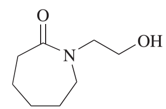
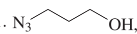
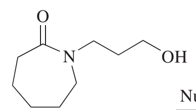
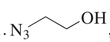
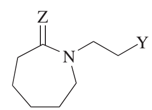
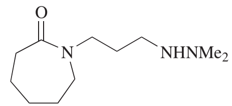
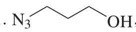
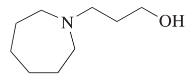
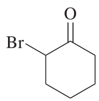
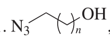
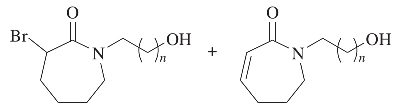
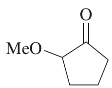
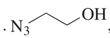
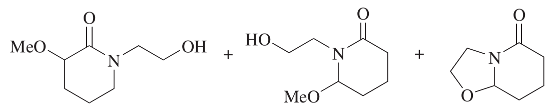
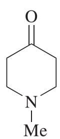
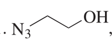
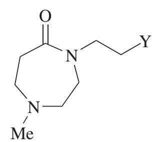
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{2-7} 	, BF_3•OEt_2, CH_2Cl_2, 0° to rt, 1 h	 I +  II R / I / II Me / (74) / (13) Ph / (66) / (10) 4-$O_2NC_6H_4$ / (70) / (22)	630
C_3 	1. , BF_3•OEt_2, CH_2Cl_2, rt, 30 min 2. $NaHCO_3$, rt, 30 min	 I (86)	95
	1. , BF_3•OEt_2, CH_2Cl_2 2. KOH	**I** (40) +  (19)	48
	1. , BF_3•OEt_2, CH_2Cl_2 2. KOH	 (87)	48
C_5 	1. , BF_3•OEt_2, CH_2Cl_2, rt, 3 h 2. $NaHCO_3$, rt, 30 min	 (96)	95

TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

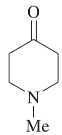
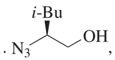
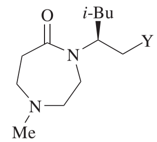
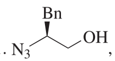
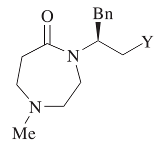
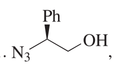
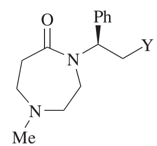
Substrate	Conditions	Product(s) and Yield(s) (%)				Refs.
C_5 	n-$C_6H_{13}N_3$, $TiCl_4$, CH_2Cl_2, rt, 16 h	 (<5)				85
C_6 	BnN_3, Promoter, CH_2Cl_2	 **I** + **II**	Promoter	**I**:**II**:BnN_3[a]		85
		I + **II** (—)	$TiCl_4$ (1.1 eq)	45:39:16		
			$TiCl_4$ (2.5 eq)	85:15:0		
			$SnCl_4$ (1.1 eq)	0:11:89		
			BF_3•OEt_2 (1.1 eq)	0:11:89		
			BF_3•OEt_2 (2.5 eq)	0:8:92		
	1. , BF_3•OEt_2, CH_2Cl_2, rt, 3 h 2. $NaHCO_3$, rt, 30 min	 (98)				95
	1. , BF_3•OEt_2, CH_2Cl_2, rt, 3 h 2. $NaHCO_3$, rt, 30 min	 (90)				95
	1. , BF_3•OEt_2, CH_2Cl_2, rt, 3 h 2. Nucleophile	 Nucleophile	Y	Z		46
		NaOH	HO	O	(98)	
		$Bu_4N^+Ph_3SiF_2^-$	F	O	(64)	
		Bu_4NI	I	O	(55)	
		NaN_3	N_3	O	(85)	
		NaCN	NC–	O	(82)	
		$NaCH(CO_2Me)_2$	$(MeO_2C)_2CH$	O	(34)	
		NaOPh	PhO	O	(74)	
		NaSPh	PhS	O	(95)	
		$NaCH(SO_2Ph)_2$	$(PhO_2S)_2CH$	O	(54)	
		$NaCH(CN)_2$	HO	$C(CN)_2$	(71)	

	1.  , BF$_3$•OEt$_2$, CH$_2$Cl$_2$, rt, 3 h 2. Me$_2$NNH$_2$	 (88)	46
	1.  , BF$_3$•OEt$_2$, CH$_2$Cl$_2$, rt, 3 h 2. NaBH$_4$	 (78)	46
	1.  , BF$_3$•OEt$_2$, CH$_2$Cl$_2$, 0° to reflux, 48 h 2. KOH		49
	1.  , BF$_3$•OEt$_2$, CH$_2$Cl$_2$, 0° to reflux, 48 h 2. KOH	 (25) (19) (10)	49
	1.  , BF$_3$•OEt$_2$, CH$_2$Cl$_2$, 0° to rt, 12 h 2. NaY, DMF, 70°, 24 h		631

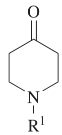
n	**I**	**II**
1	(44)	(14)
2	(42)	(10)

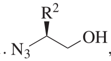
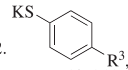
Y	
N_3	(19)
NC–	(37)
PhO	(32)
PhS	(15)
4-BrC$_6$H$_4$S	(62)
4-MeC$_6$H$_4$S	(63)
4-MeOC$_6$H$_4$S	(37)
4-(AcNH)C$_6$H$_4$S	(15)

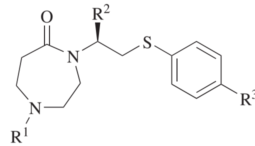
TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)			Refs.
C_6 	 1., BF_3•OEt_2, CH_2Cl_2, 0° to rt, 12 h 2. NaY, DMF, 70°, 24 h		Y		631
			N_3	(8)	
			NC–	(34)	
			PhO	(20)	
			PhS	(7)	
			4-BrC_6H_4S	(20)	
			4-MeC_6H_4S	(58)	
			4-$MeOC_6H_4S$	(34)	
			4-(AcNH)C_6H_4S	(35)	
	 1., BF_3•OEt_2, CH_2Cl_2, 0° to rt, 12 h 2. NaY, DMF, 70°, 24 h		Y		631
			N_3	(63)	
			NC–	(40)	
			PhO	(44)	
			PhS	(18)	
			4-BrC_6H_4S	(44)	
			4-MeC_6H_4S	(62)	
			4-$MeOC_6H_4S$	(40)	
			4-(AcNH)C_6H_4S	(62)	
	 1., BF_3•OEt_2, CH_2Cl_2, 0° to rt, 12 h 2. NaY, DMF, 70°, 24 h		Y		631
			N_3	(58)	
			NC–	(22)	
			PhO	(23)	
			PhS	(8)	
			4-BrC_6H_4S	(22)	
			4-MeC_6H_4S	(16)	
			4-$MeOC_6H_4S$	(20)	
			4-(AcNH)C_6H_4S	(18)	

C$_{6-8}$



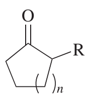
1. ,
BF$_3$•OEt$_2$, CH$_2$Cl$_2$,
0° to rt, 12 h
2. ,
DMF, 70°, 24 h

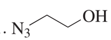


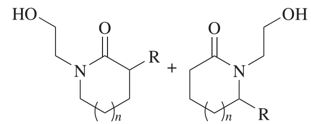
R^1	R^2	R^3	*b*	*c*
Me	H	Me	(58)	(61)
Me	H	MeO	(55)	(56)
Me	*i*-Bu	Me	(38)	(55)
Me	*i*-Bu	MeO	(85)	(47)
n-Pr	H	Me	(46)	(49)
n-Pr	H	MeO	(57)	(52)
n-Pr	*i*-Bu	Me	(56)	(58)
n-Pr	*i*-Bu	MeO	(47)	(52)

631

C$_{6-12}$



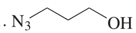
1. ,
BF$_3$•OEt$_2$, CH$_2$Cl$_2$, rt, 3 h
2. KOH

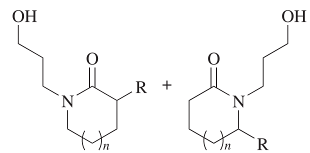


I **II**

R	*n*	**I + II**	**I:II**
Me	1	(89)	53:47
Me	2	(83)	45:55
MeO	2	(52)	91:9
Et	2	(85)	42:58
i-Pr	2	(80)	21:79
t-Bu	2	(11)	13:87
Ph	2	(93)	47:53

49

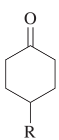
1. ,
BF$_3$•OEt$_2$, CH$_2$Cl$_2$, rt, 3 h
2. KOH



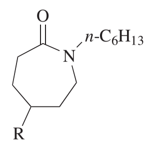
I **II**

R	*n*	**I + II**	**I:II**
Me	1	(86)	88:12
MeO	1	(76)	91:9
Me	2	(95)	55:45
Et	2	(94)	57:43
t-Bu	2	(0)	—
Ph	2	(92)	95:5

49



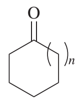
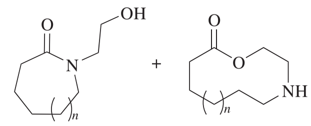
n-$C_6H_{13}N_3$, $TiCl_4$, CH_2Cl_2,
rt, 16 h



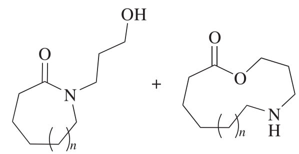
R	
H	(80)
t-Bu	(63)
Ph	(48)

85

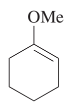
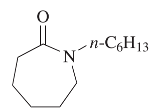
TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-12} 	1. N_3⁀⁀OH, BF_3•OEt_2, CH_2Cl_2 2. Base	 **I** + **II** (see below)	48

Base	n	**I**	**II**
KOH	1	(96)	(0)
$NaHCO_3$	1	(97)	(0)
KOH	2	(68)	(0)
$NaHCO_3$	2	(27)	(43)
KOH	3	(29)	(0)
KOH	4	(88)	(0)
$NaHCO_3$	4	(26)	(64)
KOH	5	(51)	(19)
$NaHCO_3$	5	(30)	(64)
KOH	7	(50)	(30)
$NaHCO_3$	7	(8)	(79)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. N_3⁀⁀⁀OH, BF_3•OEt_2, CH_2Cl_2 2. Base	 **I** + **II** (see below)	48

Base	n	**I**	**II**
KOH	1	(95)	(0)
$NaHCO_3$	1	(91)	(0)
KOH	2	(99)	(0)
$NaHCO_3$	2	(21)	(70)
KOH	3	(3)	(28)
KOH	4	(23)	(40)
$NaHCO_3$	4	(46)	(49)
KOH	5	(25)	(54)
$NaHCO_3$	5	(29)	(67)
KOH	7	(36)	(45)
$NaHCO_3$	7	(5)	(93)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	1. n-$C_6H_{13}N_3$, TfOH, CH_2Cl_2 2. NaI, acetone	 (27)	94

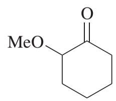
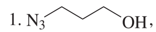
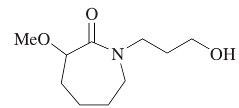
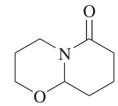
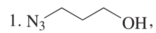
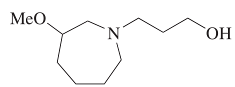
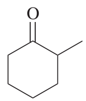
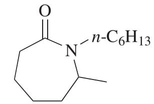
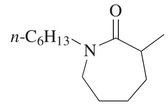
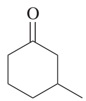
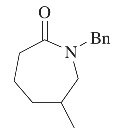
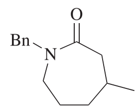
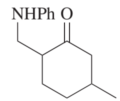
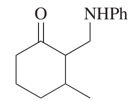
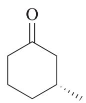
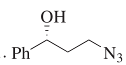
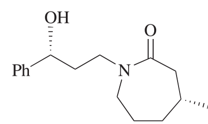
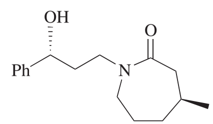
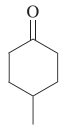
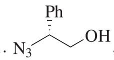
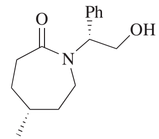
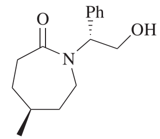
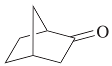
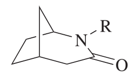
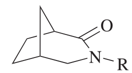
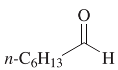
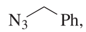
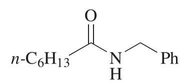
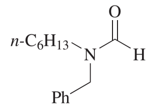
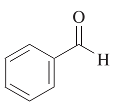
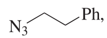
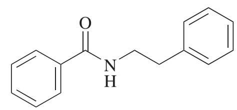
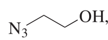
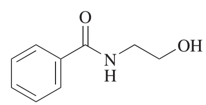
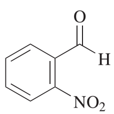
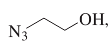
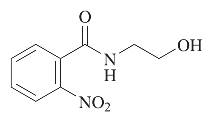
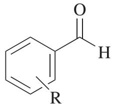
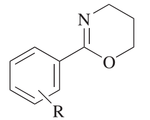
	1.  , BF_3•OEt_2, CH_2Cl_2, 0° to reflux, 48 h 2. KOH	 (61) +  (7)	49
	1.  , BF_3•OEt_2, CH_2Cl_2, 0° to reflux, 48 h 2. $NaBH_4$	 (64)	46
	n-$C_6H_{13}N_3$, $TiCl_4$, CH_2Cl_2, rt, 16 h	 **I** +  **II** **I + II** (5–19), **I**:**II** = 1.7:1	22
	BnN_3, $TiCl_4$, CH_2Cl_2, rt, 16 h	 **I** +  **II** +  **III** +  **IV** **I + II** (44), **III + IV** (11)	85
	1.  , BF_3•OEt_2, CH_2Cl_2, –82° to rt, 48 h 2. KOH	 **I** +  **II** **I + II** (90), **I**:**II** = 98:2	99

TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	1. , BF_3•OEt_2, *n*-pentane, –20°, 23 h 2. KOH	 (78) +  (22)	98
	RN_3, $TiCl_4$, CH_2Cl_2, rt, 16 h	 **I** +  **II** R | **I + II** | **I:II** *n*-C_6H_{13} | (40) | 1:5 Bn | (46) | 1:2	22
	, promoter, 17–19 h	 **I** +  **II** Promoter | **I** | **II** TFA | trace | trace $TiCl_4$ | (16) | (10)	632
	, H_2SO_4, 75°	 (10)	21
	, H_2SO_4, 75°	 (—)	21
	, H_2SO_4, 80°, 15 min	 (63)	21

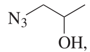


H_2SO_4, PhH, reflux

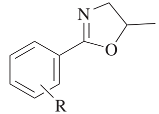


R	
4-O_2N	(70)
3-O_2N	(82)

45



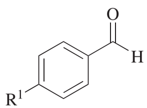
H_2SO_4, PhH, reflux

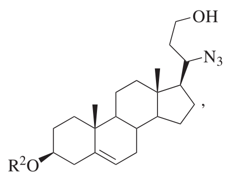


R	
4-O_2N	(53)
3-O_2N	(56)

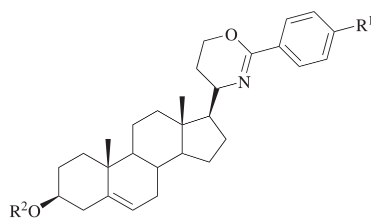
45

C_{7-8}





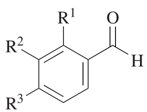
BF_3•OEt_2, CH_2Cl_2, 0°, 2 h

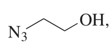


R^1	R^2	
H	H	(65)
H	Ac	(65)
Cl	H	(87)
Cl	Ac	(60)
Br	H	(82)
Br	Ac	(83)
O_2N	H	(92)
O_2N	Ac	(75)
MeO	H	(78)
MeO	Ac	(78)

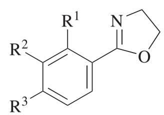
633

C_{7-9}





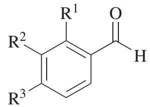
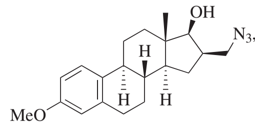
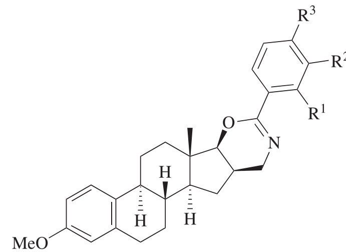
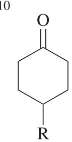
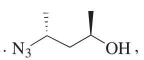
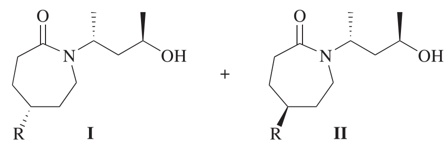
H_2SO_4, PhH, reflux



R^1	R^2	R^3	
H	H	H	(77)
HO	H	H	(15)
H	H	HO	(25)
Cl	H	Cl	trace
H	H	Cl	(75)
H	H	O_2N	(70)
H	O_2N	H	(73)
H	H	Me_2N	(10)

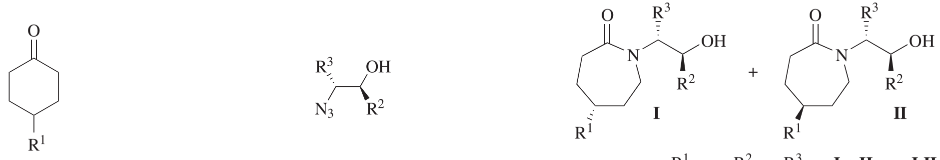
21

TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{7-9} 	 BF$_3$•OEt$_2$, CH$_2$Cl$_2$, 0° to rt, 1 h		630
C_{7-10} 	1.  , BF$_3$•OEt$_2$, CH$_2$Cl$_2$ 2. KOH	 **I** + **II**	98

R^1	R^2	R^3	
H	H	H	(82)
H	H	F	(82)
H	H	HO	(30)
H	H	O_2N	(92)
H	O_2N	H	(65)
O_2N	H	H	(30)
H	H	Cl	(88)
H	Cl	H	(62)
Cl	H	H	(26)
H	H	Br	(78)
H	H	Me	(30)
H	H	NC–	(59)
H	H	CHO	(49)
H	H	MeO	(73)
H	H	Me_2N	(22)
H	H	AcO	(87)

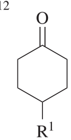
R	**I + II**	**I:II**
Me	(98)	59:41
t-Bu	(98)	60:40

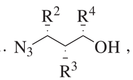


98

R^1	R^2	R^3	**I + II**	**I:II**
Me	H	Ph	(97)	78:22
Me	Ph	Ph	(51)	87:13
t-Bu	H	Ph	(83)	85:15
t-Bu	Ph	H	(73)	56:44
t-Bu	Ph	Ph	(64)	88:12

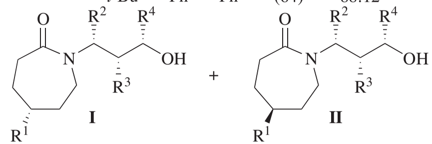
C_{7-12}



1.  ,

BF_3•OEt_2, CH_2Cl_2

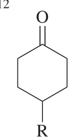
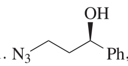
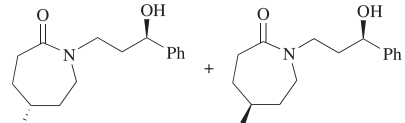
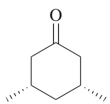
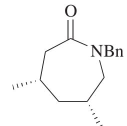
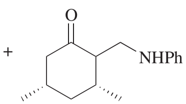
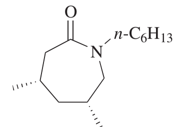
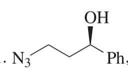
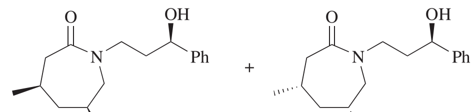
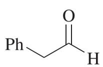
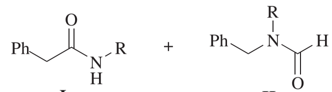
2. KOH



98

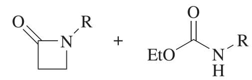
R^1	R^2	R^3	R^4	**I + II**	**I:II**
Me	H	Me	H	(93)	78:22
Me	Me	H	Me	(98)	98:2
Me	H	*i*-Pr	H	(88)	88:12
Me	Ph	H	H	(96)	89:11
Me	H	Ph	H	(93)	60:40
Me	H	H	Ph	(98)	93:7
t-Bu	H	Me	H	(98)	74:26
t-Bu	Me	H	Me	(94)	94:6
t-Bu	H	*i*-Pr	H	(85)	88:12
t-Bu	Ph	H	H	(94)	90:10
t-Bu	H	Ph	H	(98)	60:40
t-Bu	H	H	Ph	(100)	95:5
t-Bu	3,4,5-$(MeO)_3C_6H_2$	H	H	(94)	90:10
Ph	H	H	Ph	(99)	96:4

TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{7-12} 	1.  $BF_3•OEt_2$, CH_2Cl_2, –82° to rt, 48 h 2. KOH	 **I** + **II** R / **I + II** / **I:II** Me / (98) / 93:7 *t*-Bu / (100) / 98:2 Ph / (99) / 98:2	99
C_8 	BnN_3, $TiCl_4$, CH_2Cl_2, rt, 16 h	 (52) +  (35)	85
	n-$C_6H_{13}N_3$, $TiCl_4$, CH_2Cl_2, rt, 16 h	 (62)	85
	1.  $BF_3•OEt_2$, CH_2Cl_2, –82° to rt, 48 h 2. KOH	 **I** + **II** **I + II** (86), **I:II** = 99:1	98
	RN_3, promoter, 17–19 h	 **I** + **II**	632

RN_3, BF_3•OEt_2, CH_2Cl_2,

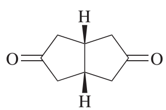
R	Promoter	**I**	**II**
n-C_6H_{13}	TFA	(19)	(13)
n-C_6H_{13}	$TiCl_4$	(29)	(26)
Bn	TFA	trace	trace
Bn	$TiCl_4$	(21)	(10)
$PhCH_2CH_2$	TFA	(16)	(16)
$PhCH_2CH_2$	$TiCl_4$	(22)	(19)

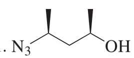


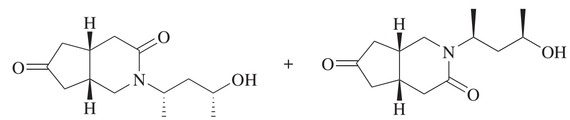
I **II**

R	**I**	**II**
Bn	(45)	(13)
n-C_6H_{13}	(58)	(40)
3-$MeOC_6H_4CH_2$	(36)	(60)
4-$MeOC_6H_4CH_2$	(27)	(35)
4-$MeO_2CC_6H_4CH_2$	(38)	(43)
4-$BrC_6H_4CH_2$	(45)	(34)

634



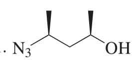
1.  ,
HCl, 0° to rt, 6 h
2. NaOH



I **II**

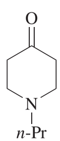
I + II (40), **I**:**II** = 3.2:1

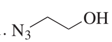
116

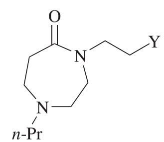
1.  ,
BF_3•OEt_2, CH_2Cl_2, 0° to rt
2. $NaHCO_3$

I + II (40), **I**:**II** = 2:1

116



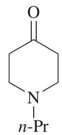
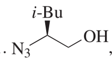
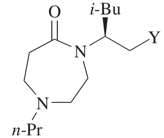
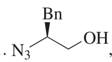
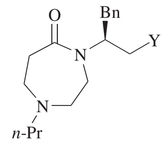
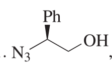
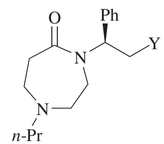
1.  ,
BF_3•OEt_2, CH_2Cl_2,
0° to rt, 12 h
2. NaY, DMF, 70°, 24 h



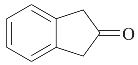
Y	
N_3	(24)
NC–	(28)
PhO	(40)
PhS	(4)
4-BrC_6H_4S	(40)
4-MeC_6H_4S	(15)
4-$MeOC_6H_4S$	(28)
4-(AcNH)C_6H_4S	(34)

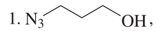
631

TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

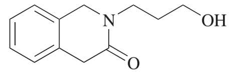
Substrate	Conditions	Product(s) and Yield(s) (%)			Refs.
C_8					
	1. , BF_3•OEt_2, CH_2Cl_2, 0° to rt, 12 h 2. NaY, DMF, 70°, 24 h		Y		631
			N_3	(22)	
			NC–	(33)	
			PhO	(41)	
			PhS	(12)	
			4-BrC_6H_4S	(41)	
			4-MeC_6H_4S	(17)	
			4-$MeOC_6H_4S$	(33)	
			4-(AcNH)C_6H_4S	(22)	
	1. , BF_3•OEt_2, CH_2Cl_2, 0° to rt, 12 h 2. NaY, DMF, 70°, 24 h		Y		631
			N_3	(35)	
			NC–	(36)	
			PhO	(37)	
			PhS	(14)	
			4-BrC_6H_4S	(37)	
			4-MeC_6H_4S	(43)	
			4-$MeOC_6H_4S$	(36)	
			4-(AcNH)C_6H_4S	(43)	
	1. , BF_3•OEt_2, CH_2Cl_2, 0° to rt, 12 h 2. NaY, DMF, 70°, 24 h		Y		631
			N_3	(37)	
			NC–	(26)	
			PhO	(17)	
			PhS	(22)	
			4-BrC_6H_4S	(33)	
			4-MeC_6H_4S	(24)	
			4-$MeOC_6H_4S$	(16)	
			4-(AcNH)C_6H_4S	(27)	

C$_9$

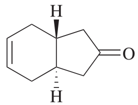


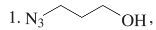


BF$_3$•OEt$_2$, CH$_2$Cl$_2$, rt, 3 h
2. NaHCO$_3$, rt, 30 min

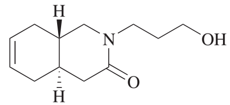


(80) 95

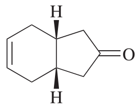


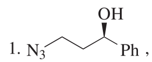


BF$_3$•OEt$_2$, CH$_2$Cl$_2$, rt, 3 h
2. NaHCO$_3$, rt, 30 min

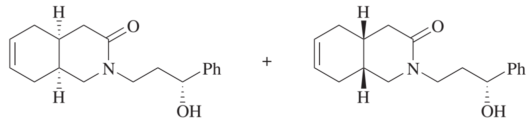


(88) 95



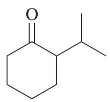


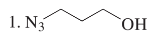
BF$_3$•OEt$_2$, CH$_2$Cl$_2$,
–82° to rt, 48 h
2. KOH



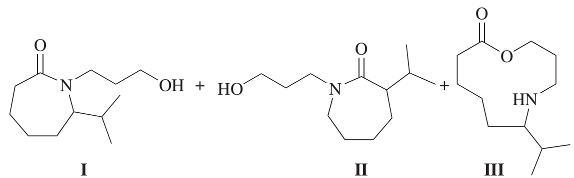
I **I + II** (57), **I**:**II** = 4:1 **II**

98





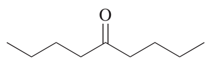
BF$_3$•OEt$_2$, CH$_2$Cl$_2$,
0° to reflux, 48 h
2. KOH

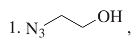


I **II** **III**

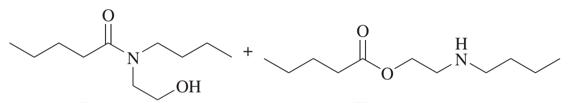
I + II + III (40), **I**:**II**:**III** = 54:23:23

49





BF$_3$•OEt$_2$, CH$_2$Cl$_2$
2. Base

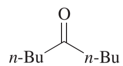
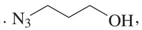
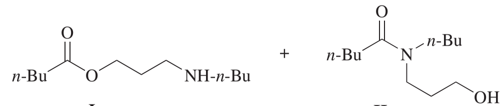
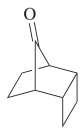
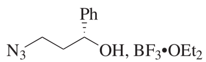
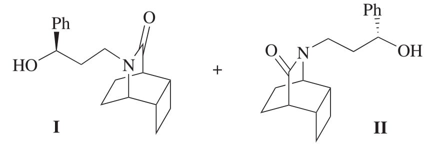
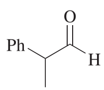
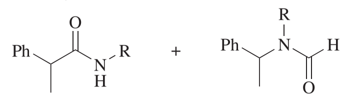


I **II**

Base	I	II
KOH	(55)	(28)
NaHCO$_3$	(6)	(92)

48

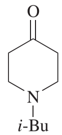
TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

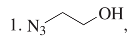
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	1. , BF_3•OEt_2, CH_2Cl_2 2. Base	 I + II	48
	, BF_3•OEt_2	 I + II	635
	RN_3, promoter, 17–19 h	 I + II	632

Base	I	II
KOH	(64)	(18)
$NaHCO_3$	(75)	(0)

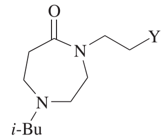
Conditions	I + II	I:II
CH_2Cl_2, 0° to rt, 1 h; reflux, 12 h	(22)	50:50
CH_2Cl_2, 0° to rt, 12 h; reflux, 5 h	(22)	56:44
CCl_4, rt, 12 h	(64)	*ca* 50:50
CCl_4, –20° to rt, 36 h	(83)	58:42

R	Promoter	I	II
n-C_6H_{13}	TFA	(23)	(8)
n-C_6H_{13}	$TiCl_4$	(35)	(27)
Bn	TFA	trace	trace
Bn	$TiCl_4$	(33)	(11)
$PhCH_2CH_2$	TFA	(13)	(5)
$PhCH_2CH_2$	$TiCl_4$	(20)	(30)



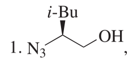


BF$_3$•OEt$_2$, CH$_2$Cl$_2$,
0° to rt, 12 h
2. NaY, DMF, 70°, 24 h

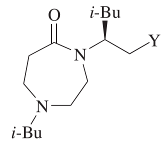


Y	
N_3	(29)
NC–	(34)
PhO	(45)
PhS	(19)
4-BrC$_6$H$_4$S	(45)
4-MeC$_6$H$_4$S	(50)
4-MeOC$_6$H$_4$S	(34)
4-(AcNH)C$_6$H$_4$S	(39)

631

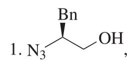


BF$_3$•OEt$_2$, CH$_2$Cl$_2$,
0° to rt, 12 h
2. NaY, DMF, 70°, 24 h

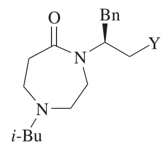


Y	
N_3	(10)
NC–	(60)
PhO	(49)
PhS	(36)
4-BrC$_6$H$_4$S	(49)
4-MeC$_6$H$_4$S	(28)
4-MeOC$_6$H$_4$S	(60)
4-(AcNH)C$_6$H$_4$S	(36)

631



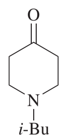
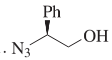
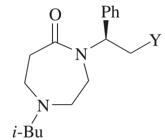
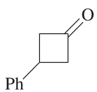
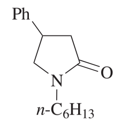
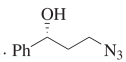
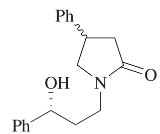
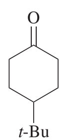
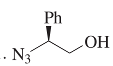
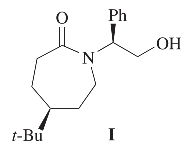
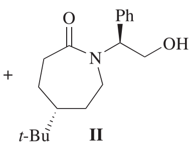
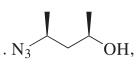
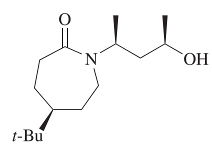
BF$_3$•OEt$_2$, CH$_2$Cl$_2$,
0° to rt, 12 h
2. NaY, DMF, 70°, 24 h

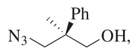


Y	
N_3	(50)
NC–	(35)
PhO	(36)
PhS	(19)
4-BrC$_6$H$_4$S	(36)
4-MeC$_6$H$_4$S	(43)
4-MeOC$_6$H$_4$S	(35)
4-(AcNH)C$_6$H$_4$S	(34)

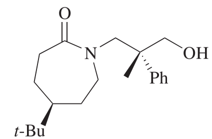
631

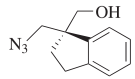
TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	1. , BF_3•OEt_2, CH_2Cl_2, 0° to rt, 12 h 2. NaY, DMF, 70°, 24 h	 Y: N_3 (53); NC- (18); PhO (27); PhS (10); 4-BrC_6H_4S (12); 4-MeC_6H_4S (19); 4-$MeOC_6H_4S$ (23); 4-$(AcNH)C_6H_4S$ (21)	631
C_{10} 	n-$C_6H_{13}N_3$, $TiCl_4$, CH_2Cl_2, rt, 16 h	 (51)	85
	1. , BF_3•OEt_2, CH_2Cl_2, –82° to rt, 48 h 2. KOH	 (82)[d]	98
	1. , BF_3•OEt_2, n-pentane, –20°, 23 h 2. KOH	 **I** +  **II** **I + II** (70), **I:II** = 7.2:1	95
	1. , BF_3•OEt_2, CH_2Cl_2 2. KOH	 (90–94)	95

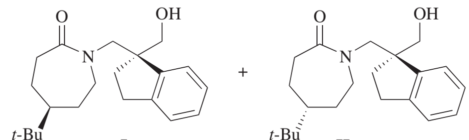


BF_3•OEt_2, CH_2Cl_2

 (99) 636

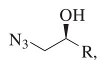


BF_3•OEt_2, CH_2Cl_2

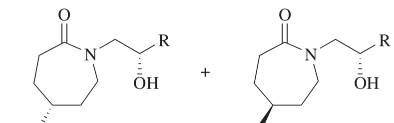


I **II**

I + II (85), **I:II** = 77:23 636

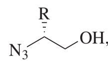


BF_3•OEt_2, CH_2Cl_2, –78°

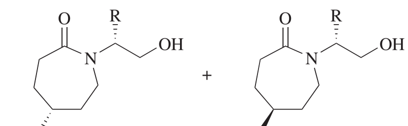


I **II** 637

R	**I + II**	**I:II**
$MeOCH_2$	(98)	97:3
c-C_6H_{11}	(91)	56:44

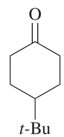
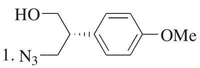
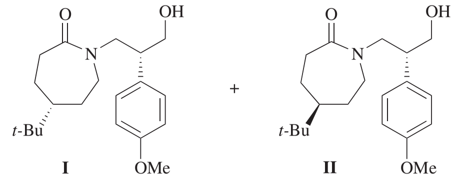
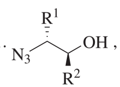
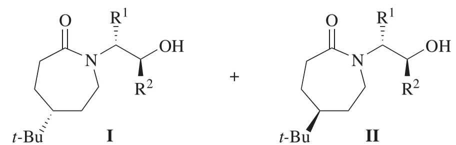


BF_3•OEt_2, CH_2Cl_2, –78°



I **II** 637

R	**I + II**	**I:II**
$MeOCH_2$	(96)	83:17
c-C_6H_{11}	(—)	75:25

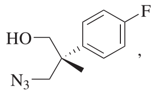
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	1. , BF_3•OEt_2, –78° to rt 2. 10% aq KOH		638
	1. , BF_3•OEt_2, CH_2Cl_2, –78° to rt 2. 10% aq KOH		638

First reaction (I + II):

Solvent	I + II	I:II
pentane/CH_2Cl_2	(78)	47:53
toluene	(97)	47:53
Et_2O	(98)	54:47
diglyme	(99)	72:28
CH_2Cl_2	(99)	47:53

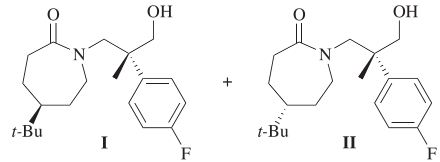
Second reaction (I + II):

R^1	R^2	I + II	I:II
H	c-C_6H_{11}	(91)	56:44
c-C_6H_{11}	H	(85)	75:25
Ph	H	(89)	85:15
4-$O_2NC_6H_4$	H	(97)	66:34
3,4,5-$(MeO)_3C_6H_2$	H	(96)	86:14

1. 

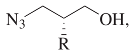
BF_3•OEt_2, CH_2Cl_2, –78° to rt

2. 10% aq KOH

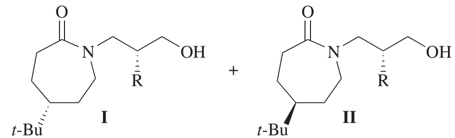


I + **II** (93), **I**:**II** = 93:7

638

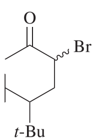


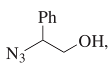
BF_3•OEt_2, CH_2Cl_2



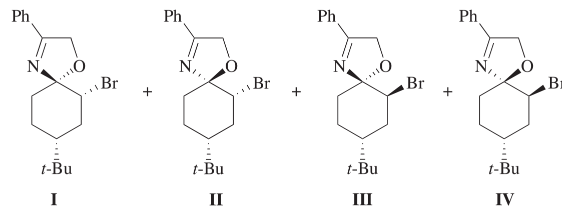
R	I + II	I:II
Me	(—)	74:26
i-Pr	(—)	88:12
Ph	(85)	64:36
4-FC_6H_4	(73)	69:31
4-$O_2NC_6H_4$	(86)	76:24
4-BrC_6H_4	(90)	68:32
4-$MeOC_6H_4$	(99)	47:53
3,4,5-$(MeO)_3C_6H_2$	(99)	43:57

636





BF_3•OEt_2, CH_2Cl_2



I + **II** + **III** + **IV** (47), **I**:**II**:**III**:**IV** = —

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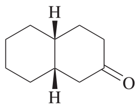
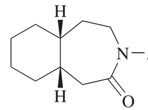
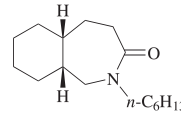
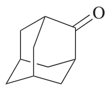
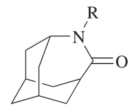
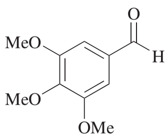
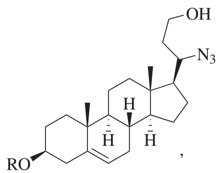
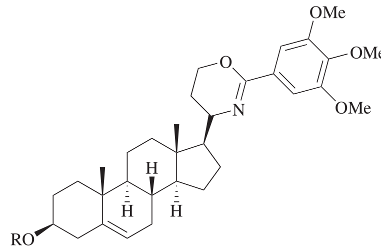
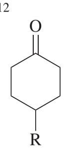
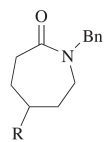
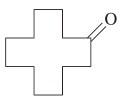
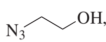
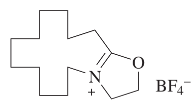
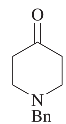
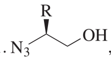
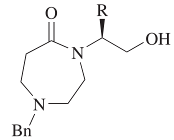
TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	n-$C_6H_{13}N_3$, $TiCl_4$, CH_2Cl_2, rt, 16 h	 (25) +  (25)	85
	RN_3, $TiCl_4$, CH_2Cl_2, rt, 16 h	 R: n-C_6H_{13} (100); Bn (98)	85
	, BF_3•OEt_2, CH_2Cl_2, 0°, 2 h	 R: H (65); Ac (80)	633
$C_{10–12}$ 	BnN_3, $TiCl_4$, CH_2Cl_2, rt, 16 h	 R: t-Bu (65); Ph (70)	85
C_{12} 	, BF_3•OEt_2, CH_2Cl_2, –5°, 3 h; reflux, 192 h	 (90)	639

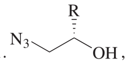


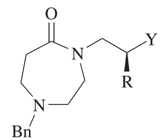
1. ,
BF$_3$•OEt$_2$, CH$_2$Cl$_2$, 0° to rt
2. NaHCO$_3$



R	
H	(79)
i-Bu	(76)
Ph	(64)
Bn	(85)

631

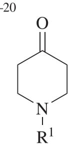
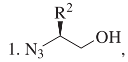
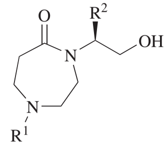
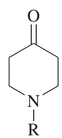
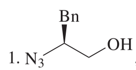
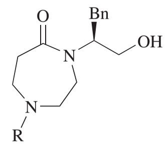
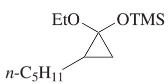
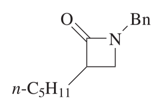
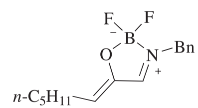
1. ,
BF$_3$•OEt$_2$, CH$_2$Cl$_2$, 0° to rt
2. NaY, DMF, 70°



R	Y	
H	N_3	(81)
H	PhO	(67)
H	PhS	(80)
H	NC–	(79)
i-Pr	N_3	(60)
i-Pr	PhO	(55)
i-Pr	PhS	(58)
i-Pr	NC–	(63)
i-Bu	N_3	(66)
i-Bu	PhO	(63)
i-Bu	PhS	(62)
i-Bu	NC–	(69)
Ph	N_3	(74)
Ph	PhO	(62)
Ph	PhS	(70)
Ph	NC–	(70)
Bn	N_3	(66)
Bn	PhO	(58)
Bn	PhS	(60)
Bn	NC–	(74)
4-BnOC$_6$H$_4$CH$_2$	N_3	(55)
4-BnOC$_6$H$_4$CH$_2$	PhO	(40)
4-BnOC$_6$H$_4$CH$_2$	PhS	(52)
4-BnOC$_6$H$_4$CH$_2$	NC–	(52)

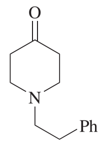
640

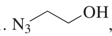
TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

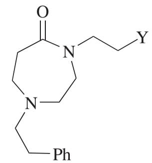
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12-20} 	 1. N_3 (azide shown), BF_3•OEt_2, TfOH, CH_2Cl_2 2. KOH, aq $NaHCO_3$	 (see table below)	641
	 1. N_3 (azide shown), promoter 2. KOH	 (see table below)	641
C_{13} 	BnN_3, BF_3•OEt_2, CH_2Cl_2, MW, 135°, 10 min	 (12) +  (5)	634

R^1	R^2	
Bn	*i*-Pr	(89)
Bn	*i*-Bu	(87)
Bn	4-$BnOC_6H_4CH_2$	(63)
Bn	$CbzNH(CH_2)_3$	(84)
Bn	$CbzNH(CH_2)_4$	(88)
Bn	$MeS(CH_2)_2$	(55)
Bn	BnO_2C	(62)
Cbz	*i*-Bu	(52)
$CbzNHCH_2CO$	*i*-Bu	(79)
Fmoc	*i*-Pr	(63)
Fmoc	*i*-Bu	(68)

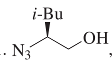
R	Promoter	
Bn	BF_3•OEt_2	(52)
Bn	TfOH	(84)
Cbz	BF_3•OEt_2	(46)
Cbz	TfOH	(51)
Fmoc	BF_3•OEt_2	(74)
Fmoc	TfOH	(55)

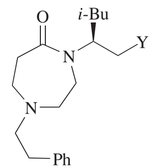


1. ,
BF$_3$•OEt$_2$, CH$_2$Cl$_2$,
0° to rt, 12 h
2. NaY, DMF, 70°, 24 h

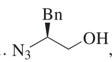


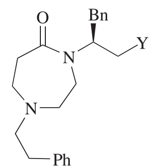
Y		
N_3	(32)	
NC–	(29)	631
PhO	(32)	
PhS	(18)	
4-BrC$_6$H$_4$S	(42)	
4-MeC$_6$H$_4$S	(41)	
4-MeOC$_6$H$_4$S	(29)	
4-(AcNH)C$_6$H$_4$S	(18)	

1. ,
BF$_3$•OEt$_2$, CH$_2$Cl$_2$,
0° to rt, 12 h
2. NaY, DMF, 70°, 24 h



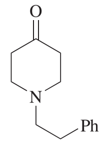
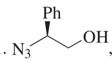
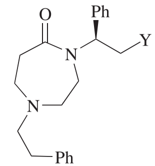
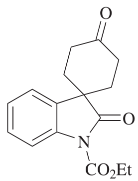
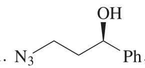
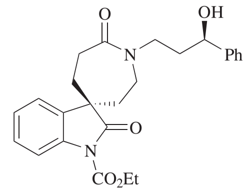
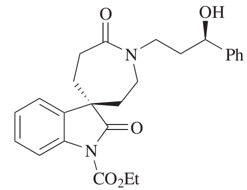
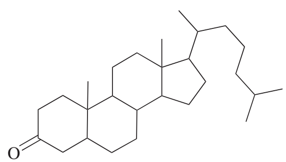
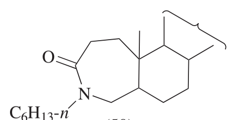
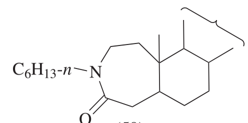
Y		
N_3	(8)	
NC–	(28)	631
PhO	(33)	
PhS	(20)	
4-BrC$_6$H$_4$S	(23)	
4-MeC$_6$H$_4$S	(29)	
4-MeOC$_6$H$_4$S	(18)	
4-(AcNH)C$_6$H$_4$S	(20)	

1. ,
BF$_3$•OEt$_2$, CH$_2$Cl$_2$,
0° to rt, 12 h
2. NaY, DMF, 70°, 24 h



Y		
N_3	(41)	
NC–	(22)	631
PhO	(30)	
PhS	(12)	
4-BrC$_6$H$_4$S	(26)	
4-MeC$_6$H$_4$S	(42)	
4-MeOC$_6$H$_4$S	(22)	
4-(AcNH)C$_6$H$_4$S	(42)	

TABLE 9. SCHMIDT REACTIONS OF ALDEHYDES AND KETONES WITH ALKYL AZIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	1. , BF_3•OEt_2, CH_2Cl_2, 0° to rt, 12 h 2. NaY, DMF, 70°, 24 h	 Y: N_3 (23); NC– (17); PhO (4); PhS (8); 4-BrC_6H_4S (7); 4-MeC_6H_4S (20); 4-$MeOC_6H_4S$ (17); 4-(AcNH)C_6H_4S (13)	631
C_{16} 	1. , BF_3•OEt_2, CH_2Cl_2, –80° to rt 2. $NaHCO_3$	 **I** +  **II** **I** + **II** (98), **I**:**II** = 87:13	476
C_{27} 	n-$C_6H_{13}N_3$, $TiCl_4$, CH_2Cl_2, rt, 16 h	 (50) +  (50)	85[e]

[a] The ratios were calculated on the basis of ^{1}H NMR integrations of the crude reaction mixtures and were normalized to 100 with the recovered azide.

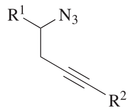
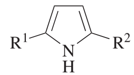
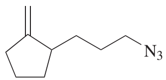
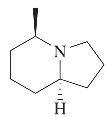
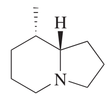
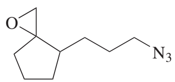
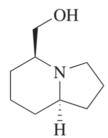
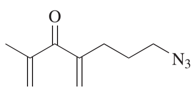
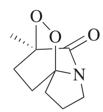
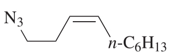
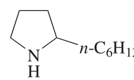
[b] Yields were obtained from reactions run on a Bodan Miniblock XT automated synthesizer.

[c] Yields were obtained from reactions run on a Chemspeed SLT100 automated synthesizer.

[d] The ratio of the two diastereomers was 65:35. The stereochemistry was not determined.

[e] The stereochemistry of the substrate was not specified in the reference.

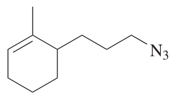
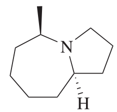
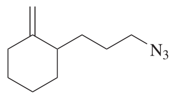
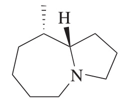
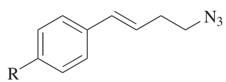
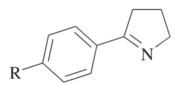
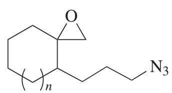
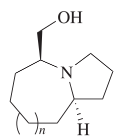
TABLE 10. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALKENES, ALKYNES, ALCOHOLS, EPOXIDES, AND OXYALLYL CATIONS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{8-12} 	(dppm)Au_2Cl_2 (2.5 mol %), $AgSbF_6$ (5 mol %), CH_2Cl_2, 35°		105
C_9 	1. TfOH, PhH 2. $NaBH_4$, MeOH	 **I** +  **II** **I** + **II** (71), **I**:**II** = 1:1	51
	1. Promoter, CH_2Cl_2 2. $NaBH_4$		104
	BF_3•OEt_2, air, –78 to 0°	 (69)	642
C_{10} 	1. $Hg(ClO_4)_2$•$3H_2O$, THF 2. $NaBH_4$	 (37)	50

R^1	R^2	
H	*n*-Bu	(76)
H	2-C_4H_3O	(61)
H	Ph	(68)
H	4-IC_6H_4	(87)
H	2-$MeOC_6H_4$	(88)
H	3-$CF_3C_6H_4$	(93)
n-Bu	*n*-Bu	(82)

Promoter	Temp (°)	
TfOH	–40	(25)
TMSOTf	–78	(21)
BF_3•OEt_2	–78	(50)
$TiCl_4$	–25	(43)
$EtAlCl_2$	–78	(63)

TABLE 10. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALKENES, ALKYNES, ALCOHOLS, EPOXIDES, AND OXYALLYL CATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	1. $Hg(ClO_4)_2$•$3H_2O$, CH_2Cl_2 2. $NaBH_4$	 (31)	50
	1. $Hg(OTf)_2$, THF 2. $NaBH_4$	**I** (45)	50
	1. TfOH, CH_2Cl_2 2. $NaBH_4$	**I** +  **II** **I** + **II** (79), **I**:**II** = 1:1	51
	1. $Hg(OTf)_2$, CH_2Cl_2 2. $NaBH_4$	**I** (87)	50
	1. $Hg(ClO_4)_2$•$3H_2O$, CH_2Cl_2 2. $NaBH_4$	**I** (84)	50
C_{10-11} 	1. TfOH, CH_2Cl_2, 0°, 30 min 2. Et_3N, rt, 15 min	 R: H (48); Cl (50); Br (40); Me (62); MeO (72)	643
	1. Et_2AlCl, CH_2Cl_2, –78°, 45 min 2. $NaBH_4$	 *n*: 1 (42); 2 (47)	644

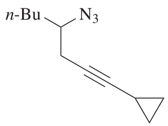
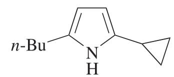
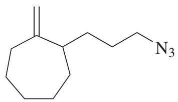
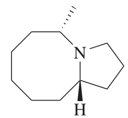
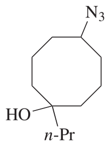
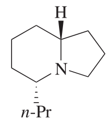
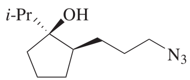
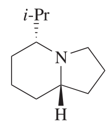
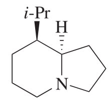
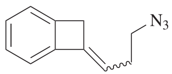
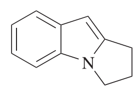
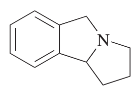
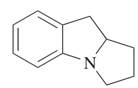
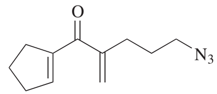
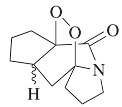
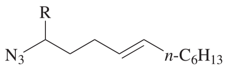
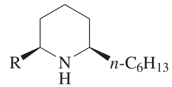
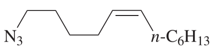
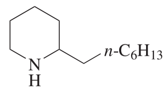
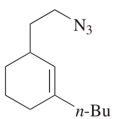
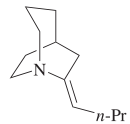
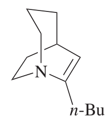
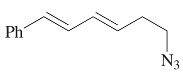
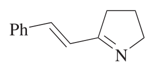
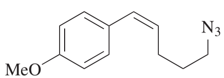
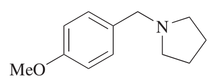
C_{11}			
	(dppm)Au_2Cl_2 (2.5 mol %), $AgSbF_3$ (5 mol %), CH_2Cl_2, 35°	 (78)	105
	1. $Hg(ClO_4)_2$•$3H_2O$, THF 2. $NaBH_4$	 (31)	50
	1. TfOH, Tf_2O, PhH 2. $NaBH_4$	 (47)	51
	1. TfOH, PhH 2. BH_3•SMe_2	 **I** +  **II** **I** + **II** (35), **I**:**II** = 1.3:1	51
	1. TfOH, PhH 2. $NaBH_4$	 **I** +  **II** +  **III** **I** + **II** + **III** (48), **I**:**II**:**III** = 3:1.3:1	102
	1. TfOH, PhH 2. BH_3•SMe_2	**II** + **III** (49), **II**:**III** = 1:1.5	102
	1. $Hg(OTf)_2$ 2. BH_3•SMe_2	**I** + **II** (50), **I**:**III** = 1.5:1	50

TABLE 10. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALKENES, ALKYNES, ALCOHOLS, EPOXIDES, AND OXYALLYL CATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	BF_3•OEt_2, air, –78 to 0°	 (60) dr = 2:1	642
C_{11-13} 	1. $Hg(ClO_4)_2$•$3H_2O$, THF 2. $NaBH_4$	 R: H (58); Et (44)	50
C_{12} 	1. $Hg(ClO_4)_2$•$3H_2O$, THF 2. $NaBH_4$	 (73)	50
	1. TfOH, PhH 2. NaOH	 **I** +  **II** — **I** + **II** (37), **I**:**II** = 1.1:1	51
	1. TfOH, CH_2Cl_2, 0°, 30 min 2. Et_3N, rt, 15 min	 (30)	643
	1. $Hg(ClO_4)_2$•$3H_2O$, THF 2. $NaBH_4$	 (43)	50

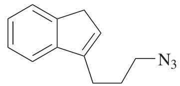
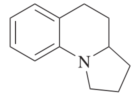
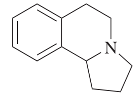
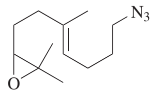
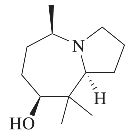
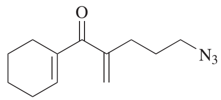
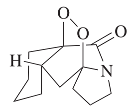
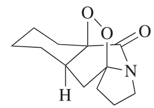
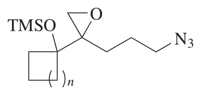
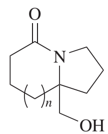
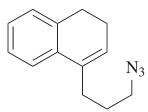
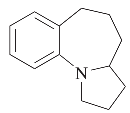
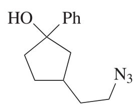
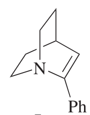
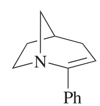
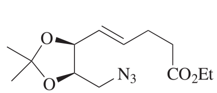
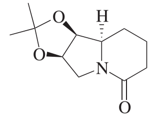
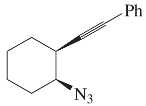
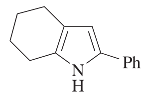
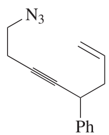
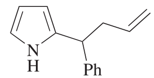
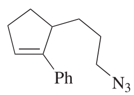
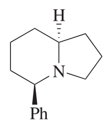
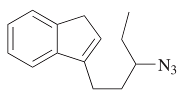
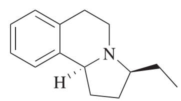
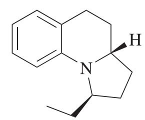
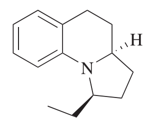
	1. TfOH, PhH 2. $NaBH_4$	 **I** +  **II** **I + II** (92), **I:II** = 2.3:1	102
	1. Et_2AlCl, CH_2Cl_2, –78°, 45 min 2. $NaBH_4$	 (36)	104
	BF_3•OEt_2, air, –78 to 0°	 **I** +  **II** **I + II** (60), **I:II** = 2:1	642
C_{12-14}			
	$TiCl_4$, CH_2Cl_2, –78° to rt	 *n* 1 (77) 2 (67) 3 (66)	645
C_{13}			
	1. TfOH, PhH 2. $NaBH_4$	 (72)	102
	1. TfOH, PhH 2. $NaBH_4$, MeOH	 **I** +  **II** **I + II** (76), **I:II** = 1.8:1	51

TABLE 10. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALKENES, ALKYNES, ALCOHOLS, EPOXIDES, AND OXYALLYL CATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}			
	1. $Hg(ClO_4)_2$•$3H_2O$, THF 2. $NaBH_4$	 (34)	50
C_{14}			
	(dppm)Au_2Cl_2 (2.5 mol %), $AgSbF_6$ (5 mol %), CH_2Cl_2, 35°	 (73)	105
	(dppm)Au_2Cl_2 (2.5 mol %), $AgSbF_6$ (5 mol %), CH_2Cl_2, 35°	 (41)	105
	1. TfOH, PhH, 15°, 5 min 2. $NaBH_4$, MeOH, 0° to rt, 24h	 (57)	101
	1. TfOH, PhH 2. $NaBH_4$	 +  +  **I** **II** **III** **I + II + III** (72), **I**:**II**:**III** = 2:1:1	102

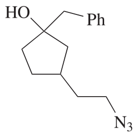
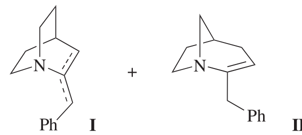
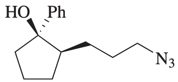
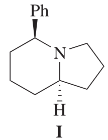
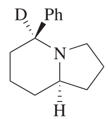
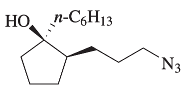
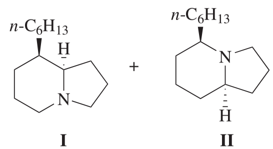
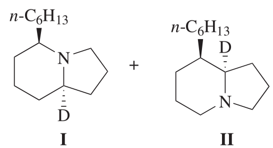
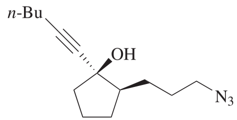
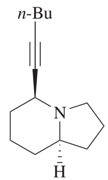
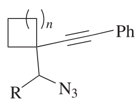
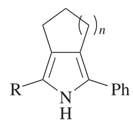
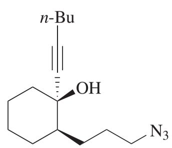
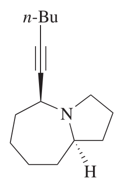
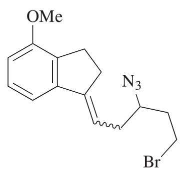
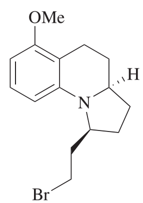
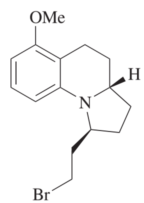
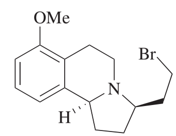
	1. TfOH, PhH 2. NaOH		**I** + **II** (21), **I**:**II** = 4.3:1	51
	1. TfOH, PhH 2. $NaBH_4$, EtOH	 (40)		51
	1. $SnCl_4$ 2. $NaBH_4$	**I** (63)		101
	1. TfOH 2. $NaBD_4$	 (50)		101
	1. TfOH, PhH 2. $NaBH_4$, MeOH		**I** + **II** (25), **I**:**II** = 1.4:1	17
	1. $SnCl_4$, CH_2Cl_2 2. BH_3•Me_2S	**I** + **II** (47), **I**:**II** = 1:1.7		17
	1. TfOH 2. $NaBD_4$		**I** + **II** (25), **I**:**II** = 1.3:1	101

TABLE 10. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALKENES, ALKYNES, ALCOHOLS, EPOXIDES, AND OXYALLYL CATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	1. $SnCl_4$, CH_2Cl_2, –78°, 10 min 2. $NaBH_4$, MeOH, rt, 20 h	 (60)	101
C_{14-21} 	$(dppm)Au_2Cl_2$ (2.5 mol %), $AgSbF_6$ (5 mol %), CH_2Cl_2, 35°	 R / *n* / yield: H 1 (80) Ph 2 (84)	105
C_{15} 	1. $SnCl_4$, CH_2Cl_2, –78°, 10 min 2. $NaBH_4$, MeOH, rt, 20 h	 (44)	101
	1. TfOH, PhH 2. $NaBH_4$	 **I** +  **II** +  **III** **I + II + III** (72), **I**:**II**:**III** = 1:1:0.6	102

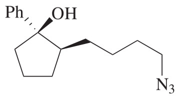
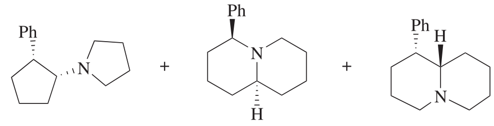
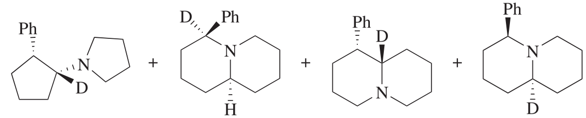
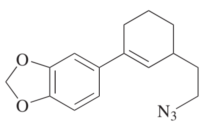
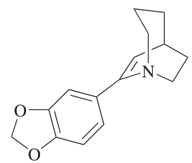
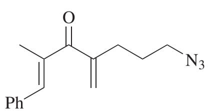
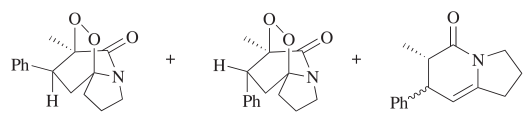
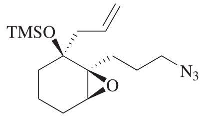
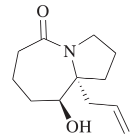
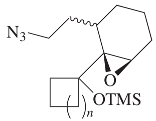
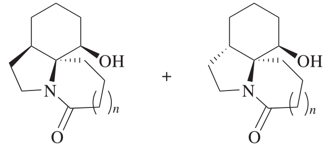
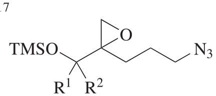
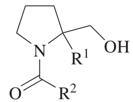
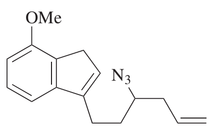
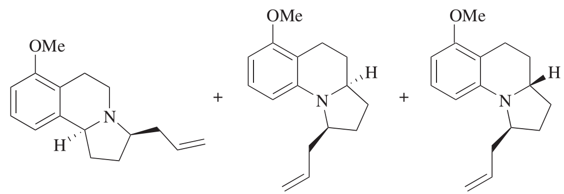
	1. TfOH, PhH 2. DIBAL-H	**I + II + III** (60), **I:II:III** = 2:1:1	102
	1. TfOH, PhH 2. L-Selectride	**I + II + III** (55), **I:II:III** = 4.5:0:1	102
	1. TfOH, PhH, 15°, 5 min 2. BH_3•SMe_2, THF, rt, 14 h	 **I** **II** **III** **I + II + III** (36), **I:II:III** = 2.3:1.9:1	101
	1. TfOH, PhH, 15°, 5 min 2. $NaBD_4$, MeOD, 0°, 24 h	 **I** **II** **III** **IV** **I + II + III + IV** (25), **I:II:III:IV** = 4:3.5:2:1	101
	1. TfOH, CH_2Cl_2, 0°, 5 min 2. NaOH	 (71)	23
	BF_3•OEt_2, air, –78 to 0°	 **I** **II** **III** dr = 5:1 **I + II + III** (72), **I:II:III** = 5:5:1	642

TABLE 10. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALKENES, ALKYNES, ALCOHOLS, EPOXIDES, AND OXYALLYL CATIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	$TiCl_4$, CH_2Cl_2, –78° to 0°	 (92)	645
C_{15-16} 	$TiCl_4$, CH_2Cl_2, –78° to 0°	 **I** + **II** *n* / **I + II** / **I:II** 1 / (78) / 7:1 2 / (92) / 8:1	645
C_{15-17} 	$TiCl_4$, CH_2Cl_2, –78° to rt	 R^1 / R^2 Ph / H / (80) Ph / Me / (95) 3-$MeOC_6H_4$ / Me / (77)	645
C_{16} 	1. TfOH, PhH 2. $NaBH_4$	 **I** + **II** + **III** **I + II + III** (86), **I:II:III** = 4:2:1	102
	1. $Hg(OTf)_2$ 2. $NaBH_4$	**I + II + III** (45), **I:II:III** = 0:2:1	50

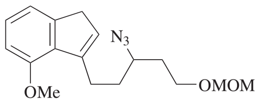
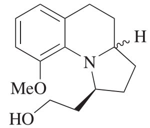
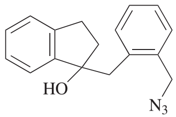
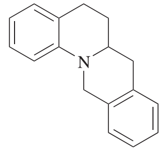
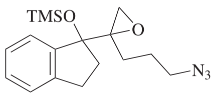
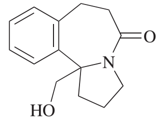
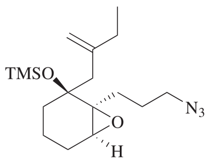
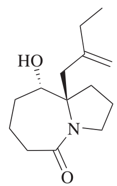
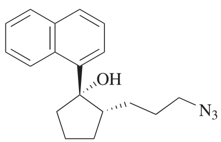
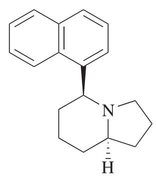
C_{17}				
	1. TfOH, PhH 2. $NaBH_4$		(47) dr = 1.2:1	102
	1. TfOH, PhH 2. BH_3•SMe_2		(67)	102
	$TiCl_4$, CH_2Cl_2, –78° to rt		(61)	645
	$TiCl_4$, CH_2Cl_2, –78 to 0°		(68)	646
C_{18}				
	1. $SnCl_4$, CH_2Cl_2, –78°, 12 min 2. BH_3•SMe_2, THF, rt, 12 h		(68)	103

TABLE 10. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALKENES, ALKYNES, ALCOHOLS, EPOXIDES, AND OXYALLYL CATIONS (*Continued*)

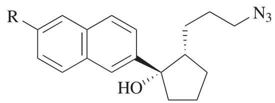
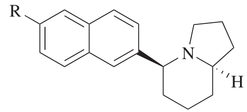
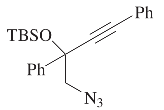
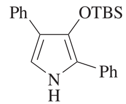
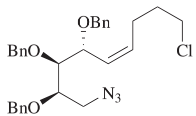
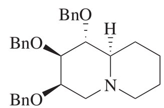
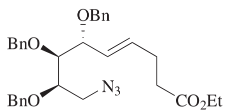
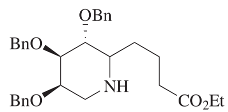
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18-19} 	1. $SnCl_4$, CH_2Cl_2, –78°, 12 min 2. BH_3•SMe_2, THF, rt, 12 h	 R: H (60); MeO (49)	103
C_{22} 	(dppm)Au_2Cl_2 (5 mol %), $AgSbF_6$ (10 mol %), $MeNO_2$, rt	 (58)	105
C_{30} 	1. $Hg(OTf)_2$, THF 2. $NaBH_4$, MeOH 3. MeONa, MeOH, reflux	 (63)	50
C_{32} 	1. $Hg(ClO_4)_2$•$3H_2O$, THF 2. $NaBH_4$, MeOH	 (41)	50

TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES

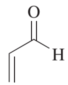
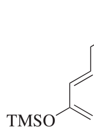
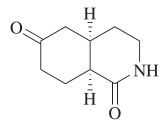
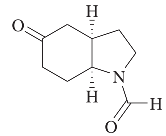
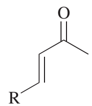
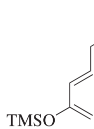
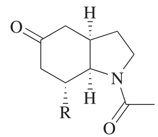
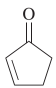
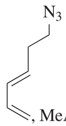
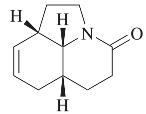
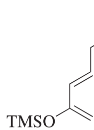
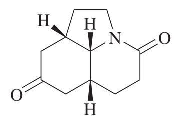
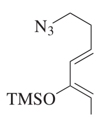
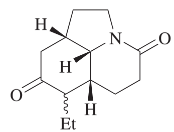
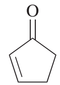
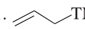
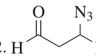
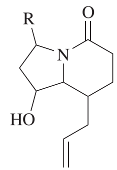
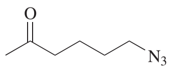
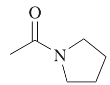
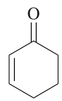
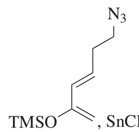
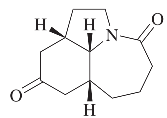
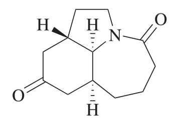
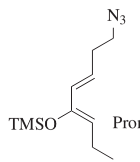
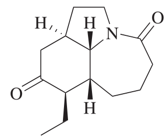
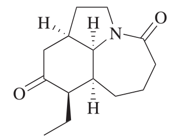
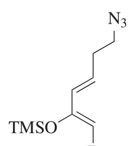
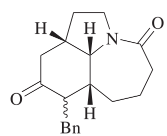
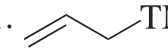
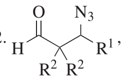
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	 , $MeAlCl_2$	 (36) +  (21)	647
C_{4-5} 	 , $SnCl_4$	 R: H (60); Me (59)	647
C_5 	 , $MeAlCl_2$	 (38)	647
	 , $SnCl_4$	 (52)	647
	 Et, $BF_3{\bullet}OEt_2$, CH_2Cl_2, –78° to rt	 (49)	648

TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

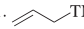
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	1. TMS, $TiCl_4$, CH_2Cl_2, –45°, 1 h 2.  R, –45°, 10 min; 0°, 6 h 3. $TiCl_4$ (2 eq), 0°, 18 h	 R: H (0); n-C_6H_{13} (0)	649
C_6 	TFA, CH_2Cl_2, rt, 16 h	 (75)	29
	, $SnCl_4$	 **I** +  **II** **I** + **II** (82), **I**:**II** = 3.4:1	647
	 Promoter	 **I** +  **II** Promoter / **I** + **II** / **I**:**II**: TMSOTf (70) 3:1; BF_3•OEt_2 (30) 0:100	650
	 Bn, BF_3•OEt_2, CH_2Cl_2, –78° to rt	 (56)	648

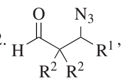
Conditions A:

1. TMS, $TiCl_4$, CH_2Cl_2, –45°, 1 h

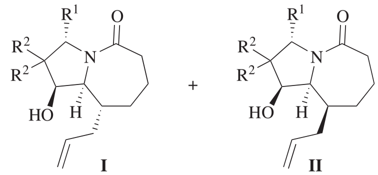
2. , –45°, 10 min; 0°, 24 h

Conditions B:

1. TMS, $TiCl_4$, CH_2Cl_2, –45°, 1 h

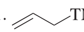
2. , –45°, 10 min; 0°, 6 h

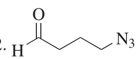
3. $TiCl_4$ (2 eq), 0°, 18 h



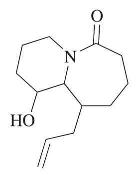
R^1	R^2	Conditions	**I + II**	**I:II**
H	H	A	(38)	6.4:1
H	H	B	(59)	2.6:1
H	Me	A	(42)	1:0
H	Me	B	(56)	1:0
n-C_6H_{13}	H	A	(36)	4.0:1
n-C_6H_{13}	H	B	(59)	1.8:1

649

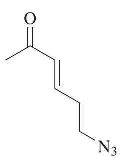
1. TMS, $TiCl_4$, CH_2Cl_2, –45°, 1 h

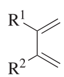
2. , –45°, 10 min; 0°, 6 h

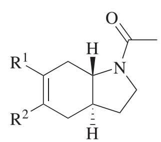
3. $TiCl_4$ (2 eq), 0°, 18 h

 (0)

649



, $MeAlCl_2$



R^1	R^2	
H	H	(54)
H	Me	(73)
Me	Me	(75)

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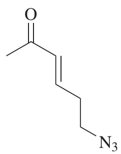
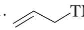
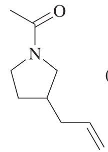
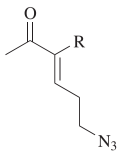
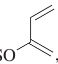
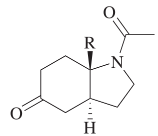
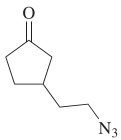
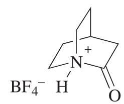
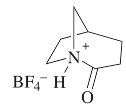
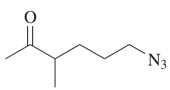
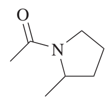
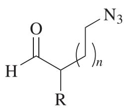
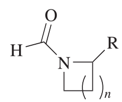
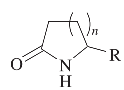
TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 	1. TMS, $TiCl_4$, CH_2Cl_2, –78°, 3 h; 0°, 5 h 2. MeOH (5 eq), rt, 45 min	 (46)	649
$C_{6–7}$ 	TMSO, $MeAlCl_2$	 R: H (71); Me (61)	647
C_7 	HBF_4, Et_2O, 20°	 **I** +  **II** **I** + **II** (38), **I**:**II** = 76:24	91
	TFA	 (75)	651
$C_{7–13}$ 	Promoter, rt, 17–19 h	 **I** +  **II**	632

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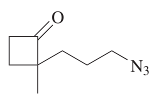
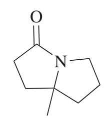
n	R	Promoter	**I**	**II**
1	allyl	TFA	(—)	(63)
1	allyl	$TiCl_4$	(—)	(90)
2	allyl	TFA	(60)	(—)
2	allyl	$TiCl_4$	(96)	(—)
3	allyl	TFA	(53)	(—)
3	allyl	$TiCl_4$	(41)	(—)
1	Bn	TFA	(—)	(77)
1	Bn	$TiCl_4$	(—)	(94)
2	Bn	TFA	(68)	(—)
2	Bn	$TiCl_4$	(85)	(—)
3	Bn	TFA	(71)	(—)
3	Bn	$TiCl_4$	(49)	(—)

C_8



TFA, CH_2Cl_2, rt



(66)

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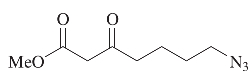
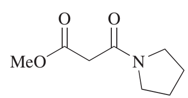
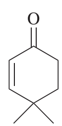


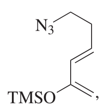
Promoter, CH_2Cl_2, rt



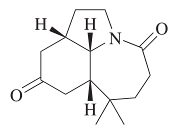
Promoter	Time	
TFA	12 h	(66)
$TiCl_4$	15 min	(64)

3





BF_3•OEt_2, CH_2Cl_2, –78° to rt



(25)

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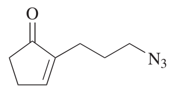
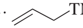
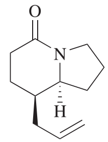
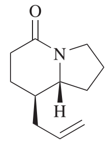
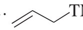
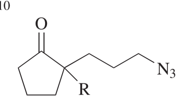
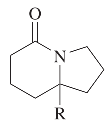
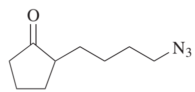
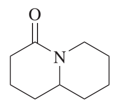
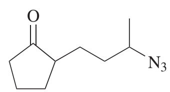
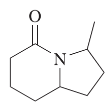
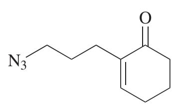
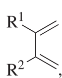
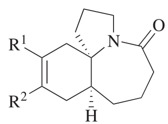
TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	1.  TMS, $TiCl_4$, CH_2Cl_2, –78°, 3 h; 0°, 5 h 2. *t*-BuOH (5 eq), rt, 45 min	 **I** +  **II** **I** + **II** (50), **I**:**II** = 64:36	649
	1.  TMS, $TiCl_4$, CH_2Cl_2, –78°, 3 h; 0°, 5 h 2. aq NH_4Cl 3. TFA	**II** (47)	649
C_{8-10} 	Promoter, CH_2Cl_2, rt		

R	Promoter	Time		Refs.
H	TFA	40 min	(83)	3
MeO_2C	TFA	16 h	(66)	29
MeO_2C	$TiCl_4$	20 min	(70)	3

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	$TiCl_4$, CH_2Cl_2, rt, 16 h	 (56)	29
	$TiCl_4$, CH_2Cl_2, rt, 16 h	 (68)	29
	, $MeAlCl_2$		647

R^1	R^2		Refs.
H	Me	(84)	647
Me	Me	(85)	

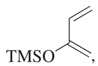
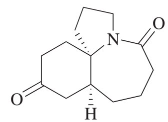
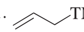
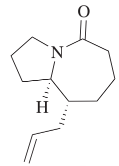
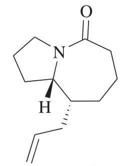
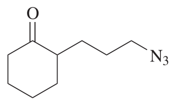
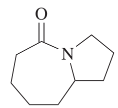
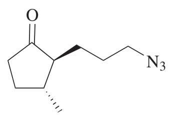
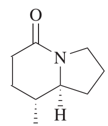
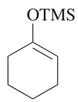
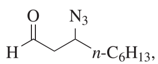
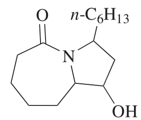
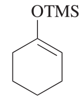
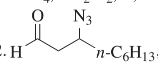
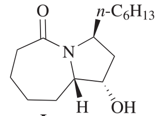
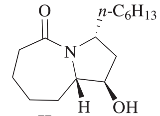
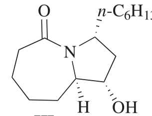
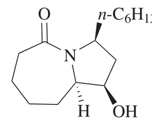
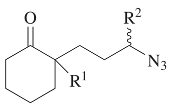
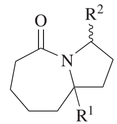
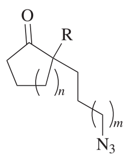
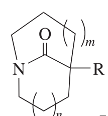
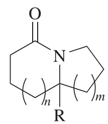
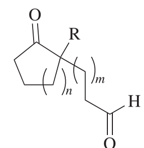
	, $MeAlCl_2$	 (91)	647
	1. TMS, $TiCl_4$, CH_2Cl_2, –78°, 3 h; 0°, 5 h 2. ROH (5 eq), rt, 45 min	 **I** +  **II** ROH / **I + II** / **I:II** MeOH / (75) / 7:3 *t*-BuOH / (79) / >9:1	649
	TFA, CH_2Cl_2, rt, 3.5 h	 (85)	29
	TFA, 0°, 40 min	 (93)	111
	, $TiCl_4$, –45°, 10 min; rt, 24 h	 (27)	649

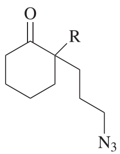
TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	1. $TiCl_4$, CH_2Cl_2, rt, 3 min 2.  –45°, 10 min; rt, 24 h	 **I** +  **II** +  **III** +  **IV** **I** + **II** + **III** + **IV** (56), **I**:(**II**+**III**+**IV**) = 56:44	649
C_{9-12} 	TFA, CH_2Cl_2, rt		3
C_{9-15} 	TfOH, CH_2Cl_2, 0°	 **I** +  **II** +  **III**	652

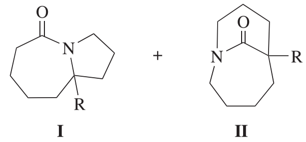
R^1	R^2	Time	
H	H	10 min	(90)
H	Me	20 min	(74)
EtO_2C	H	1 h	(93)

n	*m*	R	**I**	**II**	**III**
1	1	MeS	(0)	(43)	(0)
2	1	MeO	(23)	(52)	(0)
2	1	MeO_2C	(48)	(13)	(0)
2	1	MeS	(65)	(15)	(0)
2	2	MeS	(0)	(0)	(53)
3	1	MeS	(62)	(11)	(20)
4	1	MeS	(0)	(0)	(30)
2	1	PhS	(35)	(32)	(0)

C_{9-17}

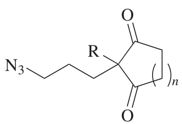


TfOH, CH_2Cl_2, 0°

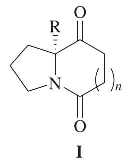


R	I + II	I:II
H	(85)	>95:5
Ph	(96)	>95:5

652



Promoter (x eq), rt



n	R	Promoter	x	Solvent	Time (h)	
1	Me	BF_3•OEt_2	4	Et_2O	24	(65)
1	Me	$TiCl_4$	2.5	Et_2O	1	(89)
1	Me	$EtAlCl_2$	2.5	Et_2O	6	(83)
1	Me	CuOTf	2.5	THF	72	(—)
1	Me	$ZnCl_2$	2.5	Et_2O	72	(—)
1	Me	$Yb(OTf)_3$	—	THF	72	(—)
2	Me	BF_3•OEt_2	4	Et_2O	24	(52)
2	Me	BF_3•OEt_2	2.5	Et_2O	24	(85)
2	Me	$TiCl_4$	1.1	Et_2O	1	(67)
2	Me	$EtAlCl_2$	1.1	Et_2O	24	(60)
2	Me	$EtAlCl_2$	2.5	Et_2O	6	(80)
3	Bn	$EtAlCl_2$	2.5	Et_2O	24	(87)

653

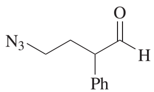
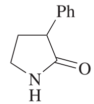
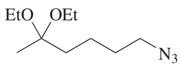
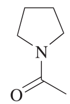
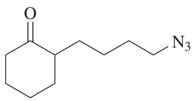
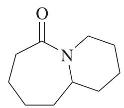
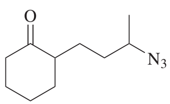
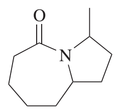
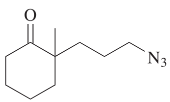
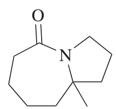
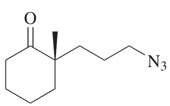
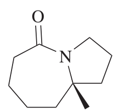
Promoter, rt, 72 h

I

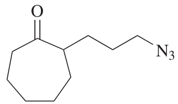
653

n	R	Promoter	Solvent		% er
1	Me	L-menthyloxyaluminum dichloride	hexane/toluene (1:1)	(35)	0
1	Me	(*S*)-BINOLAlCl	toluene	(18)	53.0:47.0
2	Me	L-menthyloxyaluminum dichloride	hexane/toluene (1:1)	(50)	52.5:47.5
2	Me	(*S*)-BINOLAlCl	toluene	(25)	52.0:48.0
3	Bn	L-menthyloxyaluminum dichloride	hexane/toluene (1:1)	(27)	0
3	Bn	(*S*)-BINOLAlCl	toluene	(10)	0

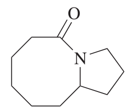
TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	TFA, CH_2Cl_2	 (29)	29
	1. TMSOTf, CH_2Cl_2, rt, 16 h 2. NaI, acetone	 (81)	94
	Promoter, CH_2Cl_2, rt, 16 h	 Promoter: TFA (0); BF_3•OEt_2 (29); $TiCl_4$ (91)	29
	TFA, CH_2Cl_2, 15 min	 (74)	29
	TFA, CH_2Cl_2, 15 min	 (87)	29
 91% ee	TFA, CH_2Cl_2, 1 h	 (87) 94.5:5.5 er	651

C_{11}

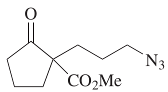


TFA, CH_2Cl_2, 3 h

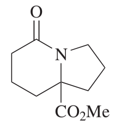


(80)

29

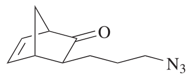


Promoter, CH_2Cl_2

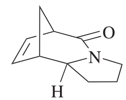


Promoter	Time	
TFA	16 h	(66)
$TiCl_4$	30 min	(70)

29

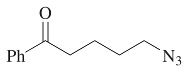


$TiCl_4$, CH_2Cl_2, 0° to rt

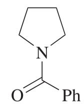


(89)

654

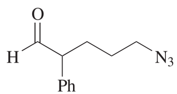


TFA, CH_2Cl_2, rt, 16 h

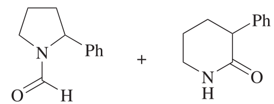


(77)

29



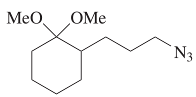
Promoter, CH_2Cl_2



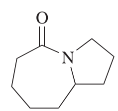
I **II**

Promoter	**I**	**II**
TFA	(81)	(8)
$AlCl_3$	(69)	(8)
$SnCl_4$	(59)	(15)
$ZnCl_2$	(48)	(17)
TMSOTf	(61)	(22)

29



1. TFA, CH_2Cl_2, rt, 16 h
2. NaI, acetone



(72)

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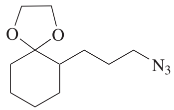
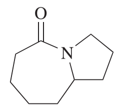
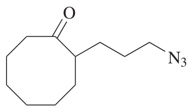
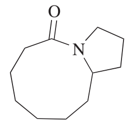
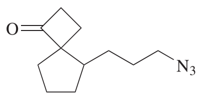
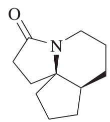
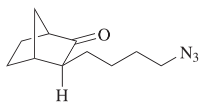
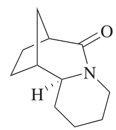
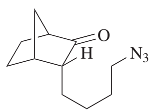
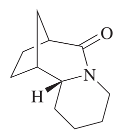
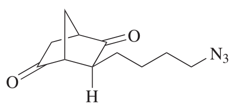
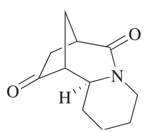
TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11} 	1. TFA, CH_2Cl_2, rt, 16 h 2. NaI, acetone	 (35)	94
	TFA, CH_2Cl_2, 16 h	 (96)	29
	$TiCl_4$, CH_2Cl_2, rt	 (39)	3
	$TiCl_4$, CH_2Cl_2	 (82)	655
	$TiCl_4$, CH_2Cl_2	 (92)	655
	$TiCl_4$, CH_2Cl_2	 (50–75)	655

C_{12}

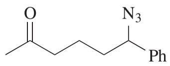
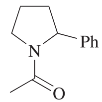
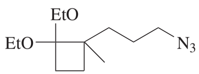
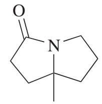
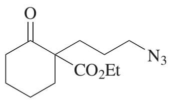
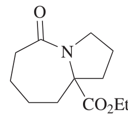
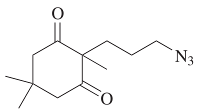
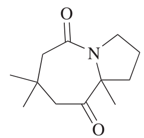
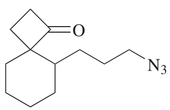
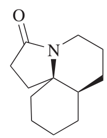
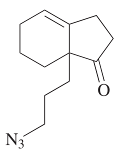
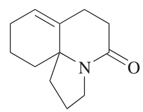
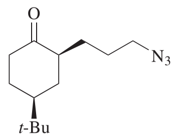
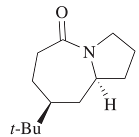
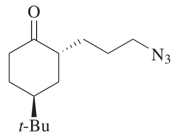
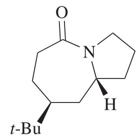
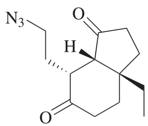
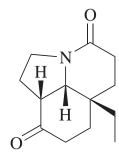
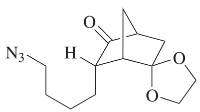
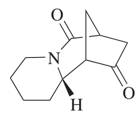
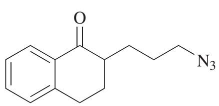
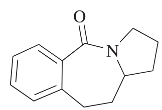
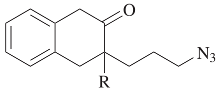
	$TiCl_4$ or TfOH, CH_2Cl_2, 0°, 15 min	 (55–58)	90
	TFA, CH_2Cl_2, rt, 16 h	 (68)	94
	TFA, CH_2Cl_2, rt, 1 h	 (93)	29
	TFA, CH_2Cl_2	 (82)	29
	$TiCl_4$, CH_2Cl_2, rt	 (81)	3
	BF_3•OEt_2, rt	 (70)	656

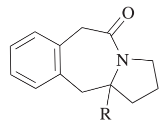
TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	TFA, CH_2Cl_2	 (96)	29
	$TiCl_4$, CH_2Cl_2	 (92)	29
	$TiCl_4$, CH_2Cl_2	 (82)	114
	$TiCl_4$, CH_2Cl_2, reflux	 (62)	115
	TfOH, CH_2Cl_2	 (45)	29

C$_{13-14}$



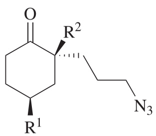
TFA, CH_2Cl_2, rt, 20 min



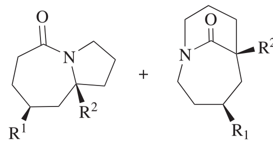
R	
H	(91)
Me	(91)

3

C$_{13-20}$



$MeAlCl_2$, CH_2Cl_2, 0°

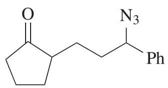


I + **II**

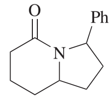
R^1	R^2	**I**	**II**
t-Bu	H	(57)	(17)
H	Ph	(96)	(—)
t-Bu	Ph	(20)	(51)
t-Bu	4-$MeOC_6H_4$	(10)	(65)

657

C$_{14}$

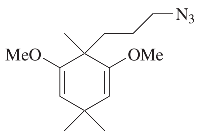


Promoter, CH_2Cl_2, 0°, 15 min

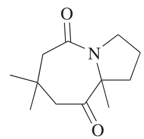


Promoter	
$TiCl_4$	(50)
TfOH	(60)

90

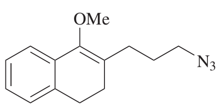


1. TfOH, CH_2Cl_2
2. NaI, acetone

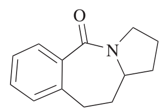


(95)

94



1. TFA, CH_2Cl_2
2. NaI, acetone



(89)

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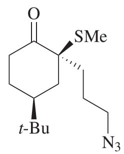
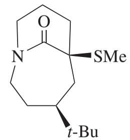
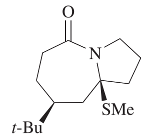
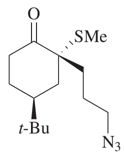
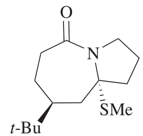
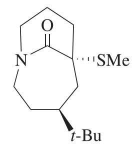
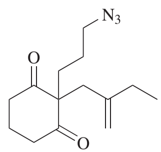
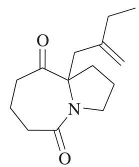
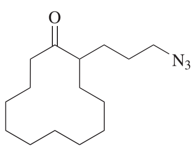
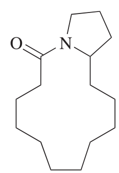
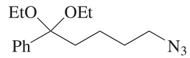
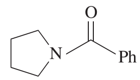
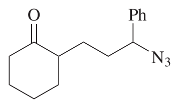
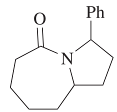
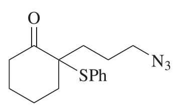
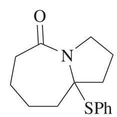
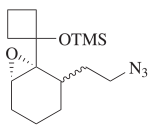
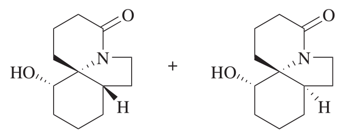
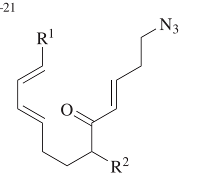
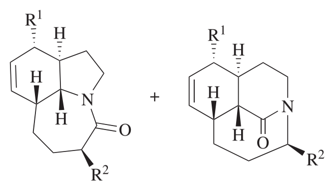
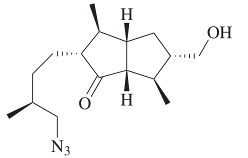
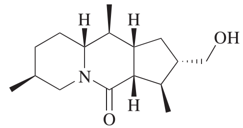
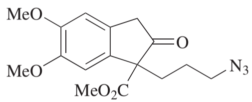
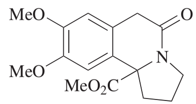
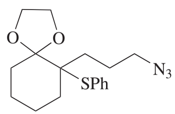
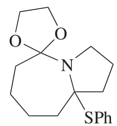
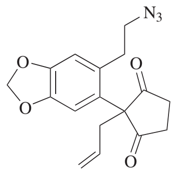
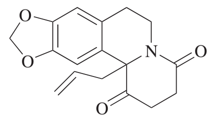
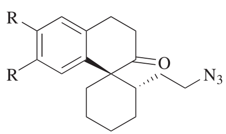
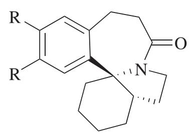
TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	TfOH, CH_2Cl_2, 0°	 **I** +  **II** **I** + **II** (74), **I**:**II** = 86:14	652
	TfOH, CH_2Cl_2, 0°	 **I** +  **II** **I** + **II** (75), **I**:**II** = >95:5	652
	$TiCl_4$, CH_2Cl_2, −78°, 15 min; rt	 (93)	658
C_{15} 	TFA, CH_2Cl_2, 2 h	 (89)	29

	1. TFA, CH_2Cl_2, rt, 16 h 2. NaI, acetone	 (79)	94
	Promoter, CH_2Cl_2, 0°, 15 min	 Promoter / TFOH (52) / $TiCl_4$ (81)	90
	TfOH, CH_2Cl_2	 (42)	29
 *cis*:*trans* = 6:1	$TiCl_4$, CH_2Cl_2, –78° to rt	 **I** + **II** **I + II** (78), **I**:**II** = 8:1	659
$C_{15–21}$ 	$MeAlCl_2$, CH_2Cl_2, reflux, 20 h	 **I** + **II**	657

R^1	R^2	**I**	**II**
H	*i*-Pr	(43)	(28)
H	Ph	(85)	(—)
$BnO(CH_2)_2$	H	(43)	(24)

TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16} 	TfOH, CH_2Cl_2, 0°, 30 min	 (79)	660
	TfOH, CH_2Cl_2, –5° to 0°, 15 min	 (54)	661, 662
C_{17} 	TMSOTf, CH_2Cl_2, 0° to rt, 40 min	 (94)	94
	$TiCl_4$, CH_2Cl_2, 0°, 40 min	 (75)	658
$C_{17–19}$ 	TFA, CH_2Cl_2, rt, 6 h	 R: H (81); MeO (85)	110

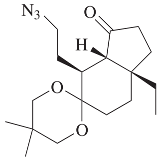
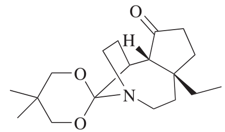
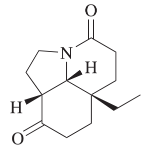
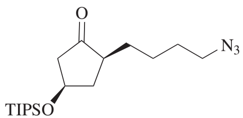
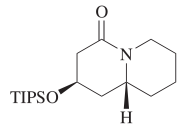
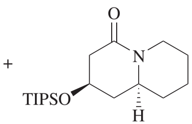
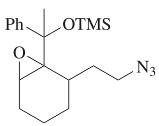
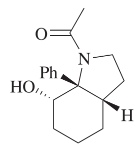
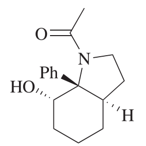
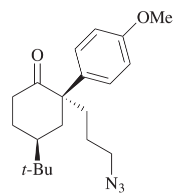
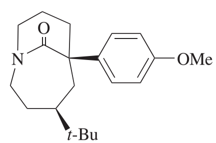
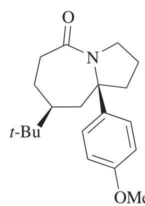
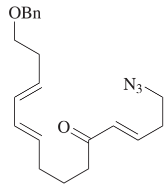
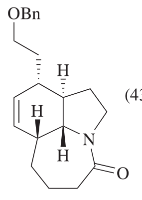
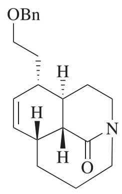
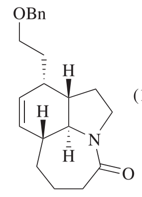
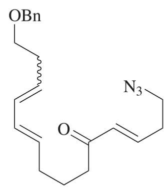
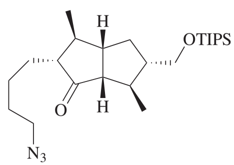
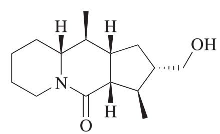
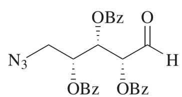
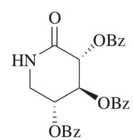
C_{18} 	$TiCl_4$, CH_2Cl_2	 (53)	114
	TFA	 (21)	114
	$TiCl_4$, CH_2Cl_2, reflux	 **I** +  **II** — **I** + **II** (79), **I**:**II** = 1.3:1	93
C_{19} 	$TiCl_4$, CH_2Cl_2, –78° to rt	 **I** +  **II** — **I** + **II** (80), **I**:**II** = 7:1	659
C_{20} 	TfOH, CH_2Cl_2, 0°	 **I** +  **II** — **I** + **II** (75), **I**:**II** = 87:13	652

TABLE 11. INTRAMOLECULAR SCHMIDT REACTIONS OF AZIDOALKYL ALDEHYDES AND KETONES (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{21}		Et_2AlCl, CH_2Cl_2, reflux, 18 h	 (43) +  (24) +  (12) **I** **II** **III**	92
		Promoter CH_2Cl_2, 45°	**I** + **II** + **III** (see below)	663

Promoter	x	**I**	**II**	**III**
$InCl_3$	2.0[a]	(20)	(22)	(18)
$AlMe_3$	1.0	(0)	(0)	(0)
Et_2AlCl	1.3[a]	(28)	(20)	(12)
Et_2AlCl	1.0	(41)	(28)	(9)
$MeAlCl_2$	1.0	(43)	(24)	(12)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{24}		TfOH, CH_2Cl_2, 0°, 30 min	 (52)	660
C_{26}		$TiCl_4$, CH_2Cl_2, 0° to rt, 18 h	 (84)	664

[a] The Promoter was added in two equal portions.

REFERENCES

[1] Smith, P. A. S. *J. Am. Chem. Soc.* **1948**, *70*, 320.
[2] De Koning, A. J. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 548.
[3] Aubé, J.; Milligan, G. L. *J. Am. Chem. Soc.* **1991**, *113*, 8965.
[4] Schmidt, K. F. *Ber. Dtsch. Chem. Ges.* **1924**, *57*, 704.
[5] Dice, J. R.; Smith, P. A. S. *J. Org. Chem.* **1949**, *14*, 179.
[6] Smith, P. A. S.; Ashby, B. *J. Am. Chem. Soc.* **1950**, *72*, 2503.
[7] Smith, P. A. S.; Horwitz, J. P. *J. Am. Chem. Soc.* **1950**, *72*, 3718.
[8] Smith, P. A. S. *J. Am. Chem. Soc.* **1954**, *76*, 431.
[9] Briggs, L. H.; De Ath, G. C.; Ellis, S. R. *J. Chem. Soc.* **1942**, 61.
[10] Briggs, L. H.; Lyttleton, J. W. *J. Chem. Soc.* **1943**, 421.
[11] Wolff, H. *Org. React.* **1946**, *3*, 307.
[12] Uyeo, S. *Pure Appl. Chem.* **1963**, *7*, 269.
[13] Koldobskii, G. I.; Tereshchenko, G. F.; Gerasimova, E. S.; Bagal, L. I. *Usp. Khim.* **1971**, *40*, 1790.
[14] Koldobskii, G. I.; Ostrovskii, V. A.; Gidaspov, B. V. *Khim. Geterotsikl. Soedin.* **1975**, 723.
[15] Koldobskii, G. I.; Ostrovskii, V. A.; Gidaspov, B. V. *Usp. Khim.* **1978**, *47*, 2044.
[16] Krow, G. R. *Tetrahedron* **1981**, *37*, 1283.
[17] Pearson, W. H. *J. Heterocycl. Chem.* **1996**, *33*, 1489.
[18] Braese, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188.
[19] Judd, W. R.; Katz, C. E.; Aubé, J. *Science of Synthesis* **2005**, *21*, 133.
[20] Smith, P. A. S. *Trans. N.Y. Acad. Sci.* **1969**, *31*, 504.
[21] Boyer, J. H.; Hamer, J. *J. Am. Chem. Soc.* **1955**, *77*, 951.
[22] Aubé, J.; Milligan, G. L.; Mossman, C. J. *J. Org. Chem.* **1992**, *57*, 1635.
[23] Pearson, W. H.; Schkeryantz, J. M. *Tetrahedron Lett.* **1992**, *33*, 5291.
[24] Pearson, W. H.; Fang, W.-k. *J. Org. Chem.* **1995**, *60*, 4960.
[25] Krow, G. R. *Org. React.* **1993**, *43*, 251.
[26] Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 1867.
[27] Richard, J. P.; Amyes, T. L.; Lee, Y.-G.; Jagannadham, V. *J. Am. Chem. Soc.* **1994**, *116*, 10833.
[28] Sprecher, M.; Kost, D. *J. Am. Chem. Soc.* **1994**, *116*, 1016.
[29] Milligan, G. L.; Mossman, C. J.; Aubé, J. *J. Am. Chem. Soc.* **1995**, *117*, 10449.
[30] Fikes, L. E.; Shechter, H. *J. Org. Chem.* **1979**, *44*, 741.
[31] Fikes, L. E.; Shechter, H. *Tetrahedron Lett.* **1976**, *17*, 2525.
[32] Bach, R. D.; Wolber, G. J. *J. Org. Chem.* **1982**, *47*, 239.
[33] Gawley, R. E. *Org. React.* **1988**, *35*, 1.
[34] Siddiqui, A. H.; Afzal, M. N.; Baig, M. H.; Lingam, G. V.; Rao, N. S. *Indian J. Chem.* **1984**, *23B*, 1108.
[35] Hewgill, F. R.; Jefferies, P. R. *J. Chem. Soc.* **1956**, 805.
[36] McEwen, W. E.; Conrad, W. E.; Werf, C. A. V. *J. Am. Chem. Soc.* **1952**, *74*, 1168.
[37] Ostrovskii, V. A.; Koldobskii, G. I.; Shirokova, N. P.; Gidaspov, B. V. *Zh. Org. Khim.* **1977**, *13*, 339.
[38] Ostrovskii, V. A.; Kuznetsov, A. V.; Koldobskii, G. I.; Shirokova, N. P.; Gidaspov, B. V. *Zh. Org. Khim.* **1975**, *11*, 1027.
[39] Astier, A.; Plat, M. M. *Tetrahedron Lett.* **1978**, *19*, 2051.
[40] Dietzsch, K. *J. Prakt. Chem.* **1965**, *27*, 34.
[41] Adam, G.; Andrieux, J.; Plat, M. M. *Tetrahedron Lett.* **1983**, *24*, 3609.
[42] Nielsen, D. R.; McEwen, W. E. *J. Am. Chem. Soc.* **1954**, *76*, 4042.
[43] Aubé, J. *Chem. Soc. Rev.* **1997**, *26*, 269.
[44] Christensen, D.; Joergensen, K. A.; Hazell, R. G. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2391.
[45] Boyer, J. H.; Canter, F. C.; Hamer, J.; Putney, R. K. *J. Am. Chem. Soc.* **1956**, *78*, 325.
[46] Gracias, V.; Milligan, G. L.; Aubé, J. *J. Org. Chem.* **1996**, *61*, 10.
[47] Forsee, J. E.; Smith, B. T.; Frank, K. E.; Aubé, J. *Synlett* **1998**, 1258.
[48] Forsee, J. E.; Aubé, J. *J. Org. Chem.* **1999**, *64*, 4381.
[49] Smith, B. T.; Gracias, V.; Aubé, J. *J. Org. Chem.* **2000**, *65*, 3771.

[50] Pearson, W. H.; Hutta, D. A.; Fang, W.-k. *J. Org. Chem.* **2000**, *65*, 8326.
[51] Pearson, W. H.; Walavalkar, R.; Schkeryantz, J. M.; Fang, W. K.; Blickensdorf, J. D. *J. Am. Chem. Soc.* **1993**, *115*, 10183.
[52] Smith, P. A. S. *Org. React.* **1946**, *3*, 337.
[53] Shechter, H.; Kirk, J. C. *J. Am. Chem. Soc.* **1951**, *73*, 3087.
[54] Conley, R. T. *J. Org. Chem.* **1958**, *23*, 1330.
[55] Sakakida, Y.; Kumanireng, A. S.; Kawamoto, H.; Yokoo, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 478.
[56] Galvez, N.; Moreno-Manas, M.; Sebastian, R. M.; Vallribera, A. *Tetrahedron* **1996**, *52*, 1609.
[57] Dickerman, S. C.; Moriconi, E. J. *J. Org. Chem.* **1955**, *20*, 206.
[58] Carr, D.; Iddon, B.; Suschitzky, H.; Parfitt, R. T. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2380.
[59] Tomita, M.; Minami, S.; Uyeo, S. *J. Chem. Soc. C* **1969**, 183.
[60] Chapman, N. B.; Shorter, J.; Utley, J. H. P. *J. Chem. Soc.* **1962**, 1824.
[61] Marsili, A. *Tetrahedron Lett.* **1963**, *4*, 1143.
[62] Evans, D.; Lockhart, I. M. *J. Chem. Soc.* **1965**, 4806.
[63] Smith, P. A. S.; Antoniades, E. P. *Tetrahedron* **1960**, *9*, 210.
[64] Misiti, D. *Annali dell'Istituto Superiore di Sanita* **1973**, *9*, 174.
[65] Carboni, S.; Da Settimo, A.; Bertini, D.; Ferrarini, P. L.; Livi, O.; Tonetti, I. *Farmaco, Ed. Sci.* **1975**, *30*, 237.
[66] Mamouni, A.; Daich, A.; Decroix, B. *J. Heterocycl. Chem.* **1996**, *33*, 1251.
[67] Krow, G. R.; Szczepanski, S. W.; Kim, J. Y.; Liu, N.; Sheikh, A.; Xiao, Y.; Yuan, J. *J. Org. Chem.* **1999**, *64*, 1254.
[68] Krow, G. R.; Cheung, O. H.; Hu, Z.; Lee, Y. B. *J. Org. Chem.* **1996**, *61*, 5574.
[69] Trofimov, F. A.; Shevchenko, L. I.; Mukhanova, T. I.; Grinev, A. N. *Khim. Geterotsikl. Soedin.* **1977**, 1040.
[70] El-Ahl, A.-A. S.; Elmorsy, S. S.; Soliman, H.; Amer, F. A. *Tetrahedron Lett.* **1995**, *36*, 7337.
[71] Misiti, D.; Moore, H. W.; Folkers, K. *Tetrahedron* **1966**, *22*, 1201.
[72] Birkofer, L.; Wegner, P. *Org. Synth.* **1970**, *50*, 107.
[73] Tokes, A. L.; Litkei, G. *Synth. Commun.* **1993**, *23*, 895.
[74] Evans, P. A.; Modi, D. P. *J. Org. Chem.* **1995**, *60*, 6662.
[75] Datta, S. K.; Grundmann, C.; Bhattacharyya, N. K. *J. Chem. Soc. C* **1970**, 2058.
[76] Resplandy, A.; Le Roux, P.; Mentzer, C. *C.R. Hebd. Sceances Acad. Sci.* **1966**, *262*, 293.
[77] ApSimon, J. W.; Hunter, N. R. *Tetrahedron Lett.* **1972**, *13*, 187.
[78] Ruediger, E. H.; Gandhi, S. S.; Gibson, M. S.; Farcasiu, D.; Uncuta, C. *Can. J. Chem.* **1986**, *64*, 577.
[79] Farcasiu, D.; Roman, M. *Chem. Ind. (London)* **1967**, 1225.
[80] Davies, A. J.; Marks, R. E. *J. Chem. Soc. C* **1968**, 2703.
[81] Mehta, G.; Rao, K. S.; Suri, S. C.; Cameron, T. S.; Chan, C. *J. Chem. Soc., Chem. Commun.* **1980**, 650.
[82] Kost, D.; Sprecher, M. *Tetrahedron Lett.* **1970**, *11*, 2535.
[83] Trost, B. M.; Vaultier, M.; Santiago, M. L. *J. Am. Chem. Soc.* **1980**, *102*, 7929.
[84] Donaruma, L. G.; Huber, M. L. *J. Org. Chem.* **1956**, *21*, 965.
[85] Desai, P.; Schildknegt, K.; Agrios, K. A.; Mossman, C.; Milligan, G. L.; Aubé, J. *J. Am. Chem. Soc.* **2000**, *122*, 7226.
[86] Molander, G. A.; Bibeau, C. T. *Tetrahedron Lett.* **2002**, *43*, 5385.
[87] Reddy, D. S.; Judd, W. R.; Aubé, J. *Org. Lett.* **2003**, *5*, 3899.
[88] Mahoney, J. M.; Smith, C. R.; Johnston, J. N. *J. Am. Chem. Soc.* **2005**, *127*, 1354.
[89] Hong, K. B.; Donahue, M. G.; Johnston, J. N. *J. Am. Chem. Soc.* **2008**, *130*, 2323.
[90] Wrobleski, A.; Aubé, J. *J. Org. Chem.* **2001**, *66*, 886.
[91] Tani, K.; Stoltz, B. M. *Nature (London)* **2006**, *441*, 731.
[92] Golden, J. E.; Aubé, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 4316.
[93] Gracias, V.; Zeng, Y.; Desai, P.; Aubé, J. *Org. Lett.* **2003**, *5*, 4999.
[94] Mossman, C. J.; Aubé, J. *Tetrahedron* **1996**, *52*, 3403.
[95] Gracias, V.; Milligan, G. L.; Aubé, J. *J. Am. Chem. Soc.* **1995**, *117*, 8047.
[96] Gracias, V.; Frank, K. E.; Milligan, G. L.; Aubé, J. *Tetrahedron* **1997**, *53*, 16241.

[97] Hünig, S. *Angew. Chem., Int. Ed.* **1964**, *3*, 548.
[98] Sahasrabudhe, K.; Gracias, V.; Furness, K.; Smith, B. T.; Katz, C. E.; Reddy, D. S.; Aubé, J. *J. Am. Chem. Soc.* **2003**, *125*, 7914.
[99] Furness, K.; Aubé, J. *Org. Lett.* **1999**, *1*, 495.
[100] Pearson, W. H.; Fang, W.-k. *J. Org. Chem.* **2001**, *66*, 6838.
[101] Pearson, W. H.; Walavalkar, R. *Tetrahedron* **2001**, *57*, 5081.
[102] Pearson, W. H.; Fang, W.-k. *J. Org. Chem.* **2000**, *65*, 7158.
[103] Pearson, W. H.; Gallagher, B. M. *Tetrahedron* **1996**, *52*, 12039.
[104] Reddy, P. G.; Varghese, B.; Baskaran, S. *Org. Lett.* **2003**, *5*, 583.
[105] Gorin, D. J.; Davis, N. R.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 11260.
[106] Cava, M. P.; Vogt, B. R. *Tetrahedron Lett.* **1964**, *5*, 2813.
[107] Misaka, Y.; Mizutani, T.; Sekido, M.; Uyeo, S. *J. Chem. Soc. Chem. Commun.* **1967**, 1258.
[108] Georg, G. I.; Guan, X.; Kant, J. *Tetrahedron Lett.* **1988**, *29*, 403.
[109] Tanaka, M.; Oba, M.; Tamai, K.; Suemune, H. *J. Org. Chem.* **2001**, *66*, 2667.
[110] Le Dreau, M. A.; Desmaele, D.; Dumas, F.; d'Angelo, J. *J. Org. Chem.* **1993**, *58*, 2933.
[111] Aubé, J.; Rafferty, P. S.; Milligan, G. L. *Heterocycles* **1993**, *35*, 1141.
[112] Wrobleski, A.; Sahasrabudhe, K.; Aubé, J. *J. Am. Chem. Soc.* **2002**, *124*, 9974.
[113] Iyengar, R.; Schildknegt, K.; Aubé, J. *Org. Lett.* **2000**, *2*, 1625.
[114] Iyengar, R.; Schildknegt, K.; Morton, M.; Aubé, J. *J. Org. Chem.* **2005**, *70*, 10645.
[115] Smith, B. T.; Wendt, J. A.; Aubé, J. *Org. Lett.* **2002**, *4*, 2577.
[116] Vidari, G.; Tripolini, M.; Novella, P.; Allegrucci, P.; Garlaschelli, L. *Tetrahedron: Asymmetry* **1997**, *8*, 2893.
[117] Donaruma, L. G.; Heldt, W. Z. *Org. React.* **1960**, *11*, 1.
[118] Shah, J. N.; Mehta, Y. P.; Shah, G. M. *J. Org. Chem.* **1978**, *43*, 2078.
[119] Moriconi, E. J.; Stemniski, M. A. *J. Org. Chem.* **1972**, *37*, 2035.
[120] Suginome, H.; Takeda, H.; Masamune, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 269.
[121] Narasaka, K.; Kusama, H.; Yamashita, Y.; Sato, H. *Chem. Lett.* **1993**, 489.
[122] Kusama, H.; Yamashita, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 373.
[123] Hoffman, R. V.; Kim, H.-O. *Tetrahedron* **1992**, *48*, 3007.
[124] Hoffman, R. V.; Salvador, J. M. *Tetrahedron Lett.* **1989**, *30*, 4207.
[125] Hoffman, R. V. *Tetrahedron* **1991**, *47*, 1109.
[126] Hoffman, R. V.; Salvador, J. M. *J. Org. Chem.* **1992**, *57*, 4487.
[127] Hoffman, R. V.; Nayyar, N. K.; Chen, W. *J. Org. Chem.* **1993**, *58*, 2355.
[128] Barton, D. H. R.; Day, M. J.; Hesse, R. H.; Pechet, M. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1764.
[129] Barton, D. H. R.; Day, M. J.; Hesse, R. H.; Pechet, M. M. *J. Chem. Soc. D* **1971**, 945.
[130] Black, D. S. C.; Watson, K. G. *Aust. J. Chem.* **1973**, *26*, 2505.
[131] Black, D. S. C.; Blackman, N. A.; Johnstone, L. M. *Aust. J. Chem.* **1979**, *32*, 2041.
[132] Johnson, G. P.; Marples, B. A. *Tetrahedron Lett.* **1984**, *25*, 3359.
[133] Johnson, G. P.; Marples, B. A. *Tetrahedron Lett.* **1985**, *26*, 4115.
[134] Black, D. S. C.; Johnstone, L. M. *Aust. J. Chem.* **1984**, *37*, 577.
[135] Black, D. S. C.; Johnstone, L. M. *Aust. J. Chem.* **1984**, *37*, 587.
[136] Zeng, Y.; Smith, B. T.; Hershberger, J.; Aubé, J. *J. Org. Chem.* **2003**, *68*, 8065.
[137] Schmitz, E. *Adv. Heterocycl. Chem.* **1963**, *2*, 83.
[138] Haddadin, M. J.; Freeman, J. P. In *Chemistry of Heterocyclic Compounds: Small Ring Heterocycles, Part 3*; Hassner, A., Ed.; Wiley: New York, 1985; Vol. 4, pp 283–350.
[139] Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703.
[140] Lipczynska-Kochany, E. *Chem. Rev.* **1991**, *91*, 447.
[141] Bolsman, T. A. B. M.; de Boer, T. J. *Tetrahedron* **1975**, *31*, 1019.
[142] Aubé, J.; Hammond, M.; Gherardini, E.; Takusagawa, F. *J. Org. Chem.* **1991**, *56*, 499.
[143] Post, A. J.; Nwaukwa, S.; Morrison, H. *J. Am. Chem. Soc.* **1994**, *116*, 6439.
[144] Emmons, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 5739.
[145] Schmitz, E.; Murawski, D. *Chem. Ber.* **1965**, *98*, 2525.
[146] Black, D. S. C.; Watson, K. G. *Aust. J. Chem.* **1973**, *26*, 2515.
[147] Aubé, J.; Burgett, P. M.; Wang, Y. *Tetrahedron Lett.* **1988**, *29*, 151.

[148] Aubé, J.; Wang, Y.; Hammond, M.; Tanol, M.; Takusagawa, F.; Vander Velde, D. *J. Am. Chem. Soc.* **1990**, *112*, 4879.
[149] Oliveros-Desherces, E.; Rivière, M.; Parello, J.; Lattes, A. *Tetrahedron Lett.* **1975**, 851.
[150] Lattes, A.; Oliveros, E.; Rivière, M.; Belzecki, C.; Mostowicz, D.; Abramskj, W.; Piccinni-Leopardi, C.; Germain, G.; Van Meerssche, M. *J. Am. Chem. Soc.* **1982**, *104*, 3929.
[151] Oliveros, E.; Rivière, M.; Malrieu, J. P.; Teichteil, C. *J. Am. Chem. Soc.* **1979**, *101*, 318.
[152] Wolfe, M. S.; Dutta, D.; Aubé, J. *J. Org. Chem.* **1997**, *62*, 654.
[153] Schultz, A. G.; Ravichandran, R. *J. Org. Chem.* **1980**, *45*, 5008.
[154] Schultz, A. G.; McMahon, W. G. *J. Org. Chem.* **1984**, *49*, 1676.
[155] Sha, C.-K.; Ouyang, S.-L.; Hsieh, D.-Y.; Hseu, T.-H. *J. Chem. Soc., Chem. Commun.* **1984**, 492.
[156] Sha, C.-K.; Ouyang, S.-L.; Hsieh, D.-Y.; Chang, R.-C.; Chang, S.-C. *J. Org. Chem.* **1986**, *51*, 1490.
[157] Kaiser, C.; Weinstock, J. *Org. Synth.* **1971**, *51*, 48.
[158] Shioiri, T.; Yamada, S. *Org. Synth.* **1984**, *62*, 187.
[159] Lebel, H.; Leogane, O. *Org. Lett.* **2005**, *7*, 4107.
[160] Almond, M. R.; Stimmel, J. B.; Thompson, E. A.; Loudon, G. M. *Org. Synth.* **1988**, *66*, 132.
[161] Stockel, R. F.; Hall, D. M. *Nature (London)* **1963**, *197*, 787.
[162] Peet, N. P.; Weintraub, P. M. *Chem. Eng. News* **1994**, *72*, 4.
[163] Ito, M.; Koyakumaru, K.-i.; Ohta, T.; Takaya, H. *Synthesis* **1995**, 376.
[164] Blandy, C.; Choukroun, R.; Gervais, D. *Tetrahedron Lett.* **1983**, *24*, 4189.
[165] TerBeek, K. J. *Chem. Eng. News* **1998**, *76*, 6.
[166] Viaud, M. C.; Rollin, P. *Synthesis* **1990**, 130.
[167] Pavlov, P. A. *Chem. Heterocycl. Compd.* **2002**, *38*, 524.
[168] Allan, R. D.; Dickenson, H. W.; Johnston, G. A. R.; Kazlauskas, R.; Tran, H. W. *Aust. J. Chem.* **1985**, *38*, 1651.
[169] Merour, J. Y.; Cossais, F.; Piroelle, S.; Mazeas, D. *J. Heterocycl. Chem.* **1994**, *31*, 87.
[170] Arcus, C. L.; Coombs, M. M. *J. Chem. Soc.* **1954**, 4319.
[171] Schuerch, C., Jr.; Huntress, E. H. *J. Am. Chem. Soc.* **1949**, *71*, 2233.
[172] Tamir, H.; Ginsburg, D. *J. Chem. Soc.* **1959**, 2921.
[173] Zakharkin, L. I.; Kalinin, V. N.; Gedymin, V. V. *Zh. Obshch. Khim.* **1973**, *43*, 1974.
[174] Takagi, S.; Hayashi, K. *Chem. Pharm. Bull.* **1959**, *7*, 183.
[175] Strassman, M.; Thomas, A. J.; Locke, L. A.; Weinhouse, S. *J. Am. Chem. Soc.* **1956**, *78*, 228.
[176] Stickings, C. E.; Townsend, R. J. *Biochem. J.* **1961**, *78*, 412.
[177] Leete, E. *J. Am. Chem. Soc.* **1963**, *85*, 3523.
[177a] Hoare, D. S. *Biochem. J.* **1963**, *87*, 284.
[178] Trown, P. W.; Sharp, M.; Abraham, E. P. *Biochem. J.* **1963**, *86*, 280.
[179] Pathak, B. *J. Indian Chem. Soc.* **1951**, *28*, 561.
[180] Caldwell, D. R.; Newman, K. *Curr. Microbiol.* **1986**, *14*, 55.
[181] Schumann, W. C.; Kumaran, K.; Landau, B. R. *Anal. Biochem.* **1978**, *90*, 141.
[182] Lee, A. W. M.; Chan, W. H.; Lam, Y. S. *Analyst (Cambridge, U.K.)* **1995**, *120*, 2841.
[183] Rabinowitz, J. L.; Palmere, R. M.; Conley, R. T. *J. Labelled Compd. Radiopharm.* **1973**, *9*, 141.
[184] Babu, B. H.; Amma, P. K. S.; Rao, S. V. *Ind. J. Technol.* **1967**, *5*, 262.
[185] Blomstrand, R. *Acta Chem. Scand.* **1954**, *8*, 1487.
[186] Phares, E. F.; Long, M. V. *J. Am. Chem. Soc.* **1955**, *77*, 2556.
[187] Koppes, W. M.; Sitzmann, M. E.; Adolph, H. G. *J. Chem. Eng. Data* **1986**, *31*, 119.
[188] Maffei, S.; Bettinetti, G. F. *Ann. Chim. (Rome)* **1959**, *49*, 1801.
[189] Takagi, S.; Hayashi, K. *Chem. Pharm. Bull.* **1959**, *7*, 99.
[190] Takagi, S.; Hayashi, K. *Chem. Pharm. Bull.* **1959**, *7*, 96.
[191] Hill, R. K.; Rhee, S.-W.; Leete, E.; McGaw, B. A. *J. Am. Chem. Soc.* **1980**, *102*, 7344.
[192] Rosenberg, H.; Paul, A. G. *Lloydia* **1971**, *34*, 372.
[193] Schuerch, C., Jr.; Huntress, E. H. *J. Am. Chem. Soc.* **1949**, *71*, 2238.
[194] Sekizawa, Y.; Maragoudakis, M.; King, T. E.; Cheldelin, V. H. *Chim. Chronika* **1965**, *30*, 131.
[195] Oae, S.; Furukawa, N.; Kise, M.; Kawanishi, M. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1212.
[196] Zbarskii, V. L.; Shutov, G. M.; Zhilin, V. F.; Orlova, E. Y. *Khim. Geterotsikl. Soedin.* **1967**, 178.

[197] Rothchild, S.; Fields, M. *J. Org. Chem.* **1951**, *16*, 1080.
[198] Hayashi, K. *Chem. Pharm. Bull.* **1959**, *7*, 187.
[199] Hayashi, K. *Chem. Pharm. Bull.* **1960**, *8*, 177.
[200] Nowatari, H.; Kuroda, Y.; Hayami, H.; Okamoto, K.; Ekimoto, H.; Takahashi, K. *Chem. Pharm. Bull.* **1989**, *37*, 2406.
[201] Lillien, I. *J. Chem. Soc. Chem. Commun.* **1968**, 1009.
[202] Allan, R. D.; Johnston, G. A. R.; Twitchin, B. *Aust. J. Chem.* **1979**, *32*, 2517.
[203] Roe, A. M.; Burton, R. A.; Reavill, D. R. *J. Chem. Soc. Chem. Commun.* **1965**, 582.
[204] Wei, Y. *Chin. J. App. Chem.* **1990**, *7*, 70.
[205] Atkins, R. L.; Wilson, W. S. *J. Org. Chem.* **1986**, *51*, 2572.
[206] Rutherford, K. G.; Ing, S. Y.-S.; Thibert, R. J. *Can. J. Chem.* **1965**, *43*, 541.
[207] Minor, J. T.; Vanderwerf, C. A. *J. Org. Chem.* **1952**, *17*, 1425.
[208] McNamara, A. J.; Stothers, J. B. *Can. J. Chem.* **1964**, *42*, 2354.
[209] Baumgarten, H. E.; Bower, F. A.; Okamoto, T. T. *J. Am. Chem. Soc.* **1957**, *79*, 3145.
[210] Leete, E. *J. Am. Chem. Soc.* **1959**, *81*, 3948.
[211] Granger, R.; Girard, J. P.; Boussinesq, J. *C.R. Hebd. Sceances Acad. Sci.* **1966**, *263*, 90.
[212] Kalmykova, V. D.; Bogdanov, M. N.; Okromchedlidze, N. P.; Zhmaeva, I. V.; Efremov, V. Y. *Vysokomol. Soedin.* **1966**, *8*, 1586.
[213] Munk, V. P.; Cham, S. T.; Fenton, R. R.; Hocking, R. K.; Hambley, T. W. *Aust. J. Chem.* **2002**, *55*, 523.
[214] Hewgill, F. R.; Jefferies, P. R.; Macbeth, A. K. *J. Chem. Soc.* **1954**, 699.
[215] Newman, M. S.; Wiseman, E. H. *J. Org. Chem.* **1961**, *26*, 3208.
[216] Sladkov, A. M.; Vitt, S. V. *Zh. Obshch. Khim.* **1956**, *26*, 1130.
[217] Zbarskii, V. L.; Sonis, M. A.; Orlova, E. Y. *Zh. Prikl. Khim.* **1971**, *44*, 2656.
[218] Woodroofe, C. C.; Zhong, B.; Lu, X.; Silverman, R. B. *J. Chem. Soc., Perkin Trans. 1* **2000**, 55.
[219] Palmere, R. M.; Conley, R. T. *J. Org. Chem.* **1970**, *35*, 2703.
[220] Shibata, S.; Yamazaki, M. *Pharm. Bull.* **1957**, *5*, 501.
[221] Schrecker, A. W. *J. Org. Chem.* **1957**, *22*, 33.
[222] Hayashi, K. *Chem. Pharm. Bull.* **1959**, *7*, 912.
[223] Granger, R.; Nau, P.; Nau, J. *Bull. Soc. Chim. Fr.* **1960**, 1225.
[224] Granger, R.; Nau, P.; Nau, J. *C.R. Hebd. Sceances Acad. Sci.* **1958**, *246*, 3467.
[225] Granger, R.; Nau, P.; Nau, J. *Bull. Soc. Chim. Fr.* **1958**, 1441.
[226] Granger, R.; Nau, P.; Nau, J. *Compt. Rend.* **1957**, *245*, 2315.
[227] Meinwald, J.; Gassman, P. G. *J. Am. Chem. Soc.* **1960**, *82*, 2857.
[228] Chow, A. W.; Jakas, D. R.; Hoover, J. R. E. *Tetrahedron Lett.* **1966**, *7*, 5427.
[229] Fort, A. W.; Roberts, J. D. *J. Am. Chem. Soc.* **1956**, *78*, 584.
[230] Rosenberg, H.; Stohs, S. J. *Lloydia* **1974**, *37*, 313.
[231] Kornblum, N.; Iffland, D. C. *J. Am. Chem. Soc.* **1949**, *71*, 2137.
[232] Nozoe, T.; Kitahara, Y.; Doi, K.; Funamizu, M.; Terasawa, T. *Tohoku Daigaku Hisui Yoeki Kagaku Kenkyusho Hokoku* **1961**, *10*, 199.
[233] Sicher, J.; Tichy, M.; Zavada, J.; Krupicka, J. *Collect. Czech. Chem. Commun.* **1968**, *33*, 1438.
[234] Granger, R.; Girard, J. P. *C.R. Hebd. Sceances Acad. Sci.* **1963**, *256*, 4236.
[235] Kursanov, D. N.; Vitt, S. V. *Zh. Obshch. Khim.* **1955**, *25*, 2509.
[236] Urabe, H.; Yamakawa, T.; Sato, F. *Tetrahedron: Asymmetry* **1992**, *3*, 5.
[237] Jawdosiuk, M.; Kovacic, P. *Synth. Commun.* **1983**, *13*, 53.
[238] Newman, M. S.; Gildenhorn, H. L. *J. Am. Chem. Soc.* **1948**, *70*, 317.
[239] Balenovic, K.; Bregant, N. *J. Chem. Soc.* **1965**, 5131.
[240] Stetter, H.; Loehr, V.; Simos, A. *Justus Liebigs Ann. Chem.* **1977**, 999.
[241] Dittmer, D. C.; Silverstein, A.; Lempka, L. P. *J. Org. Chem.* **1959**, *24*, 651.
[242] Shiotani, S.; Mitsuhashi, K. *Chem. Pharm. Bull.* **1966**, *14*, 324.
[243] Smith, C. R.; RajanBabu, T. V. *J. Org. Chem.* **2009**, *74*, 3066.
[244] Sicher, J.; Tichy, M.; Sipos, F. *Collect. Czech. Chem. Commun.* **1966**, *31*, 2238.
[245] Izumi, K.; Kitamikado, T.; Sugiura, S.; Kato, K.; Hori, M.; Fujimura, H. *Yakugaku Zasshi* **1973**, *93*, 1349.

[246] Shirley, D. A.; Brody, S. S.; Sheehan, W. C. *J. Org. Chem.* **1957**, *22*, 495.
[247] Koptyug, V. A.; Gerasimova, T. N.; Tabatskaya, A. A. *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk* **1966**, 62.
[248] Szmant, H. H.; McIntosh, J. J. *J. Am. Chem. Soc.* **1951**, *73*, 4356.
[249] Weisburger, E. K. *J. Org. Chem.* **1956**, *21*, 698.
[250] Weisburger, E. K.; Weisburger, J. H. *J. Org. Chem.* **1955**, *20*, 1396.
[251] Grantham, P. H.; Weisburger, E. K.; Weisburger, J. H. *J. Org. Chem.* **1961**, *26*, 1008.
[252] Migachev, G. I.; Andrievskii, A. M.; Dokunikhin, N. S. *Zh. Vses. Khim. Ova.* **1976**, *21*, 237.
[253] Nielsen, A. T.; Norris, W. P.; Atkins, R. L.; Vuono, W. R. *J. Org. Chem.* **1983**, *48*, 1056.
[254] Brouard, J. P.; Michailidis, A.; Resplandy, A. *C.R. Hebd. Sceances Acad. Sci.* **1974**, *278*, 475.
[255] De Koning, A. J. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 147.
[256] Rutherford, K. G.; Newman, M. S. *J. Am. Chem. Soc.* **1957**, *79*, 213.
[257] Inouye, H.; Ueda, S.; Inoue, K.; Hayashi, T.; Hibi, T. *Tetrahedron Lett.* **1975**, *16*, 2395.
[258] Nayak, U. R. *Indian J. Chem.* **1972**, *10*, 315.
[259] Hall, D. M.; Mahboob, S.; Turner, E. E. *J. Chem. Soc.* **1950**, 1842.
[260] Baxter, R. M.; Kandel, S. I.; Okany, A. *Tetrahedron Lett.* **1961**, *2*, 596.
[261] Furukawa, M.; Okawara, T.; Noguchi, Y.; Terawaki, Y. *Chem. Pharm. Bull.* **1979**, *27*, 2795.
[262] Badger, G. M.; Seidler, J. H. *J. Chem. Soc.* **1954**, 2329.
[263] Hamama, W. S.; Hammouda, M.; Afsah, E. M. *J. Prakt. Chem.* **1987**, *329*, 62.
[264] Gregory, H.; Leete, E. *Chem. Ind. (London)* **1960**, 1242.
[265] Hill, R. K.; Muench, K. *J. Org. Chem.* **1957**, *22*, 1276.
[266] Leete, E.; Ghosal, S. *Tetrahedron Lett.* **1962**, *3*, 1179.
[267] Nagao, Y.; Misono, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1723.
[268] Reddy, R. P.; Ravindranath, A.; Ramaiah, T. S.; Rao, M. V. *Ind. J. Chem. Sci.* **1987**, *1*, 45.
[269] Singh, P.; Rangaswami, S. *Tetrahedron Lett.* **1967**, *8*, 149.
[270] Davies, A. J.; Donald, A. S. R.; Marks, R. E. *J. Chem. Soc. C* **1967**, 2109.
[271] Pavlov, P. A. *Chem. Heterocycl. Compd.* **2001**, *37*, 1199.
[272] Schuerch, C., Jr. *J. Am. Chem. Soc.* **1948**, *70*, 2293.
[273] Smith, P. A. S.; Yu, T.-Y. *J. Org. Chem.* **1952**, *17*, 1281.
[274] Yeh, M. Y.; Tien, H. J.; Huang, L. Y.; Chen, M. H. *J. Chin. Chem. Soc.* **1983**, *30*, 29.
[275] Pavlov, P. A. *Russ. J. Org. Chem.* **2001**, *37*, 1310.
[276] Nonomura, S. *Yakugaku Zasshi* **1955**, *75*, 225.
[277] Ropp, G. A.; Bonner, W. A.; Clark, M. T.; Raaen, V. F. *J. Am. Chem. Soc.* **1954**, *76*, 1710.
[278] Makhova, N. N.; Blinnikov, A. N.; Khmel'nitskii, L. I. *Mendeleev Commun.* **1995**, 56.
[279] Bunce, S. C.; Cloke, J. B. *J. Am. Chem. Soc.* **1954**, *76*, 2244.
[280] Hurd, C. D.; Moffat, J. *J. Am. Chem. Soc.* **1951**, *73*, 613.
[281] Ah-Kow, G.; Paulmier, C.; Pastour, P. *Bull. Soc. Chim. Fr.* **1976**, 151.
[282] Eshghi, H.; Hassankhani, A.; Mosaddegh, E. *J. Chem. Res. (M)* **2006**, 218.
[283] Zook, H. D.; Paviak, S. C. *J. Am. Chem. Soc.* **1955**, *77*, 2501.
[284] Birkofer, L.; Storch, I. *Chem. Ber.* **1953**, *86*, 749.
[285] Pozgan, F.; Krejan, M.; Polanc, S.; Kocevar, M. *Heterocycles* **2006**, *69*, 123.
[286] Yadav, J. S.; Reddy, B. V. S.; Reddy, U. V. S.; Praneeth, K. *Tetrahedron Lett.* **2008**, *49*, 4742.
[287] Smith, P. A. S.; Berry, W. L. *J. Org. Chem.* **1961**, *26*, 27.
[288] Eshghi, H. *J. Chin. Chem. Soc.* **2006**, *53*, 987.
[289] Eshghi, H.; Hassankhani, A. *Synth. Commun.* **2006**, *36*, 2211.
[290] Chiba, T.; Sasaki, M.; Sakaki, J.; Kato, T. *Yakugaku Zasshi* **1983**, *103*, 1024.
[291] Chiba, T.; Sakaki, J.; Kato, T. *Yakugaku Zasshi* **1984**, *104*, 587.
[292] Szmant, H. H.; McIntosh, J. J. *J. Am. Chem. Soc.* **1950**, *72*, 4835.
[293] Krati, N.; Roizard, D.; Brembilla, A.; Lochon, P. *Bull. Soc. Chim. Fr.* **1989**, 443.
[294] Nimgirawath, S.; Anulakanapakorn, K. *J. Sci. Soc. Thailand* **1982**, *8*, 119.
[295] Conley, R. T. *Chem. Ind. (London)* **1958**, 438.
[296] Prager, R. H.; Tippett, J. M.; Ward, A. D. *Aust. J. Chem.* **1978**, *31*, 1989.
[297] Riemschneider, R.; Kluge, A. *Monatsh. Chem.* **1953**, *84*, 522.
[298] Li, Z.; Jin, Z.; Yin, B.; Imafuku, K. *J. Heterocycl. Chem.* **1987**, *24*, 779.
[299] Imafuku, K.; Furuya, M.; Jin, Z. T. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 609.

300 Doi, K. *Bull. Chem. Soc. Jpn.* **1961**, *34*, 501.
301 Parkin, B. A.; Hedrick, G. W. *J. Am. Chem. Soc.* **1958**, *80*, 2899.
302 Cristau, H.-J.; Marat, X.; Vors, J.-P.; Pirat, J.-L. *Tetrahedron Lett.* **2003**, *44*, 3179.
303 Bridson-Jones, F. S.; Buckley, G. D. *J. Chem. Soc.* **1951**, 3009.
304 Schwartzman, L. H.; Corson, B. B. *J. Am. Chem. Soc.* **1954**, *76*, 781.
305 Benson, F. R.; Hartzel, L. W.; Savell, W. L. *J. Am. Chem. Soc.* **1951**, *73*, 4457.
306 Graham, S. L.; Shepard, K. L.; Anderson, P. S.; Baldwin, J. J.; Best, D. B.; Christy, M. E.; Freedman, M. B.; Gautheron, P.; Habecker, C. N.; Hoffman, J. M.; Lyle, P. A; Michelson, S. R.; Ponticello, G. S.; Robb, C. M.; Schwan, H.; Smith, A. M.; Smith, R. L.; Sondey, J. M.; Strohmaier, K. M.; Sugrue, M. F.; Varga, S. L. *J. Med. Chem.* **1989**, *32*, 2548.
307 Matsuki, Y.; Shoji, F. *Nippon Kagaku Zasshi* **1965**, *86*, 1067.
308 Cuingnet, E.; Tarterat-Adalberon, M. *Bull. Soc. Chim. Fr.* **1965**, 3734.
309 Cais, M.; Narkis, N. *J. Organomet. Chem.* **1965**, *3*, 188.
310 Yeh, M. Y.; Tien, H. J.; Nonaka, T. *J. Org. Chem.* **1983**, *48*, 1382.
311 Yamato, M.; Obe, S. *Yakugaku Zasshi* **1970**, *90*, 1549.
312 Oba, M.; Tanaka, M.; Kurihara, M.; Suemune, H. *Helv. Chim. Acta* **2002**, *85*, 3197.
313 Schaefer, H. G.; Schmitt, E. W. *Chem.-Ztg.* **1971**, *95*, 420.
314 Moreno-Manas, M.; Trepat, E.; Sebastian, R. M.; Vallribera, A. *Tetrahedron: Asymmetry* **1999**, *10*, 4211.
315 Arcus, C. L.; Marks, R. E. *J. Chem. Soc.* **1956**, 1627.
316 Modi, S. P.; Archer, S. *J. Org. Chem.* **1989**, *54*, 5189.
317 Badger, G. M.; Howard, R. T.; Simons, A. *J. Chem. Soc.* **1952**, 2849.
318 Gajcy, K.; Librowski, T.; Lochynski, S. *Lett. Org. Chem.* **2009**, *6*, 186.
319 Donati, C.; Prager, R. H.; Weber, B. *Aust. J. Chem.* **1989**, *42*, 787.
320 Matsuki, Y.; Ito, I. *Nippon Kagaku Zasshi* **1967**, *88*, 751.
321 Nightingale, D. V.; Maienthal, M. *J. Am. Chem. Soc.* **1950**, *72*, 4823.
322 Sofan, M. A.; Fouda, A. M.; Asfah, E. M. *Pol. J. Chem.* **2004**, *78*, 837.
323 Chapman, N. B.; Hughes, C. G.; Scrowston, R. M. *J. Chem. Soc. C* **1971**, 463.
324 Ichiro, M. *Bull. Chem. Soc. Jpn.* **1961**, *34*, 580.
325 Ganguly, S.; Razdan, B. *Indian J. Heterocycl. Chem.* **2005**, *14*, 253.
326 Hickman, J. A.; Wibberley, D. G. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2954.
327 Kohlbrenner, P. J.; Schuerch, C. *J. Am. Chem. Soc.* **1955**, *77*, 6066.
328 Tardella, P. A.; Di Maio, G. *Ann. Chim. (Rome)* **1972**, *62*, 200.
329 Duong, T.; Prager, R. H.; Were, S. T. *Aust. J. Chem.* **1983**, *36*, 1431.
330 Ishida, N.; Imafuku, K. *J. Heterocycl. Chem.* **1990**, *27*, 887.
331 Westland, R. D.; McEwen, W. E. *J. Am. Chem. Soc.* **1952**, *74*, 6141.
332 Charpentier-Morize, M. *Bull. Soc. Chim. Fr.* **1954**, 497.
333 Schmid, H. J.; Hunger, A.; Hoffmann, K. *Helv. Chim. Acta* **1956**, *39*, 607.
334 Arcus, C. L.; Coombs, M. M. *J. Chem. Soc.* **1953**, 3698.
335 Seto, S.; Ogura, K. *Bull. Chem. Soc. Jpn.* **1960**, *33*, 1084.
336 Mejer, S. *Roczniki Chemii* **1962**, *36*, 1115.
337 Palmere, R. M.; Conley, R. T.; Rabinowitz, J. L. *J. Org. Chem.* **1972**, *37*, 4095.
338 Bhattacharya, S.; Chakraborti, K.; Rao, R. R. *Indian J. Chem.* **1986**, *25B*, 133.
339 Cauquil, G.; Casadevall, E.; Casadevall, A. *Bull. Soc. Chim. Fr.* **1962**, 608.
340 Vita-Finzi, P.; Arbasino, M. *Ann. Chim. (Rome)* **1964**, *54*, 1165.
341 Rosenmund, P.; Sauer, D.; Trommer, W. *Chem. Ber.* **1970**, *103*, 496.
342 Lancelot, J. C.; Letois, B.; Rault, S.; Nguyen Huy, D.; Saturnino, C.; Robba, M. *Gazz. Chim. Ital.* **1991**, *121*, 301.
343 Hutchison, G. I.; Marshall, P. A.; Prager, R. H.; Tippett, J. M.; Ward, A. D. *Aust. J. Chem.* **1980**, *33*, 2699.
344 Kroeck, F. W.; Kroehnke, F. *Chem. Ber.* **1971**, *104*, 1629.
345 Palazzo, S. *Ann. Chim. (Rome)* **1959**, *49*, 835.
346 Chen, I.-L.; Chang, K.-M.; Miaw, C.-L.; Liao, C.-H.; Chen, J.-J.; Wang, T.-C. *Bioorg. Med. Chem.* **2007**, *15*, 6527.

[347] Nozoe, T.; Takase, K.; Tada, M. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1948.
[348] Campbell, N.; Leadill, W. K.; Wilshire, J. F. K. *J. Chem. Soc.* **1951**, 1404.
[349] Luzina, O. A.; Polovinka, M. P.; Salakhutdinov, N. F.; Tolstikov, G. A. *Chem. Nat. Compd.* **2009**, *45*, 251.
[350] Furmeier, S.; Metzger, J. O. *Eur. J. Org. Chem.* **2003**, 885.
[351] Baker, R. W.; Kyasnoor, R. V.; Sargent, M. V. *Tetrahedron Lett.* **1999**, *40*, 3475.
[352] Wiener, C.; Schroeder, C. H.; West, B. D.; Link, K. P. *J. Org. Chem.* **1962**, *27*, 3086.
[353] Boyer, J. H.; Sanders, M., Jr. *J. Org. Chem.* **1961**, *26*, 1644.
[354] Doorenbos, N. J.; Singh, H. *J. Pharm. Sci.* **1962**, *51*, 418.
[355] De Ruggieri, P.; Ferrari, C.; Gandolfi, C. *Gazz. Chim. Ital.* **1961**, *91*, 655.
[356] Abraham, J.; Jindal, D. P.; Singh, H. *Indian J. Chem.* **1989**, *28B*, 1051.
[357] Bentley, K. W.; Hardy, D. G.; Smith, A. C. B. *J. Chem. Soc. C* **1969**, 2235.
[358] Chen, I. L.; Chen, J.-Y.; Shieh, P.-C.; Chen, J.-J.; Lee, C.-H.; Juang, S.-H.; Wang, T.-C. *Bioorg. Med. Chem.* **2008**, *16*, 7639.
[359] Bentley, K. W.; Bower, J. D.; Smith, A. C. B. *J. Chem. Soc. C* **1969**, 2241.
[360] Jaz, J.; Davreux, J. P. *Tetrahedron Lett.* **1966**, *7*, 277.
[361] Sekiguchi, H. *Bull. Soc. Chim. Fr.* **1965**, 691.
[362] Watanab, H.; Kuwat, S.; Koyam, S. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 143.
[363] Mitsuhashi, K.; Nomura, K. *Chem. Pharm. Bull.* **1965**, *13*, 951.
[364] Tamura, Y.; Kita, Y. *Chem. Pharm. Bull.* **1971**, *19*, 1735.
[365] Hutchison, G. I.; Prager, R. H.; Ward, A. D. *Aust. J. Chem.* **1980**, *33*, 2477.
[366] Elderfield, R. C.; Losin, E. T. *J. Org. Chem.* **1961**, *26*, 1703.
[367] Potti, N. D.; Nobles, W. L. *J. Pharm. Sci.* **1968**, *57*, 1785.
[368] Duong, T.; Prager, R. H.; Tippett, J. M.; Ward, A. D.; Kerr, D. I. B. *Aust. J. Chem.* **1976**, *29*, 2667.
[369] Rosenberg, M. G.; Haslinger, U.; Brinker, U. H. *J. Org. Chem.* **2002**, *67*, 450.
[370] Duong, T.; Prager, R. H.; Ward, A. D.; Kerr, D. I. B. *Aust. J. Chem.* **1976**, *29*, 2651.
[371] Ivanov, E. I.; Konup, I. P.; Konup, L. A.; Stepanov, D. E.; Grishchuk, L. V.; Vysotskaya, V. V. *Khim.-Farm. Zh.* **1993**, *27*, 37.
[372] Kralicek, J.; Kondelikova, J.; Kubanek, V. *Collect. Czech. Chem. Commun.* **1972**, *37*, 1130.
[373] Khuthier, A. H.; Robertson, J. C. *J. Org. Chem.* **1970**, *35*, 3760.
[374] Hughes, C. G.; Lewars, E. G.; Rees, A. H. *Can. J. Chem.* **1974**, *52*, 3327.
[375] Reinisch, G.; Bara, H.; Klare, H. *Chem. Ber.* **1966**, *99*, 856.
[376] Arya, V. P.; Shenoy, M. S. J. *Indian J. Chem.* **1972**, *10*, 815.
[377] Tamura, Y.; Yoshimura, Y.; Kita, Y. *Chem. Pharm. Bull.* **1971**, *19*, 1068.
[378] Mitsuhashi, K.; Nomura, K.; Watanabe, I.; Minami, N. *Chem. Pharm. Bull.* **1969**, *17*, 1572.
[379] Tochtermann, W.; Heuer, M. *Chem. Ber.* **1982**, *115*, 2125.
[380] Pozgan, F.; Polanc, S.; Kocevar, M. *Heterocycles* **2002**, *56*, 379.
[381] Rickards, R. W.; Smith, R. M. *Tetrahedron Lett.* **1966**, *7*, 2361.
[382] Naito, T.; Okumura, J.; Kasai, K.; Masuko, K.; Hoshi, H.; Kamachi, H.; Kawaguchi, H. *J. Antibiot.* **1977**, *30*, 698.
[383] Miyake, Y.; Shimadzu, H.; Hashimoto, N.; Ishida, Y.; Shibakawa, M.; Nishimura, T. *J. Labelled Compd. Radiopharm.* **2000**, *43*, 983.
[384] Torisawa, Y.; Nishi, T.; Minamikawa, J.-i. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 448.
[385] Di Maio, G.; Tardella, P. A. *Gazz. Chim. Ital.* **1961**, *91*, 1345.
[386] Hassner, A.; Ferdinandi, E. S.; Isbister, R. J. *J. Am. Chem. Soc.* **1970**, *92*, 1672.
[387] Lansbury, P. T.; Mancuso, N. R. *J. Am. Chem. Soc.* **1966**, *88*, 1205.
[388] Arcus, C. L.; Marks, R. E.; Coombs, M. M. *J. Chem. Soc.* **1957**, 4064.
[389] Conley, R. T.; Nowak, B. E. *J. Org. Chem.* **1961**, *26*, 692.
[390] Mehta, G.; Rao, K. S. *Indian J. Chem.* **1982**, *21B*, 981.
[391] Mehta, G.; Suri, S. C. *Tetrahedron Lett.* **1980**, *21*, 3821.
[392] Bardakos, V.; Sucrow, W. *Chem. Ber.* **1978**, *111*, 1780.
[393] Ortega, R.; Ravina, E.; Masaguer, C. F.; Areias, F.; Brea, J.; Loza, M. I.; Lopez, L.; Selent, J.; Pastor, M.; Sanz, F. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 1773.

[394] Mphahlele, M. J.; Moekwa, T. B. *J. Heterocycl. Chem.* **2006**, *43*, 905.
[395] Klar, H. *Arch. Pharm.* **1976**, *309*, 550.
[396] Sudan, S.; Gupta, R.; Kachroo, P. L.; Gupta, D. K.; Bhutani, K. K. *Indian J. Chem.* **1992**, *31B*, 610.
[397] Grunewald, G. L.; Dahanukar, V. H. *J. Heterocycl. Chem.* **1994**, *31*, 1609.
[398] Moore, H. W.; Shelden, H. R. *J. Org. Chem.* **1967**, *32*, 3603.
[399] Seeboth, H. *Monatsberichte der Deutschen Akademie der Wissenschaften zu Berlin* **1964**, *6*, 268.
[400] Maio, G. D.; Permutti, V. *Tetrahedron* **1966**, *22*, 2059.
[401] Hunter, N. R.; Khan, M. Z.; Marat, K.; El-Kabbani, O. A. L.; Delbaere, L. T. J. *Can. J. Chem.* **1987**, *65*, 137.
[402] Carter, K. N. *J. Org. Chem.* **1966**, *31*, 4257.
[403] Sasaki, T.; Eguchi, S.; Toru, T. *J. Org. Chem.* **1970**, *35*, 4109.
[404] Sasaki, T.; Eguchi, S.; Toru, T. *J. Chem. Soc. D* **1969**, 1285.
[405] Duddeck, H.; Brosch, D.; Koppetsch, G. *Tetrahedron* **1985**, *41*, 3753.
[406] Mehta, G.; Pandey, P. N.; Usha, R.; Venkatesan, K. *Indian J. Chem.* **1981**, *20B*, 177.
[407] Mehta, G.; Srikrishna, A. *Indian J. Chem.* **1980**, *19B*, 997.
[408] Afsah, E. M.; Metwally, M. A.; Khalifa, M. M. *Monatsh. Chem.* **1984**, *115*, 303.
[409] Clive, D. L. J.; Li, Z.; Yu, M. *J. Org. Chem.* **2007**, *72*, 5608.
[410] Valderrama, J. A.; Pessoa-Mahana, H.; Tapia, R. *Synth. Commun.* **1992**, *22*, 629.
[411] Jones, G. *J. Chem. Soc. C* **1967**, 1808.
[412] Casey, M.; Donnelly, J. A.; Ryan, J. C.; Ushioda, S. *ARKIVOC* **2003**, 310.
[413] Sasaki, T.; Eguchi, S.; Toru, T. *J. Org. Chem.* **1971**, *36*, 2454.
[414] Mehta, G.; Chaudhury, B.; Singh, V. K.; Usha, R.; Varughese, K. I.; Venkatesan, K. *Indian J. Chem.* **1981**, *20B*, 186.
[415] Greco, C. V.; Gray, R. P. *Tetrahedron* **1970**, *26*, 4329.
[415a] Zukerman-Schpector, J.; Biaggio, F. C.; Rufinoh, A. R.; Caracelli, I. *Acta Crystallogr.* **1999**, *C55*, 416.
[416] Mitsuhashi, K.; Nomura, K.; Miyoshi, F. *Chem. Pharm. Bull.* **1971**, *19*, 1983.
[417] Dinda, B.; Das, S. K.; Hajra, A. K.; Bhattacharya, A.; De, K.; Chel, G.; Achari, B. *Indian J. Chem.* **1999**, *38B*, 577.
[418] Escale, R.; El Khayat, A.; Vidal, J. P.; Girard, J. P.; Rossi, J. C. *J. Heterocycl. Chem.* **1984**, *21*, 1033.
[419] Arcus, C. L.; Barrett, G. C. *J. Chem. Soc.* **1961**, 1408.
[420] Kocevar, M.; Polanc, S.; Tisler, M.; Vercek, B. *Heterocycles* **1990**, *30*, 227.
[421] Richter, R.; Tucker, B.; Ulrich, H. *J. Org. Chem.* **1983**, *48*, 1694.
[422] Hjelte, N. S.; Agback, T. *Acta Chem. Scand.* **1964**, *18*, 191.
[423] Guzikowski, A. P.; Cai, S. X.; Espitia, S. A.; Hawkinson, J. E.; Huettner, J. E.; Nogales, D. F.; Tran, M.; Woodward, R. M.; Weber, E.; Keana, J. F. W. *J. Med. Chem.* **1996**, *39*, 4643.
[424] Guzikowski, A. P.; Whittemore, E. R.; Woodward, R. M.; Weber, E.; Keana, J. F. W. *J. Med. Chem.* **1997**, *40*, 2424.
[425] Dallemagne, P.; Tembo, O.; Rault, S.; Robba, M. *Bull. Soc. Chim. Fr.* **1989**, 98.
[426] Evans, D. D.; Weale, J.; Weyell, D. J. *Aust. J. Chem.* **1973**, *26*, 1333.
[427] Kralicek, J.; Kondelikova, J.; Kubanek, V.; Smrckova, H. *Sb. Vys. Sk. Chem. Techn.* **1973**, *C18*, 17.
[428] Kralicek, J.; Kondelikova, J.; Krivinkova, D. *Collect. Czech. Chem. Commun.* **1971**, *36*, 3275.
[429] Tafesse, L.; Kyle, D. J. *Comb. Chem. High Throughput Screen.* **2004**, *7*, 153.
[430] Mehta, G.; Singh, V.; Pandy, P. N.; Cameron, T. S.; Gardner, P. A. *J. Chem. Soc., Chem. Commun.* **1982**, 217.
[431] Mehta, G.; Suri, S. C. *Tetrahedron Lett.* **1980**, *21*, 2093.
[432] Balamurali, R.; Prasad, K. J. R. *Heterocycl. Commun.* **2000**, *6*, 153.
[433] Kocevar, M.; Stanovnik, B.; Tisler, M. *Monatsh. Chem.* **1988**, *119*, 597.
[434] Kissing, W.; Witkop, B. *Chem. Ber.* **1975**, *108*, 1623.
[435] Kondelikova, J.; Kralicek, J.; Smolikova, J.; Blaha, K. *Collect. Czech. Chem. Commun.* **1973**, *38*, 523.

[436] Doomes, E. *J. Heterocycl. Chem.* **1976**, *13*, 371.
[437] Lansbury, P. T.; Mancuso, N. R. *Tetrahedron Lett.* **1965**, *6*, 2445.
[438] Brouard, J. P.; Resplandy, A. *C.R. Hebd. Sceances Acad. Sci.* **1975**, *280*, 885.
[439] Arcus, C. L.; Coombs, M. M.; Evans, J. V. *J. Chem. Soc.* **1956**, 1498.
[440] Pan, H.-L.; Fletcher, T. L. *J. Heterocycl. Chem.* **1970**, *7*, 313.
[441] Yashiro, T.; Naito, T.; Iwauchi, S.; Ito, T. *Nagoya-Shiritsu Daigaku Yakugakubu Kenkyu Nenpo* **1978**, 19.
[442] Plostnieks, J. *J. Org. Chem.* **1966**, *31*, 634.
[443] Shutske, G. M. *J. Heterocycl. Chem.* **1990**, *27*, 1617.
[444] Gatta, F.; Del Giudice, M. R.; Pomponi, M.; Marta, M. *Heterocycles* **1992**, *34*, 991.
[445] Valderrama, J. A.; Pessoa-Mahana, H.; Tapia, R. *J. Heterocycl. Chem.* **1993**, *30*, 203.
[446] Pinder, R. M. *J. Chem. Soc. C* **1969**, 1690.
[447] Blaney, F.; Faulkner, D.; McKervey, M. A. *Synth. Commun.* **1973**, *3*, 435.
[448] Perico, A.; Triolo, A.; Viti, G.; Mannucci, C.; Caviglioli, G.; Cocchini, A.; Pestellini, V.; Paoli, P.; Dapporto, P. *J. Pharm. Sci.* **1994**, *83*, 137.
[449] Yashiro, T.; Shirai, H. *Nagoya-Shiritsu Daigaku Yakugakubu Kenkyu Nenpo* **1975**, *23*, 49.
[450] Werner, L. H.; Ricca, S.; Mohacsi, E.; Rossi, A.; Arya, V. P. *J. Med. Chem.* **1965**, *8*, 74.
[451] Flemming, C. A.; Gandhi, S. S.; Gibson, M. S.; Ruediger, E. H. *Can. J. Chem.* **1982**, *60*, 624.
[452] Kobayashi, S.; Tokumoto, T.; Koike, T.; Iizuka, K.; Irie, H.; Uyeo, S. *Chem. Pharm. Bull.* **1986**, *34*, 2443.
[453] Stephenson, E. F. M. *J. Chem. Soc.* **1949**, 2620.
[454] Jones, D. H. *J. Chem. Soc. C* **1969**, 1642.
[455] Koehl, M.; Fleischhacker, W. *Arch. Pharm. (Weinheim, Ger.)* **1983**, *316*, 481.
[456] Migachev, G. I.; Grekhova, N. G.; Terent'ev, A. M. *Khim. Geterotsikl. Soedin.* **1981**, 388.
[457] Minami, S.; Tomita, M.; Takamatsu, H.; Uyeo, S. *Chem. Pharm. Bull.* **1965**, *13*, 1084.
[458] Resplandy, A.; Brouard, J. P. *Compt. Rend.* **1975**, *280*, 669.
[459] Hamama, W. S.; Hammouda, M.; Kandeel, E. M.; Afsah, E. M. *Zhonghua Yaoxue Zazhi* **1992**, *44*, 25.
[460] Campaigne, E.; Huffman, J. C.; Yodice, R. *J. Heterocycl. Chem.* **1981**, *18*, 135.
[461] Berney, D.; Schuh, K. *Helv. Chim. Acta* **1976**, *59*, 2059.
[462] Vaidya, S. P. M.; Nayak, U. R. *Indian J. Chem.* **1986**, *25B*, 581.
[463] Shiotani, S.; Kometani, T. *Chem. Pharm. Bull.* **1973**, *21*, 1053.
[464] Hammouda, M.; Hamama, W. S.; Afsah, E. M. *J. Prakt. Chem.* **1987**, *329*, 520.
[465] Mehta, G.; Singh, V. *Tetrahedron Lett.* **1978**, *19*, 4591.
[466] Hino, K.; Nagai, Y.; Uno, H.; Masuda, Y.; Oka, M.; Karasawa, T. *J. Med. Chem.* **1988**, *31*, 107.
[467] Irie, H.; Nishitani, Y.; Sugita, M.; Tamoto, K.; Uyeo, S. *J. Chem. Soc., Perkin Trans. 1* **1972**, 588.
[468] Nelson, J. D.; Modi, D. P.; Evans, P. A. *Org. Synth.* **2003**, *79*, 165.
[469] Nunn, A. J.; Rowell, F. J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2697.
[470] Bencze, W. L.; Barsky, L. I. *J. Med. Chem.* **1971**, *14*, 40.
[471] Krapcho, J.; Turk, C. F. *J. Med. Chem.* **1966**, *9*, 191.
[472] Huet, J.; Sado-Odeye, M.; Martin, M.; Guibet, P.; Linee, P.; Lacroix, P.; Quiniou, P.; Laurent, J. *Eur. J. Med. Chem.* **1974**, *9*, 376.
[473] Blaser, R.; Imfeld, P.; Schindler, O. *Helv. Chim. Acta* **1969**, *52*, 2197.
[474] Hertler, W. R.; Sharkey, W. H.; Anderson, B. C. *Macromolecules* **1976**, *9*, 523.
[475] Werner, L. H.; Ricca, S.; Rossi, A.; De Stevens, G. *J. Med. Chem.* **1967**, *10*, 575.
[476] Pellegrino, S.; Clerici, F.; Contini, A.; Leone, S.; Pilati, T.; Gelmi, M. L. *Tetrahedron* **2009**, *65*, 1995.
[477] Delyatitskaya, L. G.; Petrova, M. V.; Grinberga, S.; Tonkikh, N. N.; Strakov, A. Y. *Chem. Heterocycl. Compd.* **2000**, *36*, 728.
[478] Hamama, W. S.; Hammouda, M.; Afsah, E. M. *Z. Naturforsch., Teil B* **1988**, *43*, 483.
[479] Bergman, J.; Brimert, T. *Acta Chem. Scand.* **1999**, *53*, 48.
[480] Berney, D.; Jauner, T. *Helv. Chim. Acta* **1975**, *58*, 74.
[481] Nagarajan, K.; Shah, R. K. *J. Chem. Soc., Chem. Commun.* **1973**, 926.
[482] Sare, H. J.; Stephenson, E. F. M. *J. Chem. Soc. C* **1969**, 1149.

[483] Marsili, I. A. *Ann. Chim. (Rome)* **1962**, *52*, 3.
[484] Marsili, A.; Ricci, P. *Ann. Chim. (Rome)* **1962**, *52*, 112.
[485] Shirai, H.; Yashiro, T.; Sato, T. *Chem. Pharm. Bull.* **1969**, *17*, 1564.
[486] Klemm, L. H.; Weisert, A. *J. Heterocycl. Chem.* **1965**, *2*, 15.
[487] Hunter, W. H.; Tupper, D. E. *J. Chem. Soc., Perkin Trans. 1* **1987**, 707.
[488] Rosenmund, P.; Trommer, W.; Dorn-Zachertz, D.; Ewerdwalbesloh, U. *Liebigs Ann. Chem.* **1979**, 1643.
[489] Buege, A.; Locke, C.; Koehler, T.; Huhn, P. *Arch. Pharm.* **1994**, *327*, 99.
[490] Hammouda, M. *Indian J. Chem.* **1993**, *32B*, 1181.
[491] Bognar, R.; Makleit, S.; Radics, L.; Seki, I. *Org. Prep. Proced. Int.* **1973**, *5*, 49.
[492] Hammouda, M.; Kandeel, E. e. D.; Hamama, W.; Afsah, E. *Arch. Pharmacal Res.* **1993**, *16*, 68.
[493] Guthrie, R. W.; Henry, W. A.; Immer, H.; Wong, C. M.; Valenta, Z.; Wiesner, K. *Collect. Czech. Chem. Commun.* **1966**, *31*, 602.
[494] Uyeo, S.; Irie, H.; Yoshitake, A.; Ito, A. *Chem. Pharm. Bull.* **1965**, *13*, 427.
[495] Uyeo, S.; Shirai, H.; Koshiro, A.; Yashiro, T.; Kagei, K. *Chem. Pharm. Bull.* **1966**, *14*, 1033.
[496] Bleeker, C.; Kunick, C. *Pharmazie* **1999**, *54*, 645.
[497] Tolkunov, S. V.; Kal'nitskii, M. N.; Khizhan, A. I.; Suikov, S. Y.; Zubritskii, M. Y. *Khim. Geterotsikl. Soedin.* **1995**, 1124.
[498] Boes, M.; Fleischhacker, W.; Kratzel, M. *J. Heterocycl. Chem.* **1982**, *19*, 1113.
[499] Resplandy, A.; Le Roux, P. *C.R. Hebd. Sceances Acad. Sci.* **1967**, *265*, 1181.
[500] Cerbai, G.; Turbanti, L.; Baldacci, G. P.; Tellini, N. *Farmaco, Ed. Sci.* **1972**, *27*, 939.
[501] Misaka, Y.; Mizutani, T.; Sekido, M.; Uyeo, S. *J. Chem. Soc. C* **1968**, 2954.
[502] Matkovics, B.; Gondos, G.; Tarodi, B. *Acta Chim. Acad. Sci. Hung.* **1968**, *57*, 119.
[503] Zlotos, D. P.; Meise, W. *Heterocycles* **1997**, *45*, 2137.
[504] Matkovics, B.; Tarodi, B.; Belaspiri, L. *Acta Chim. Acad. Sci. Hung.* **1974**, *80*, 79.
[505] Yashiro, T.; Shirai, H. *Chem. Pharm. Bull.* **1970**, *18*, 164.
[506] Singh, H.; Parashar, V. V. *Tetrahedron Lett.* **1966**, *7*, 983.
[507] Singh, H.; Malhotra, R. K.; Parashar, V. V. *Tetrahedron Lett.* **1973**, *14*, 2587.
[508] Matkovics, B.; Tegyey, Z. *Acta Chim. Acad. Sci. Hung.* **1974**, *80*, 211.
[509] Bergemann, S.; Brecht, R.; Buttner, F.; Guenard, D.; Gust, R.; Seitz, G.; Stubbs, M. T.; Thoret, S. *Bioorg. Med. Chem.* **2003**, *11*, 1269.
[509a] Singh, H.; Parashar, V. V.; Mathur, R. B. *Indian J. Chem.* **1972**, *10*, 241.
[510] Matkovics, B.; Gondos, G. *Kem. Kozl.* **1969**, *31*, 287.
[511] Hazama, N.; Irie, H.; Mizutani, T.; Shingu, T.; Takada, M.; Uyeo, S.; Yoshitake, A. *J. Chem. Soc. C* **1968**, 2947.
[512] Henin, J.; Gardent, J. *J. Heterocycl. Chem.* **1986**, *23*, 975.
[513] Benn, M.; Shaw, R. *Can. J. Chem.* **1974**, *52*, 2936.
[514] Singh, H.; Gupta, S. K.; Padmanabhan, S.; Paul, D.; Bhardwaj, T. R. *Indian J. Chem.* **1977**, *15B*, 101.
[515] Morita, Y.; Hesse, M.; Renner, U.; Schmid, H. *Helv. Chim. Acta* **1976**, *59*, 532.
[516] Marsili, A.; Saettone, M. F.; Scartoni, V. *Tetrahedron* **1968**, *24*, 4993.
[517] Singh, H.; Bhardwaj, T. R.; Paul, D. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1987.
[518] Hara, S. *Pharm. Bull.* **1955**, *3*, 209.
[519] Doorenbos, N. J.; Havranek, R. E. *J. Org. Chem.* **1965**, *30*, 2474.
[520] Cristofoli, W. A.; Benn, M. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1825.
[521] Singh, H.; Padmanabhan, S.; Bose, A. D.; Kugajevsky, I. *J. Chem. Soc., Perkin Trans. 1* **1972**, 993.
[522] Siddiqui, A. H.; Baig, M. H.; Lakshmi, C. *Aust. J. Chem.* **1977**, *30*, 2271.
[523] Ahmad, M. S.; Siddiqui, A. H.; Shafiullah; Logani, S. C. *Aust. J. Chem.* **1969**, *22*, 271.
[524] Doorenbos, N. J.; Singh, H. *J. Pharm. Sci.* **1961**, *50*, 628.
[525] Ahmad, M. S.; Husain, S. R.; Husain, M.; Choudhry, Z. H. *Indian J. Chem.* **1978**, *16B*, 559.
[526] Singh, H.; Bhutani, K. K. *Indian J. Chem.* **1978**, *16B*, 95.
[527] Singh, H.; Bhutani, K. K.; Gupta, L. R. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1210.
[528] Ahmad, M. S.; Alam, Z. *Indian J. Chem.* **1988**, *27B*, 336.
[529] Dave, V.; Stothers, J. B.; Warnhoff, E. W. *Can. J. Chem.* **1979**, *57*, 1557.

[530] Ahmad, M. S.; Alam, Z. *Indian J. Chem.* **1988**, *27B*, 1001.
[531] Ahmad, M. S.; Shafiullah; Siddiqi, A. H. *Indian J. Chem.* **1969**, *7*, 1167.
[532] Mushfiq, M.; Iqbal, N. *J. Chem. Res. (S)* **1986**, 254.
[533] Singh, H.; Mathur, R. B.; Sharma, P. P. *J. Chem. Soc., Perkin Trans. 1* **1972**, 990.
[534] Irismetov, M. P.; Tsvetkova, G. Y.; Goryaev, M. I. *Zh. Obshch. Khim.* **1977**, *47*, 941.
[535] Singh, H.; Bhardwaj, T. R.; Kumar, M.; Singh, B. *Indian J. Chem.* **1986**, *25B*, 1118.
[536] Singh, H.; Bhardwaj, T. R. *Indian J. Chem.* **1978**, *16B*, 617.
[537] Ahmad, M. S.; Farooq, Z. *Indian J. Chem.* **1977**, *15B*, 233.
[538] Irismetov, M. P.; Goryaev, M. I.; Alibaeva, K. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1980**, 45.
[539] Matkovics, B.; Balazs, G.; Balaspiri, L. *Acta Physica et Chemica* **1975**, *21*, 181.
[540] Singh, H.; Malhotra, R. K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1404.
[541] Dave, V.; Stothers, J. B.; Warnhoff, E. W. *Can. J. Chem.* **1980**, *58*, 2666.
[542] Singh, H.; Padmanabhan, S. *Indian J. Chem.* **1972**, *10*, 355.
[543] Romachenko, G. N.; Goryaev, M. I.; Irismetov, M. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1972**, *22*, 67.
[544] Matkovics, B.; Tegyey, Z.; Resch, M.; Sirokman, F.; Boga, E. *Acta Chim. Acad. Sci. Hung.* **1970**, *66*, 333.
[545] Matkovics, B.; Gondos, G.; Tegyey, Z. *Acta Chim. Acad. Sci. Hung.* **1967**, *53*, 417.
[546] Ahmad, M. S.; Waris, F. *Indian J. Chem.* **1977**, *15B*, 1141.
[547] Irismetov, M. P.; Lazareva, L. A.; Praliev, K. D.; Kiseleva, E. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1994**, 78.
[548] Siddiqui, A. H.; Rajeshwar, K.; Baig, M. H.; Siddiqui, H. U. *Indian J. Chem.* **1984**, *23B*, 435.
[549] Siddiqui, A. H.; Memariani, M.; Ramesh, D.; Siddiqui, A. H. U.; Rao, V. U. M. *J. Ind. Chem. Soc.* **1990**, *67*, 39.
[550] Siddiqui, A. H.; Ramesh, D.; Reddy, K. S.; Memariani, M.; Rao, N. S. *J. Ind. Chem. Soc.* **1988**, *65*, 672.
[551] Stevenson, R. *J. Org. Chem.* **1963**, *28*, 188.
[552] Siddiqui, A. H.; Rao, K. V.; Venkatesham, I. A.; Ahmed, I.; Rao, U. M. *Acta Cienc. Indica, Chem.* **1990**, *16C*, 7.
[553] Siddiqui, A. H.; Rao, K. V.; Memariani, M.; Reddy, V. *Orient. J. Chem.* **1988**, *4*, 22.
[554] Siddiqui, A. H.; Rao, K. V.; Venkatesham, I. A.; Rao, U. M. *Acta Cienc. Indica, Chem.* **1989**, *15*, 101.
[555] Rao, K. L.; Ramraj, S. K.; Sundararamaiah, T. *J. Ind. Chem. Soc.* **1980**, *57*, 833.
[556] Ramaiah, T. S.; Ramraj, S. K.; Govardhan, C.; Rao, V. V. *J. Ind. Chem. Soc.* **1982**, *59*, 975.
[557] Sundararamaiah, T.; Ramraj, S. K.; Rao, K. L.; Bai, V. V. *J. Ind. Chem. Soc.* **1976**, *53*, 664.
[558] Barnes, C. S.; Barton, D. H. R.; Fawcett, J. S.; Thomas, B. R. *J. Chem. Soc.* **1952**, 2339.
[559] Dickerman, S. C.; Lindwall, H. G. *J. Org. Chem.* **1949**, *14*, 530.
[560] Arya, V. P.; Kaul, C. L.; Grewal, R. S.; David, J.; Talwalker, P. K.; Shenoy, S. J. *Indian J. Chem.* **1977**, *15B*, 720.
[561] Paquette, L. A.; Scott, M. K. *J. Org. Chem.* **1968**, *33*, 2379.
[562] Merour, J. Y.; Coadou, J. Y. *Tetrahedron Lett.* **1991**, *32*, 2469.
[563] Paquette, L. A.; Wise, L. D. *J. Org. Chem.* **1965**, *30*, 228.
[564] Paquette, L. A.; Wise, L. D. *J. Am. Chem. Soc.* **1965**, *87*, 1561.
[565] Skalitzky, D. J.; Marakovits, J. T.; Maegley, K. A.; Ekker, A.; Yu, X.-H.; Hostomsky, Z.; Webber, S. E.; Eastman, B. W.; Almassy, R.; Li, J.; Curtin, N. J.; Newell, D. R.; Calvert, A. H.; Griffin, R. J.; Golding, B. T. *J. Med. Chem.* **2003**, *46*, 210.
[566] Kaye, P. T.; Mphahlele, M. J. *Synth. Commun.* **1995**, *25*, 1495.
[567] Bose, A. K.; Hoffman, W. A.; Manhas, M. S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2343.
[568] Dickerman, S. C.; Besozzi, A. J. *J. Org. Chem.* **1954**, *19*, 1855.
[569] Still, I. W. J.; Thomas, M. T.; Clish, A. M. *Can. J. Chem.* **1975**, *53*, 276.
[570] Wuensch, K. H.; Stahnke, K. H.; Ehlers, A. *Chem. Ber.* **1970**, *103*, 2302.
[571] Tapia, R. A.; Centella, C. *Synth. Commun.* **2004**, *34*, 2757.
[572] Misiti, D.; Gatta, F.; Landi-Vittory, R. *J. Heterocycl. Chem.* **1971**, *8*, 231.
[573] Misiti, D.; Rimatori, V.; Gatta, F. *J. Heterocycl. Chem.* **1973**, *10*, 689.

[574] Lebosquain, D.; Decroix, B. *Heterocycles* **1993**, *36*, 2303.
[575] Venugopal, V. K.; Rao, N.; Rahman, M. F.; Bhalerao, U. T.; Thyagarajan, G. *Indian J. Chem.* **1981**, *20B*, 156.
[576] Sasaki, T.; Eguchi, S.; Kiriyama, T. *J. Org. Chem.* **1971**, *36*, 2061.
[577] Marchalin, S.; Decroix, B. *J. Heterocycl. Chem.* **1994**, *31*, 495.
[578] Geneste, P.; Kamenka, J. M.; Vidal, Y.; Fauquet, J. P.; Morel, E.; Muller, P.; Warolin, C. *Eur. J. Med. Chem.* **1978**, *13*, 53.
[579] Hester, J. B., Jr.; Rudzik, A. D.; Veldkamp, W. *J. Med. Chem.* **1970**, *13*, 827.
[580] Levai, A.; Timar, T.; Frank, L.; Hosztafi, S. *Heterocycles* **1992**, *34*, 1523.
[581] Hohenlohe-Oehringen, K. *Monatsh. Chem.* **1965**, *96*, 257.
[582] Daich, A.; Decroix, B. *J. Heterocycl. Chem.* **1991**, *28*, 1881.
[583] Ittyerah, P. I.; Mann, F. G. *J. Chem. Soc.* **1958**, 467.
[584] Amer, F. A.; Hammouda, M.; El-Ahl, A. A. S.; Abdel-Wahab, B. F. *Synth. Commun.* **2009**, *39*, 416.
[585] Shridhar, D. R.; Sastry, C. V. R.; Lal, B. *Indian J. Chem.* **1983**, *22B*, 300.
[586] Shridhar, D. R.; Sarma, C. R.; Krishna, R. R.; Sachdeva, Y. P. *Indian J. Chem.* **1979**, *17B*, 155.
[587] Gatta, F.; Landi Vittory, R.; Nunez Barrios, G.; Tomassetti, M. *Annali dell'Istituto Superiore di Sanita* **1971**, *7*, 533.
[588] Coombs, M. M. *J. Chem. Soc.* **1958**, 4200.
[589] Afsah, E. M.; Hammouda, M.; El-Fedawy, M. G. *Zhonghua Yaoxue Zazhi* **1993**, *45*, 29.
[590] Haerter, H. P.; Stauss, U.; Osiecki, J. H.; Schindler, O. *Chimia* **1976**, *30*, 50.
[591] Daich, A.; Decroix, B. *J. Heterocycl. Chem.* **1996**, *33*, 873.
[592] Marchalin, S.; Decroix, B. *Heterocycles* **1995**, *41*, 689.
[593] Harrow, T. A.; Harrison, C. E.; Williamson, W. R. N. *J. Chem. Soc. C* **1971**, 2098.
[594] Pigeon, P.; Decroix, B. *J. Heterocycl. Chem.* **1997**, *34*, 375.
[595] Misiti, D.; Rimatori, V. *Tetrahedron Lett.* **1970**, 947.
[596] Misiti, D.; Rimatori, V. *Annali dell'Istituto Superiore di Sanita* **1973**, *9, Pt 2–3*, 150.
[597] Bagolini, C.; De Witt, P.; Pacifici, L.; Ramacci, M. T. *J. Med. Chem.* **1978**, *21*, 476.
[598] Shirai, H.; Hayazaki, T. *Yakugaku Zasshi* **1970**, *90*, 352.
[599] Ichii, T. *Yakugaku Zasshi* **1962**, *82*, 999.
[600] Buzas, A.; Cossais, F.; Jacquet, J. P. *Bull. Soc. Chim. Fr.* **1972**, 4397.
[600a] Kaye, P. T.; Whittal, R. D. *S. Afr. J. Chem.* **1991**, *44*, 56.
[600b] Kaye, P. T.; Mphahlele, M. J.; Brown, M. E. *J. Chem. Soc., Perkin Trans. 2* **1995**, 835.
[601] Bhavani, N.; Natarajan, D. *J. Ind. Chem. Soc.* **1993**, *70*, 259.
[602] Carboni, S.; Da Settimo, A.; Bertini, D.; Ferrarini, P. L.; Livi, O.; Tonetti, I. *Farmaco, Ed. Sci.* **1976**, *31*, 322.
[603] Shirai, H.; Hayazaki, T.; Maki, A. *Yakugaku Zasshi* **1971**, *91*, 1228.
[604] Merour, J. Y.; Piroelle, S.; Faure, R. *J. Heterocycl. Chem.* **1994**, *31*, 141.
[605] Mphahlele, M. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3477.
[606] Kawamoto, H.; Matsuo, T.; Morosawa, S.; Yokoo, A. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3898.
[607] Ried, W.; Bopp, H. *Synthesis* **1978**, 211.
[608] Begley, M. J.; Whittaker, N. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2830.
[609] Chellappa, J.; Pandiarajan, K.; Rangarajan, T. *Indian J. Chem.* **1982**, *21B*, 778.
[610] Yamawaki, Y.; Watanabe, M.; Yamamura, S.; Saito, S. *Yakugaku Zasshi* **1977**, *97*, 135.
[611] Chattopadhyay, F.; Mallik, A. K. *J. Indian Chem. Soc.* **2008**, *85*, 1057.
[612] Boyer, J. H.; Canter, F. C. *J. Am. Chem. Soc.* **1955**, *77*, 3287.
[613] Dietzsch, K. *J. Prakt. Chem.* **1963**, *20*, 202.
[614] Yukawa, Y.; Tanaka, K. *Mem. Inst. Sci. Ind. Res., Osaka Univ.* **1957**, *14*, 199.
[615] Alberici, G. F.; Andrieux, J.; Adam, G.; Plat, M. M. *Tetrahedron Lett.* **1983**, *24*, 1937.
[616] Adam, G.; Andrieux, J.; Plat, M. *Tetrahedron* **1985**, *41*, 399.
[617] Arcus, C. L.; Mesley, R. J. *J. Chem. Soc.* **1953**, 178.
[618] Tietz, R. F.; McEwen, W. E. *J. Am. Chem. Soc.* **1955**, *77*, 4007.
[619] Kuhn, L. P.; DiDomenico, J. *J. Am. Chem. Soc.* **1950**, *72*, 5777.
[620] Ege, S. N.; Sherk, K. W. *J. Am. Chem. Soc.* **1953**, *75*, 354.

[621] McEwen, W. E.; Mehta, N. B. *J. Am. Chem. Soc.* **1952**, *74*, 526.
[622] Arcus, C. L.; Lucken, E. A. *J. Chem. Soc.* **1955**, 1634.
[623] McEwen, W. E.; Gilliland, M.; Sparr, B. I. *J. Am. Chem. Soc.* **1950**, *72*, 3213.
[624] Tanga, M. J.; Reist, E. J. *J. Heterocycl. Chem.* **1986**, *23*, 747.
[625] Berger, A.; McEwen, W. E.; Kleinberg, J. *J. Am. Chem. Soc.* **1961**, *83*, 2274.
[626] Batchu, V. R.; Barange, D. K.; Kumar, D.; Sreekanth, B. R.; Vyas, K.; Reddy, E. A.; Pal, M. *Chem. Commun.* **2007**, 1966.
[627] Arseniyadis, S.; Wagner, A.; Mioskowski, C. *Tetrahedron Lett.* **2004**, *45*, 2251.
[628] Pearson, W. H.; Fang, W.-K. *Isr. J. Chem.* **1997**, *37*, 39.
[629] Song, D.; Rostami, A.; West, F. G. *J. Am. Chem. Soc.* **2007**, *129*, 12019.
[630] Hajnal, A.; Wolfling, J.; Schneider, G. *Synlett* **2002**, 1077.
[631] Fenster, E.; Rayabarapu, D. K.; Zhang, M.; Mukherjee, S.; Hill, D.; Neuenswander, B.; Schoenen, F.; Hanson, P. R.; Aubé, J. *J. Comb. Chem.* **2008**, *10*, 230.
[632] Lee, H.-L.; Aubé, J. *Tetrahedron* **2007**, *63*, 9007.
[633] Woelfling, J.; Oravecz, E. A.; Ondre, D.; Mernyak, E.; Schneider, G.; Toth, I.; Szecsi, M.; Julesz, J. *Steroids* **2006**, *71*, 809.
[634] Grecian, S.; Desai, P.; Mossman, C.; Poutsma, J. L.; Aubé, J. *J. Org. Chem.* **2007**, *72*, 9439.
[635] Braun, I.; Rudroff, F.; Mihovilovic, M. D.; Bach, T. *Synthesis* **2007**, 3896.
[636] Katz, C. E.; Aubé, J. *J. Am. Chem. Soc.* **2003**, *125*, 13948.
[637] Ribelin, T.; Katz, C. E.; English, D. G.; Smith, S.; Manukyan, A. K.; Day, V. W.; Neusenswander, B.; Poutsma, J. L.; Aubé, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 6233.
[638] Katz, C. E.; Ribelin, T.; Withrow, D.; Basseri, Y.; Manukyan, A. K.; Bermudez, A.; Nuera, C. G.; Day, V. W.; Powell, D. R.; Poutsma, J. L.; Aubé, J. *J. Org. Chem.* **2008**, *73*, 3318.
[639] Zhu, W.-J.; Wu, P.; Liang, X.-M.; Dong, Y.-H.; Zhang, J.-J.; Yuan, H.-Z.; Qi, S.-H.; Meng, X.-Q.; Wu, J.-P.; Chen, F.-H.; Wang, D.-Q. *J. Agric. Food Chem.* **2008**, *56*, 6547.
[640] Fenster, E.; Smith, B. T.; Gracias, V.; Milligan, G. L.; Aubé, J. *J. Org. Chem.* **2008**, *73*, 201.
[641] Ramanathan, S. K.; Keeler, J.; Lee, H.-L.; Reddy, D. S.; Lushington, G.; Aubé, J. *Org. Lett.* **2005**, *7*, 1059.
[642] Rostami, A.; Wang, Y.; Arif, A. M.; McDonald, R.; West, F. G. *Org. Lett.* **2007**, *9*, 703.
[643] Molina, P.; Alcantara, J.; Lopez-Leonardo, C. *Synlett* **1995**, 363.
[644] Reddy, P. G.; Varghese, B.; Baskaran, S. *Org. Lett.* **2003**, *5*, 583.
[645] Gu, P.; Zhao, Y.-M.; Tu, Y. Q.; Ma, Y.; Zhang, F. *Org. Lett.* **2006**, *8*, 5271.
[646] Zhao, Y.-M.; Gu, P.; Tu, Y.-Q.; Fan, C.-A.; Zhang, Q. *Org. Lett.* **2008**, *10*, 1763.
[647] Zeng, Y.; Reddy, D. S.; Hirt, E.; Aubé, J. *Org. Lett.* **2004**, *6*, 4993.
[648] Frankowski, K. J.; Neuenswander, B.; Aubé, J. *J. Comb. Chem.* **2008**, *10*, 721.
[649] Huh, C. W.; Somal, G. K.; Katz, C. E.; Pei, H.; Zeng, Y.; Douglas, J. T.; Aubé, J. *J. Org. Chem.* **2009**, *74*, 7618.
[650] Zeng, Y.; Aubé, J. *J. Am. Chem. Soc.* **2005**, *127*, 15712.
[651] Grecian, S.; Aubé, J. *Org. Synth.* **2007**, *84*, 347.
[652] Szostak, M.; Yao, L.; Aubé, J. *Org. Lett.* **2009**, *11*, 4386.
[653] Lertpibulpanya, D.; Marsden, S. P. *Org. Biomol. Chem.* **2006**, *4*, 3498.
[654] Ghosh, P.; Judd, W. R.; Ribelin, T.; Aubé, J. *Org. Lett.* **2009**, *11*, 4140.
[655] Wendt, J. A.; Aubé, J. *Tetrahedron Lett.* **1996**, *37*, 1531.
[656] Zhang, X.-M.; Wang, M.; Tu, Y.-Q.; Fan, C.-A.; Jiang, Y.-J.; Zhang, S.-Y.; Zhang, F.-M. *Synlett* **2008**, 2831.
[657] Yao, L.; Aubé, J. *J. Am. Chem. Soc.* **2007**, *129*, 2766.
[658] Zhao, Y.-M.; Gu, P.; Zhang, H.-J.; Zhang, Q.-W.; Fan, C.-A.; Tu, Y.-Q.; Zhang, F.-M. *J. Org. Chem.* **2009**, *74*, 3211.
[659] Gu, P. M.; Zhao, Y. M.; Tu, Y. Q.; Wang, M.; Zhang, S. Y. *Chin. Chem. Lett.* **2007**, *18*, 917.
[660] Wrobleski, A.; Sahasrabudhe, K.; Aubé, J. *J. Am. Chem. Soc.* **2004**, *126*, 5475.
[661] Kumar, P. S.; Kapat, A.; Baskaran, S. *Tetrahedron Lett.* **2008**, *49*, 1241.
[662] Kapat, A.; Kumar, P. S.; Baskaran, S. *Beilstein J. Org. Chem.* **2007**, *3*, 49.
[663] Frankowski, K. J.; Golden, J. E.; Zeng, Y.; Lei, Y.; Aubé, J. *J. Am. Chem. Soc.* **2008**, *130*, 6018.
[664] Norris, P.; Horton, D.; Levine, B. R. *Tetrahedron Lett.* **1995**, *36*, 7811.

CHAPTER 2

THE NEBER REARRANGEMENT

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CONTENTS

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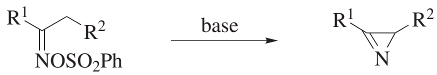
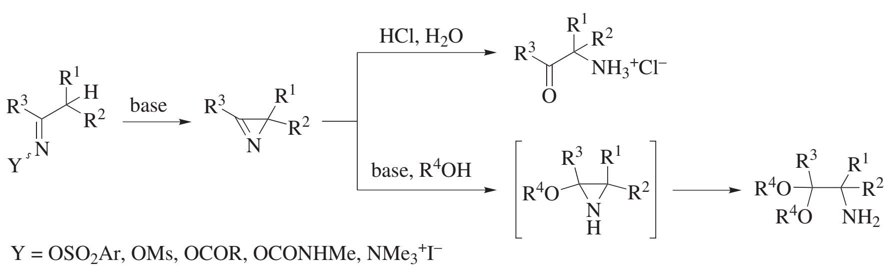
INTRODUCTION

In its original form the Neber rearrangement, discovered during an investigation of the reactions of *O*-acyl and *O*-sulfonyl ketoximes, involves the base-promoted conversion of the latter into 2*H*-azirines (Eq. 1).[1]



(Eq. 1)

Subsequent papers by the discoverer describe in detail the full panoply of reactions, intermediates, and byproducts associated with the reaction.[2–6] Key studies by Cram and Hatch confirmed both the 2*H*-azirine structure proposed by Neber and the further transformations of this reactive species.[7,8] Prior to these two papers the novelty and usefulness of the new rearrangement was infrequently noticed.[9–11] This chapter is devoted to the base-promoted rearrangement of oxime *O*-derivatives, commonly *O*-sulfonates, representing the original "Neber" rearrangement, and the similar reaction of *N*,*N*,*N*-trimethylhydrazonium iodides, the "modified Neber" rearrangement discovered by Smith.[12] These substrates react with bases to provide 2*H*-azirines or, upon subsequent aqueous, acidic work-up, α-amino ketones. When the reaction is performed using an excess of base in alcohol solvents the corresponding α-amino ketal is formed from the 2*H*-azirine via the unstable 2-alkoxy aziridine, and may be isolated or hydrolyzed in situ to the α-amino ketone. Scheme 1 summarizes the transformations that are discussed in this chapter and covered in the Tabular Survey, which includes all published examples through December 2009.



Scheme 1

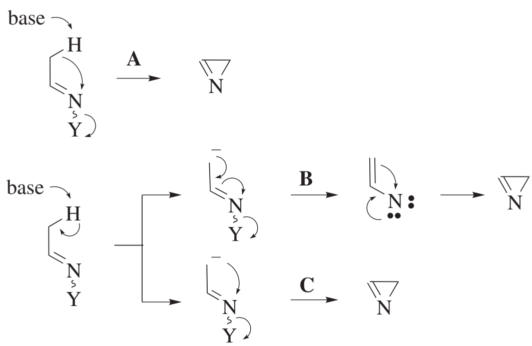
This chapter also discusses side-products encountered in these transformations and provides a comparison of the title reaction with some of the alternative routes to 2*H*-azirines, α-amino ketones, and α-amino ketals.

Only one review is devoted specifically to the Neber rearrangement,[13] but several others cover the rearrangement, generally as an adjunct of 2*H*-azirine chemistry.[14–20]

MECHANISM AND STEREOCHEMISTRY

Neither the mechanism of the Neber rearrangement, nor whether a single mechanism operates for all substrates under all conditions, is firmly established. In this section, evidence for mechanisms that have been proposed will be presented and evaluated.

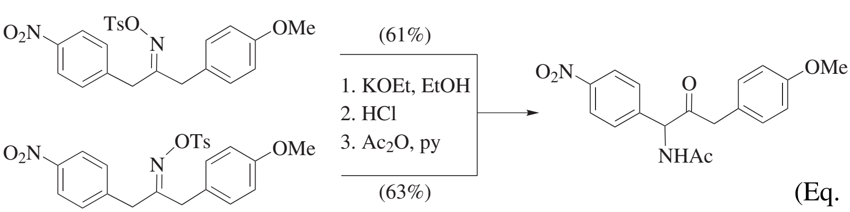
With respect to the mechanism for 2*H*-azirine formation, the three options that have been frequently discussed[7,8,13,17,20–26] are shown in Scheme 2.



Scheme 2

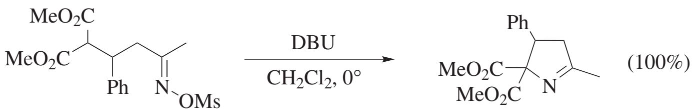
Path A involves a concerted process wherein proton removal is accompanied by carbon–nitrogen bond formation. Paths B and C involve the intermediacy of an aza-allyl anion that is converted to the 2*H*-azirine either via a vinyl nitrene (path B) or via carbon–nitrogen bond formation that is synchronous with the departure of the leaving group (path C).

An early study that has significance for all of these paths established that, in contrast to the Beckmann rearrangement, the geometry of the oxime derivative does not necessarily dictate the site selectivity of the reaction.[21,22] In the example shown in Eq. 2, cyclization of the (*E*)- and (*Z*)-isomers, under conditions where their rate of equilibration was shown to be negligible, produces the same α-acetamido ketone after acidic hydrolysis and *N*-acetylation, showing that in this system the site selectivity is determined by carbon–nitrogen bond formation at the more acidic site.



(Eq. 2)

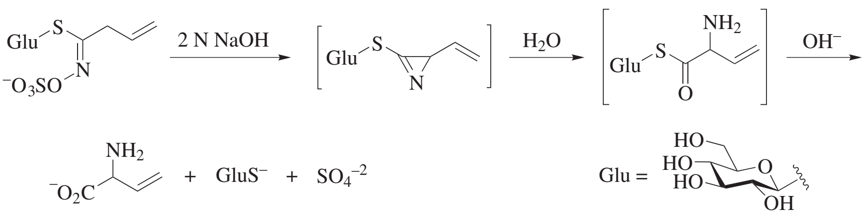
In contrast to Neber rearrangements, the successful formation of 5- and 6-membered rings by the attack of a stabilized carbanion on an *O*-sulfonyl oxime does require that the nucleophile be situated *anti* to the nitrogen–oxygen bond (Eq. 3).[27] The isomeric oxime mesylate gives none of the cyclized product.



(Eq. 3)

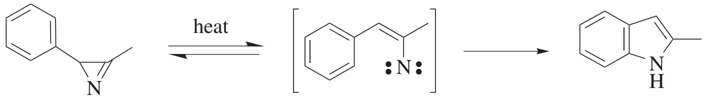
Neber rearrangements are frequently conducted using either isomer mixtures or single isomers of unknown geometry. When separated isomers are treated with base, there is no example where one isomer gives a Neber product and the other fails to do so. The influence of geometry and local steric hindrance on site selectivity when the choice is between α-protons of similar acidity is discussed and exemplified in the Scope and Limitations section.

The possibility of concerted loss of a proton with displacement of the leaving group (path A) is suggested by a single result (Scheme 3).[28] Reaction of the (*Z*)-allylglucosinolate anion[29] with aqueous base involves a Neber rearrangement followed by ring-opening of the 2*H*-azirine to produce a thiol ester, which is then hydrolyzed to vinylglycinate anion. Consistent with a concerted process, no incorporation of deuterium at the α-position of the amino acid is seen when the reaction is conducted in D_2O.[28] An alternative explanation would involve the formation of an aza-allyl anion that cyclizes faster than it reprotonates.[30]



Scheme 3

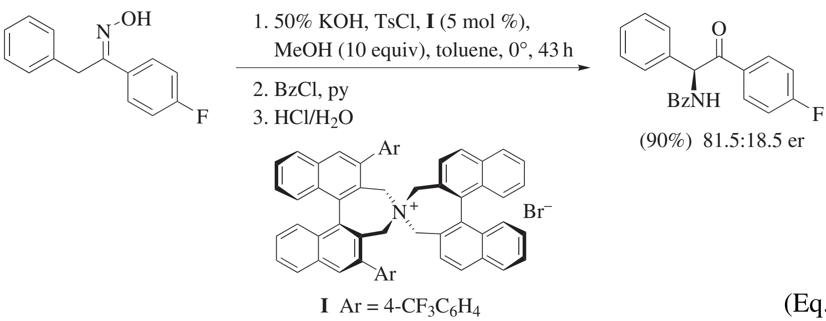
The formation of a vinyl nitrene by rapid carbanion decomposition[8,22] (path B) or by a concerted elimination would also be compatible with the lack of deuterium incorporation. A nitrene has been frequently proposed to be an intermediate in the Neber rearrangement,[13,14,16,17] by analogy to the suggested intermediacy of the same species in the thermal conversion of vinyl azides to 2*H*-azirines.[24,31–37] This latter route to 2*H*-azirines is discussed in the Comparison with Other Methods section. Vinyl nitrenes do convert to 2*H*-azirines in a reversible process,[24] as demonstrated by the fact that the rate of racemization of enantiomerically enriched 3-methyl-2-phenyl-2*H*-azirine on heating is far greater than the rate of the irreversible cyclization that ultimately forms 2-methylindole (Eq. 4).[35] It has been reported that a vinyl nitrene intermediate has been captured in such reactions as an iminophosphorane, but subsequent work explained the result by a different mechanism.[37] Hassner has provided a thorough discussion of the kinetics, energies, mechanisms, and available experimental data concerning the relationships between vinyl azides, vinyl nitrenes, and azirines.[24]



(Eq. 4)

However, the preponderance of experimental evidence[24,36] and calculations[32,33,38] now supports a concerted, conrotatory[32] ring-closure with loss of nitrogen for the vinyl azide to $2H$-azirine conversion, rather than the two-step mechanism involving a vinyl nitrene.

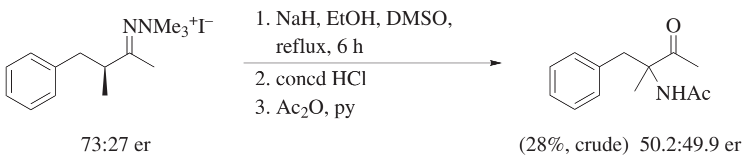
With respect to the possibility of nitrenes as intermediates in the Neber rearrangement, the observation of substantial enantiomeric enrichment in cyclizations of O-sulfonyl oximes using a chiral, enantiopure quaternary ammonium salt as a phase-transfer catalyst (Eq. 5)[25] is not consistent with the intermediacy of a neutral vinyl nitrene, but is consistent with the association of an intermediate (planar) aza-allyl anion with the chiral catalyst in the nonpolar organic phase, supporting path C. A poor fit for binding of the anion to the cation is proposed to account for the low level of enantiomeric induction observed when the isomeric oxime derivative is subjected to the same conditions. Similar effects on binding account for the drastically reduced enantioselectivity of the reaction when the nonpolar phase is absent, or when the $-OSO_2Ar$ group is replaced by an $-OSO_2Me$ group.



(Eq. 5)

An alternative explanation for these results, footnoted in the publication,[25] suggests the selective removal of one of the enantiotopic protons with simultaneous ring closure (path A). However, the necessary placement of the cation-associated hydroxide ion between the neutral substrate and the chiral cation makes a tight association of the cation with the substrate very unlikely.

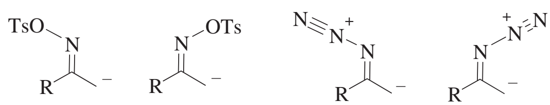
Furthermore, treating an enantiomerically enriched hydrazonium iodide with a strong base under typical Neber rearrangement conditions affords the near-racemic product (Eq. 6),[39] which implies the formation of an aza-allyl zwitterion.



(Eq. 6)

The formation and significant persistence of these zwitterions is also consistent with the mechanisms that lead to the formation of pyrroles[40] and pyridines[41] as side-products in Neber rearrangements of hydrazonium derivatives, as discussed later in the Limitations and Side-Products section. Analogous O-sulfonyl oxime rearrangements do not form these products, suggesting that the carbanions derived from these substrates convert into the $2H$-azirine more rapidly than their zwitterionic counterparts, as would be expected on the basis of the more labile leaving group.

The energy barrier to interconversion of the isomeric aza-allyl anions **1** and **2** is not known from experiment or calculation. However, calculations and low-temperature IR spectroscopy studies on vinyl azides indicate a very low barrier to equilibration of the isomers **3** and **4**, with preferred loss of dinitrogen from the *anti*-isomer.[32]



1 **2** **3** **4**

SCOPE AND LIMITATIONS

General Considerations

Whereas both oxime[8] and hydrazonium[42] derivatives of aldehydes give nitriles when treated with a base, the majority of suitably activated ketoximes and the corresponding N,N,N-trimethylhydrazonium salts will undergo Neber rearrangements, provided that an α-hydrogen is available. As noted in the preceding section, the success of the reaction is not dependent upon the configuration of the oxime derivative, and isomeric mixtures or single isomers of unknown configurations are often employed. Activated amidoximes also react to form 3-amino-$2H$-azirines or their hydrolysis products. Some failed attempts to induce Neber reactions are discussed in the Limitations and Side-Products section. Although O-tosyl oximes and hydrazonium iodides are the derivatives most frequently employed, many other oxime derivatives are also suitable substrates. As expected, other sulfonates including benzenesulfonates,[43–45] 2,4,6-trimethylbenzenesulfonates,[46] and methanesulfonates[47,48] are as effective as tosylates. In addition, Neber reactions involving 4-nitrobenzoates,[49] carbamates,[50] acetates,[51] trifluoroacetates,[52] and trichloroacetates[53,54] are known. Although few direct comparisons are available (Eq. 7),[5,11,12] most of the examples in the Tabular Survey lead to the conclusion that the choice of leaving group has no predictable effect on the yield of the $2H$-azirine or the derived α-amino ketone or α-amino ketal.

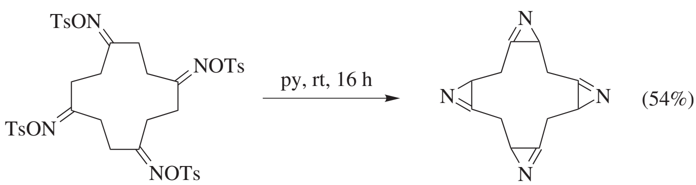
(Eq. 7)

X = NOTs (69–76%)
X = $NMe_3^+I^-$ (67%)

A variety of bases are successfully employed and their advantages and disadvantages are discussed in the subsections below. Because equivalent results are obtained in Neber rearrangements of both activated oximes and *N*,*N*,*N*-trimethylhydrazonium salts, the subsections are arranged according to product type (2*H*-azirines, α-amino ketones, and α-amino ketals) to correspond with the organization of the Tabular Survey. Issues of reaction site- and diastereoselectivity are discussed and exemplified in a separate subsection, while enantioselective reactions are treated within each subsection.

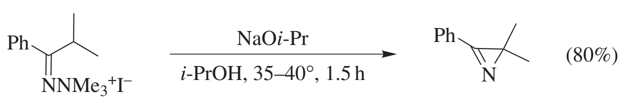
Scope

Synthesis of 2*H*-Azirines. Activated ketoximes and amidoximes and also *N*,*N*,*N*-trimethylhydrazonium salts derived from ketones are all successfully converted into 2*H*-azirines. In the majority of transformations involving oxime derivatives, an anion-stabilizing group is present. This is not a structural requirement as shown by the formation of a product containing four 2*H*-azirine units from a non-conjugated precursor (Eq. 8).[55] The successful use of a very weak base for this cyclization is unusual, and may reflect the inductive effect of the heteroatom substituents around the carbon skeleton.

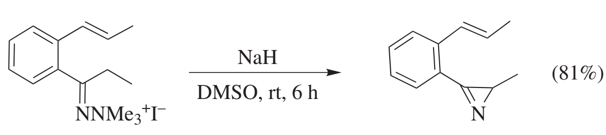


(Eq. 8)

Stronger bases are usually required to bring about cyclization when no anion-stabilizing groups are present at the site of carbon−nitrogen bond formation. Alternatively, modified Neber rearrangements of *N*,*N*,*N*-trimethylhydrazonium salts are frequently employed for the preparation of 2*H*-azirines from such substrates. Sodium isopropoxide in *i*-PrOH and sodium hydride in DMSO are the preferred base/solvent combinations, as shown in Eqs. 9[56] and 10.[57] The majority of reactions provide yields exceeding 70%.



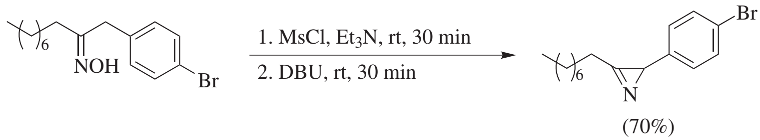
(Eq. 9)



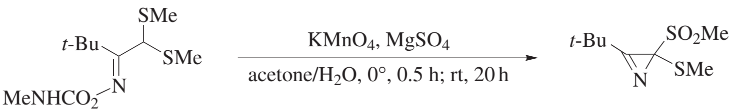
(Eq. 10)

A variety of substituted 2*H*-azirines are prepared by cyclizing *O*-sulfonyl oximes that do bear an additional anion-stabilizing group. Although the strong amidine base DBU is effective (Eq. 11),[47] weaker bases will cyclize this class of substrate. When two anion-stabilizing substituents are present, cyclization to the

2*H*-azirine occurs under near-neutral conditions, even with a carbamate leaving group (Eq. 12).[50]



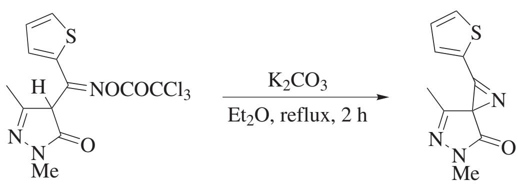
(Eq. 11)



(81%)

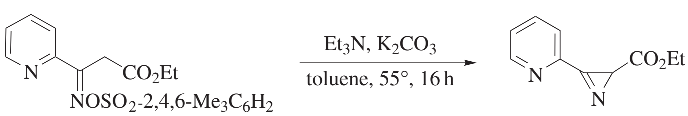
(Eq. 12)

The Neber rearrangement tolerates a variety of oxime activating groups, including *O*-(trifluoroacetate)[54] and *O*-(trichloroacetate), of which the latter has been used in the preparation of spirocyclic 2*H*-azirines (Eq. 13).[58] In addition, Mitsunobu conditions cyclize oximes via in situ activation.[47]

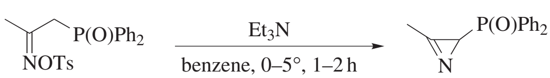


(54%) (Eq. 13)

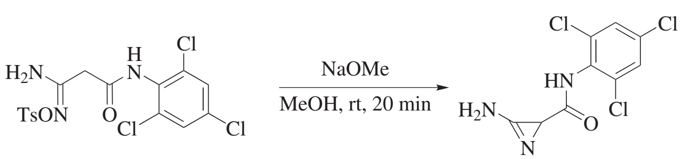
O-Sulfonyl oximes derived from β-keto esters (Eq. 14)[46] and the related β-keto phosphonates[59,60] and phosphine oxides (Eq. 15)[61] also cyclize efficiently to form 2*H*-azirines. *O*-Tosyl amidoximes are converted into 3-amino-2*H*-azirines (Eq. 16).[62]



(94%) (Eq. 14)

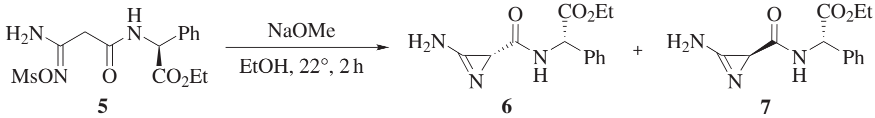


(89%) (Eq. 15)



(88%) (Eq. 16)

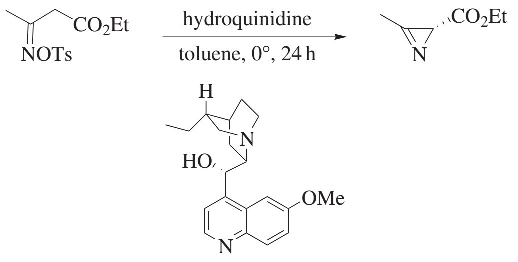
Synthesis of Chiral, Non-Racemic 2H-Azirines. O-Methanesulfonyl amidoxime **5** cyclizes to the 3-amino-2H-azirines **6** and **7** with high diastereoselectivity (Eq. 17).[63]



6 + **7** (82%), **6**:**7** = 96:4

(Eq. 17)

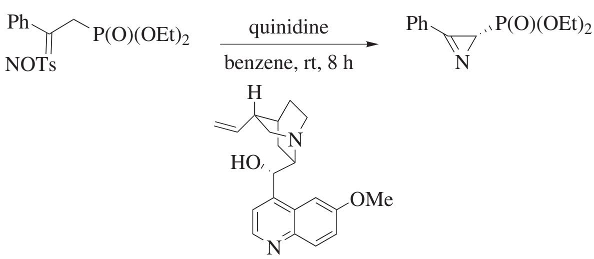
Chiral, enantiopure tertiary amine bases effect enantioselective cyclizations of O-sulfonyl oximes that contain an additional anion-stabilizing group; representative examples are shown in Eqs. 18[64] and 19.[59,60] Enantiomeric excesses are modest, reaching 65–70% after optimization. Polymer-bound chiral, non-racemic amines also accomplish these cyclizations but do not afford higher enantiomeric excesses.[59–61,65]



(74%) 85:15 er

hydroquinidine

(Eq. 18)



(85%) 82.5:17.5 er

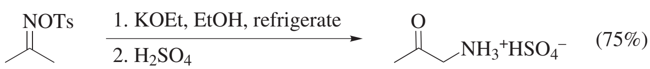
quinidine

(Eq. 19)

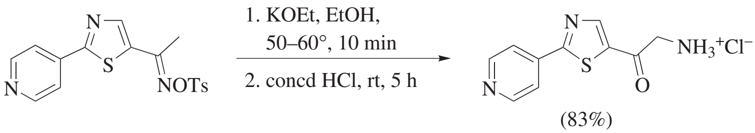
Synthesis of α-Amino Ketones. Preparations of these substances represent the most common use of the Neber rearrangement and O-sulfonyl oximes are the precursors most frequently employed. The vast majority of these preparations use a cyclization step followed by in situ hydrolysis with aqueous acid and subsequent isolation of the salt of the α-amino ketone by direct crystallization. As will be discussed in a later section dealing with side-reactions, α-amino ketones in their free-base form readily self-condense unless they are sterically hindered. For most of these two-step preparations of the salts of α-amino ketones, either sodium or potassium methoxide or ethoxide in the corresponding alcohol is employed in the rearrangement step. The composition of the product mixture at this stage is usually not determined. It is likely that excess of the alkoxide causes at least partial conversion of the $2H$-azirine to the α-amino ketal. However, both of these substances hydrolyze with acid to afford the desired product.

For the majority of these reactions a full product analysis is not available. The divergent yields reported for closely related and even identical substrates, and the isolation of a single isomer when others may also be present, may reflect the isolation of the major product by crystallization. The presence of water in the alcohol solvent is expected to diminish the yield by hydrolyzing some of the $2H$-azirine to the α-amino ketone, which will not survive the basic conditions. Water is also deleterious to the corresponding reactions of N,N,N-trimethylhydrazonium salts, causing hydrolysis of the starting material to the ketone.[39]

Diverse substrates have been subjected to the cyclization–acidic hydrolysis sequence. Examples in which a methyl group is substituted with the amino group include the simplest ketoxime (Eq. 20)[5] and more elaborate heterocyclic systems (Eq. 21).[66] A variety of *O*-tosyl aryl-ring-substituted acetophenone oximes are converted under similar conditions to the corresponding α-amino ketone salts.[6,10,11,67] However, poor yields are obtained from the corresponding *O*-acyl oximes using sodium hydride as the cyclizing agent.[68]

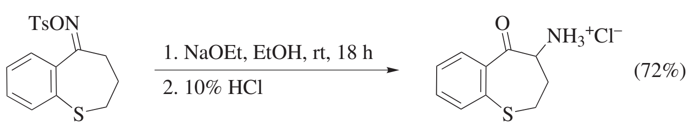


(Eq. 20)

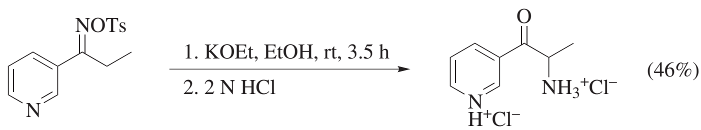


(Eq. 21)

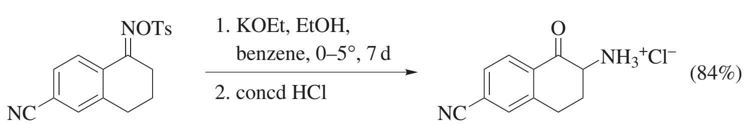
Introduction of the amino group at secondary carbons is also facile, as illustrated by Eqs. 22,[69] 23,[70] and 24.[71] Equation 24 shows that a cyano group is tolerated.



(Eq. 22)

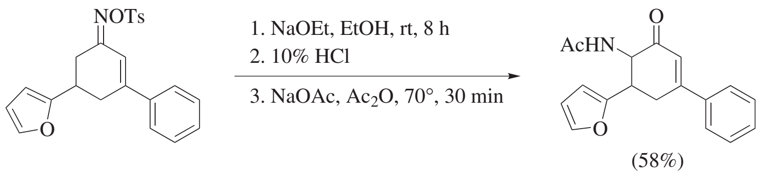


(Eq. 23)



(Eq. 24)

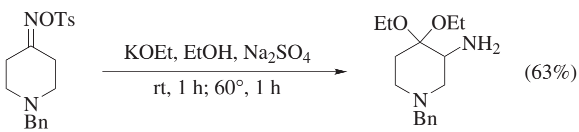
α,β-Unsaturated ketones behave normally in Neber rearrangements involving the α′-position, although examples are limited in number. Several 6-amino-3,5-diaryl-2-cyclohexenones are made and isolated as the *N*-acetyl compounds in acceptable yields under standard conditions (Eq. 25).[72] The relative configuration of the products was not specified. Lower yields are reported for similar reactions of 3-aryl-2-cyclohexenone derivatives.[73]



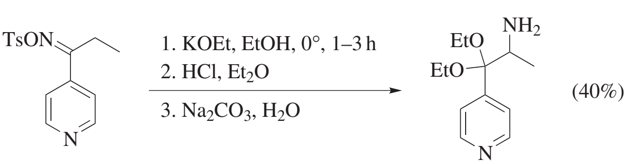
(Eq. 25)

N,*N*,*N*-Trimethylhydrazonium salts are less frequently converted into the corresponding α-amino ketones. An example where the amino group is introduced at a tertiary carbon is provided in the preparation of 2-amino-2-phenylcyclohexanone in the Experimental Procedures section. Catalyzed, enantioselective formation of α-amino ketones was discussed in the Mechanism and Stereochemistry section (Eq. 5).[25]

Synthesis of α-Amino Ketals. As discussed earlier, a 2*H*-azirine formed in alkoxide/alcohol mixtures can react further to produce the corresponding α-amino ketal as the final product. In some cases an intermediate treatment with anhydrous acid followed by either basification or recrystallization of the α-amino ketal salt is employed.[59] Isolated 2*H*-azirines are also converted into the corresponding amino ketals.[4] As expected, yields of α-amino ketals fall in the same range as those obtained in α-amino ketone preparations (Eqs. 26[74] and 27[75]). α-Amino ketal formation is limited to MeOH and EtOH: with NaO*i*-Pr in *i*-PrOH, the intermediate 2-(isopropoxy)aziridine can form, but does not react further to give the ketal.[76]



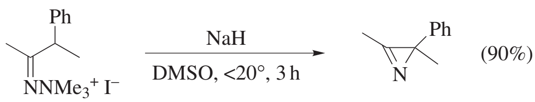
(Eq. 26)



(Eq. 27)

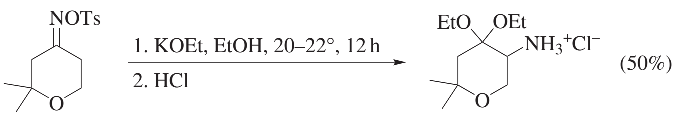
Site Selectivity and Diastereoselectivity in the Formation of 2*H*-Azirines, α-Amino Ketones, and α-Amino Ketals. With regard to site selectivity and diastereoselectivity, the number of examples in which the total product analysis is available limits the generalizations that can be made, particularly with respect to diastereoselectivity. α-Amino ketones are isolated as crystalline salts and the possible presence of a minor isomer is not investigated in most publications. When the α-amino ketal is the isolated product, reports of isomeric composition are available for a few substrates.

Site selectivity is strongly influenced by the presence of anion-stabilizing groups (Eqs. 2, 11, and 15). Carbon–nitrogen bond formation at the more acidic carbon takes place irrespective of the configuration of the starting oxime derivative. The same directing effect is seen when hydrazonium salts are cyclized (Eq. 28).[77]

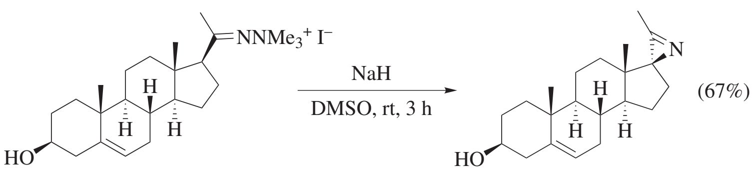


(Eq. 28)

In the absence of a second, anion-stabilizing group the influence of steric effects on site selectivity is ambiguous. An example in which the less hindered carbon is the site of carbon–nitrogen bond formation is shown in Eq. 29 (the isomeric product was not reported),[78] but in a steroid, formation of the bond to a methine rather than a methyl carbon is seen (Eq. 30).[79]

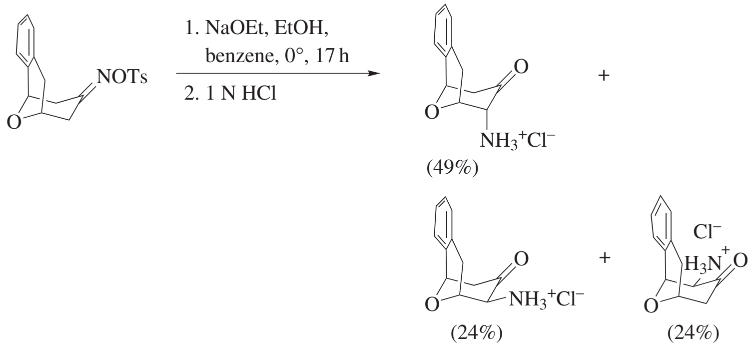


(Eq. 29)



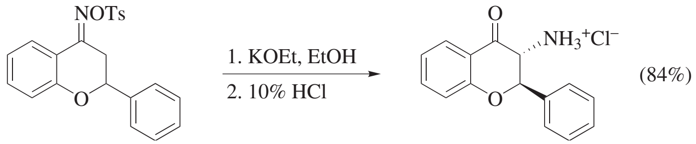
(Eq. 30)

In contrast to the above examples, when very similar positions are available, nonselective reactions can result (Eq. 31).[80]



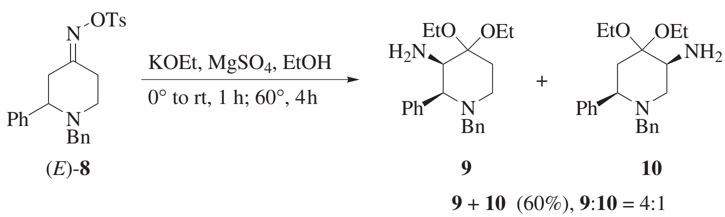
(Eq. 31)

Neber rearrangement of the *O*-tosyl oxime derived from 2-phenylchroman-4-one (flavanone)[81,82] affords a product subsequently shown[83] to be the *trans*-α-amino ketone (Eq. 32),[81] whereas reaction of the corresponding 2-methyl compound forms both isomers.[84]

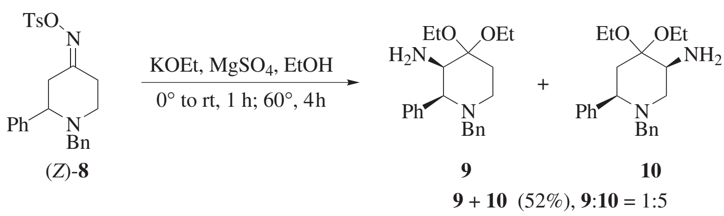


(Eq. 32)

Exclusive formation of *cis*-isomers is seen from 2-phenyl-4-piperidinone derivative **8** (Eqs. 33 and 34).[74] In this system, the separate oxime isomers give the same relative configuration of the products but different ratios of constitutional isomers **9** and **10**. The new carbon−nitrogen bond prefers to form *anti* to the original oxime nitrogen−oxygen bond. When the 2-substituent is 1-benzenesulfonylindol-2-yl, a similar directing effect of the oxime geometry is seen, although the (*Z*)-oxime gives a mixture of the *cis*- and *trans*-5-amino ketals.[85]



(Eq. 33)



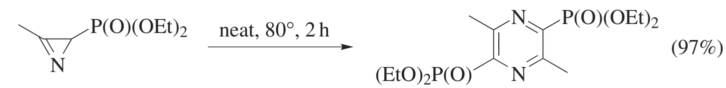
(Eq. 34)

A stereospecific Neber rearrangement to afford an α-amino ketone in a hexahydrobenzofuran system is described in the Experimental Procedures section.[86]

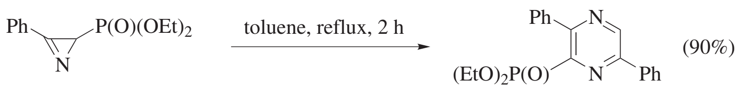
Limitations and Side-Products

No identified, consistent structural features prevent the successful closure of either activated oximes or *N*,*N*,*N*-trimethylhydrazonium derivatives. As noted earlier, when the α-amino ketal is the desired product, the substrate cannot contain groups that are sensitive to prolonged exposure to an alkali metal methoxide or ethoxide in the corresponding alcohol solvent. Side-products formed in Neber rearrangements are usually derived from further transformations of the initially formed 2*H*-azirine or of the α-amino ketone that is obtained from it by hydrolysis.

Formation of Dihydropyrazines and Pyrazines. Unless they are sterically hindered, α-amino ketones readily self-condense to form dihydropyrazines that undergo facile oxidation, usually by air, to the corresponding pyrazines.[87–90] Consequently, the latter are encountered as side-products in Neber rearrangements.[1,2,76,91] Although pyrazines most commonly result from a basification step following acidic hydrolysis of the initial cyclization products, other mechanisms are known for special substitution patterns. Simple thermal decomposition of 2-phosphinyl and 2-phosphoryl-2*H*-azirines produces pyrazines.[92] The product structure depends on the nature of the substituents on the 2*H*-azirine; 3-alkyl-2*H*-azirine-2-phosphonates form tetrasubstituted pyrazines (Eq. 35) whereas the corresponding 3-phenyl compounds form trisubstituted pyrazines (Eq. 36).[92]



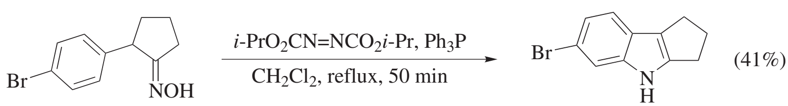
(Eq. 35)



(Eq. 36)

A nitrile ylide is the suggested intermediate in these thermal reactions,[92] with dimerization to a dihydropyrazine followed either by oxidation or elimination. The same products are also obtained by treating the precursor *O*-tosyl oximes with piperidine or diethylamine at room temperature.[92] In these reactions, conversion to the 2*H*-azirine followed by addition of the secondary amine to the carbon–nitrogen double bond, ring-opening to an α-amino ketone equivalent, dimerization, and final oxidation or elimination seems a likely route to the final pyrazines.

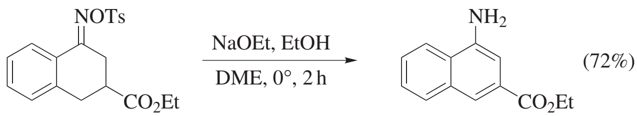
Formation of Indoles. As noted in the Mechanism and Stereochemistry section (Eq. 4), appropriately substituted 2*H*-azirines form indoles on heating, typically at 140–180°.[35,93–101] For the majority of indole syntheses of this type the starting material is the vinyl azide, which initially converts into the 2*H*-azirine as discussed below in the Comparison with Other Methods section. One example of the formation of an indole as the direct product under Neber rearrangement conditions at a significantly lower temperature is known (Eq. 37).[47] In this reaction the expected (strained) 2*H*-azirine is not isolable, but converts in situ to the indole at 40°.



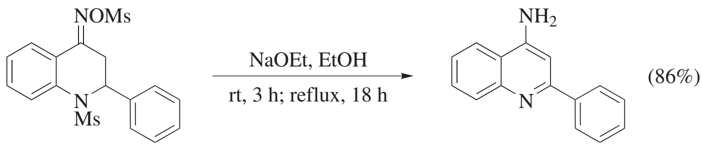
(Eq. 37)

Formation of Other Side-Products. Further transformations of the intermediate 2*H*-azirine, or interactions of that species or other intermediates with the aza-allyl zwitterions derived from trimethylhydrazonium derivatives, lead to different side-products.

Some 1-tetralone oxime derivatives bearing a C-3 carbon substituent[102–104] afford the corresponding 1-amino naphthalene under typical Neber conditions (Eq. 38).[102] A similar reaction occurs with the *N*,*O*-dimesylate of 1-oximino-3-phenyltetrahydroquinoline (Eq. 39).[105] Mechanisms involving an azirine,[102] a simple tautomerization–elimination sequence,[103] or a nitrene intermediate[105] have been suggested. The transformation of tetralone and cyclohexenone oximes to the corresponding amino naphthalenes and anilines is more frequently accomplished under acidic conditions (the Semmler–Wolff reaction).[106,107]

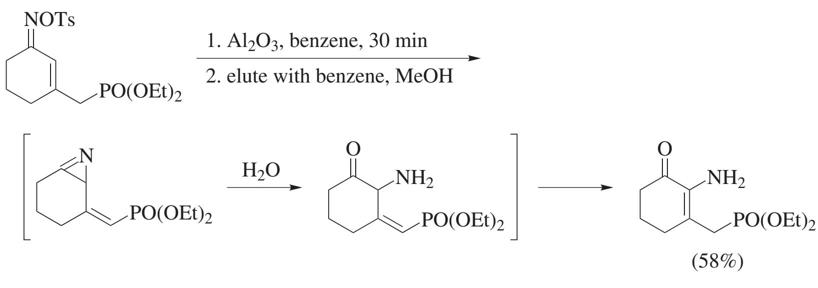


(Eq. 38)



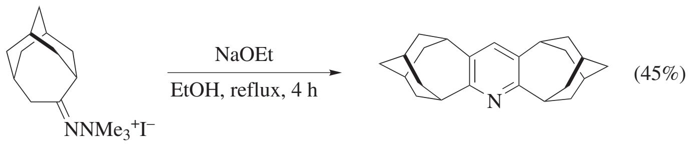
(Eq. 39)

In a vinylogous Neber rearrangement conducted on alumina, hydrolysis of the 2*H*-azirine to the α-amino ketone followed by tautomerization accounts for the observed product (Eq. 40).[108]

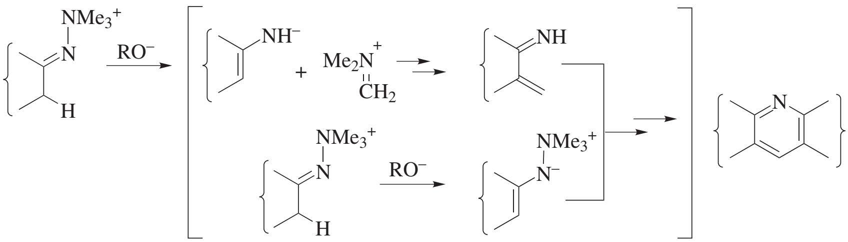


(Eq. 40)

By analogy to the proposed intermediates involved in the formation of pyridine derivatives in the thermal decomposition of trimethylhydrazonium tetrafluoroborates,[109] the corresponding base-promoted reaction shown in Eq. 41[41] is suggested to be the result of an initial fragmentation of a hydrazonium ion into an enamine anion and the *N*,*N*-dimethyl methyleneiminium ion (Eq. 42). Recombination via a Mannich reaction with β-elimination forms an unsaturated imine, and a subsequent conjugate addition–cyclization with the anion of the starting hydrazonium salt generates the new 6-membered ring.[41]

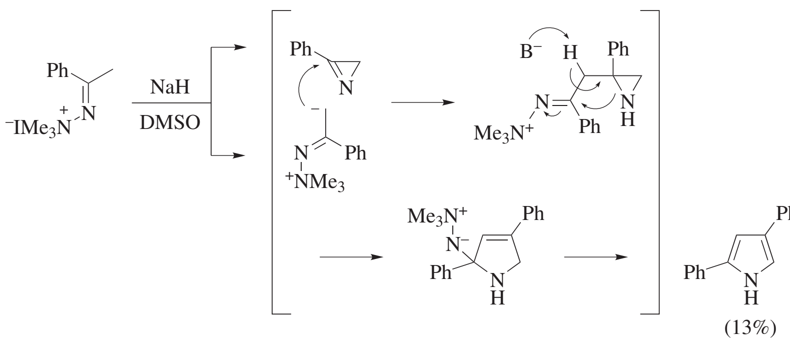


(Eq. 41)



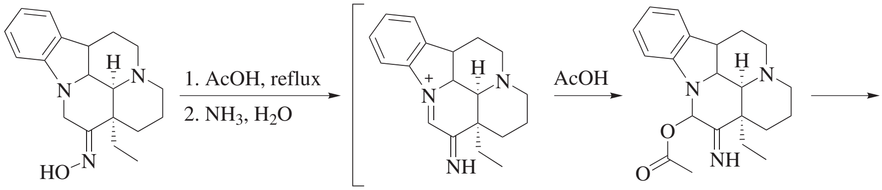
(Eq. 42)

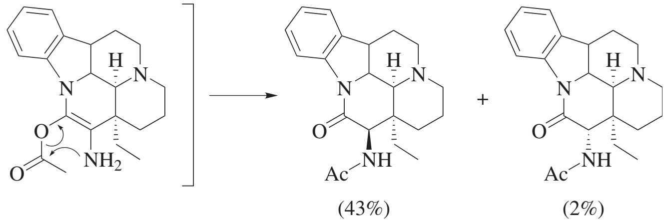
A pyrrole is also produced in an attempted Neber rearrangement. The mechanism for pyrrole formation (Eq. 43)[40] is suggested by reports of similar reactions of $2H$-azirines with enolates.[40,77,110] As shown earlier (Eq. 7), the same substrate undergoes a normal Neber rearrangement when treated with NaOEt in EtOH.[12]



(Eq. 43)

The transformation shown in Eq. 44 is suggested to involve a $2H$-azirine with a double bond shift followed by hydrolytic ring-opening.[111] However, $2H$-azirine formation under acidic conditions is unlikely and the double bond shift in $2H$-azirines has been experimentally discounted;[22,112] a more likely route would involve the conjugated iminium ion shown.

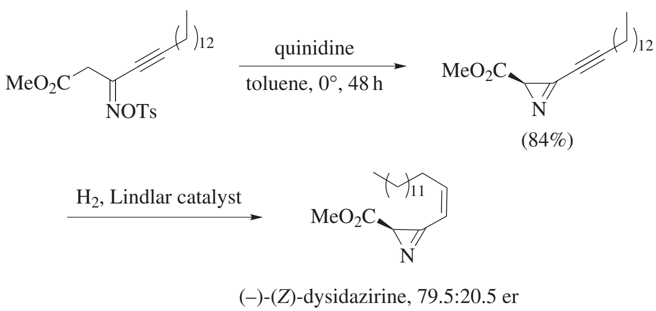




(Eq. 44)

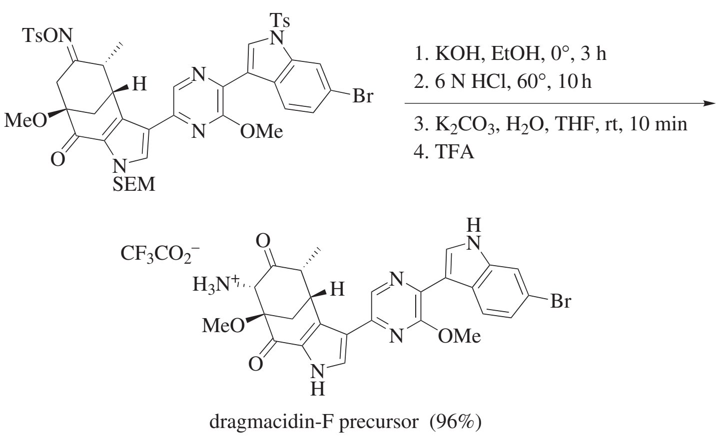
APPLICATIONS TO SYNTHESIS

Of a number of natural products that contain a $2H$-azirine ring, a $2H$-azirine-2-carboxylic acid derivative, dysidazirine, is synthesized in enantiomerically enriched form by a Neber rearrangement, using the reaction of an O-tosyl oxime with quinidine (Scheme 4).[113]



Scheme 4

An α-amino ketone produced via a Neber rearrangement is used in the synthesis of dragmacidin-F (Eq. 45).[114,115]



(Eq. 45)

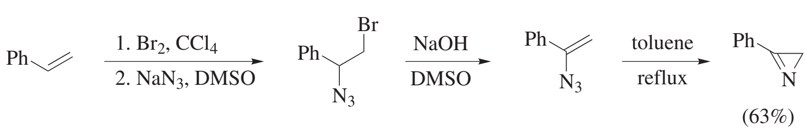
COMPARISON WITH OTHER METHODS

The ability of the Neber rearrangement to produce $2H$-azirines and/or α-amino ketones by hydrolysis, facilitating the synthesis of the large variety of heterocycles that may be derived from them, sparked a vigorous interest in alternate ways to make $2H$-azirines. The many reactions that form and exploit these reactive molecules now comprise an important chapter in the literature of heterocyclic chemistry. In addition to the Neber rearrangement, several other effective synthetic approaches to the azirines are known. The thermal and photochemical reactions of vinyl azides have found extensive application, as have the rearrangements of isoxazoles and oxazoles. In addition to these reactions, Neber-like reactions that afford products derived from intermediate $2H$-azirines and miscellaneous routes to azirines are discussed below. Alternative routes to α-amino ketones from ketones are also discussed.

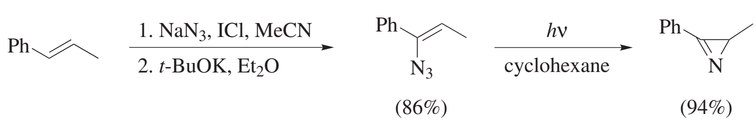
Other Routes to 2*H*-Azirines

2*H*-Azirines from Vinyl Azides. The discovery of the facile thermal rearrangement of vinyl azides to $2H$-azirines,[116] and subsequently of a photochemical version,[117] led to the development of a variety of routes to vinyl azides.[118–120] These methods have, in turn, fostered many studies of the conversion of vinyl azides into $2H$-azirines,[118,119] and $2H$-azirine-derived products,[15,17,121–124] such as amino acids,[125] aziridines,[126,127] indoles,[92,128] azepines,[128] isoxazoles,[129] oxazoles,[24,130] furoxanes,[128] carbazoles,[128] pyrroles,[121,128,131] pyridines,[128] pyridones,[128] pyrazines,[1,92] and open-chain nitriles and isonitriles.[24]

Most of the $2H$-azirine substitution patterns that are available via the Neber rearrangement may also be made via the thermal or photochemical rearrangement of a vinyl azide. Different methods for vinyl azide preparation allow different classes of starting materials to be employed. Schemes 5[132–134] and 6[135] show the formation of vinyl azides from alkenes by the addition of a halogen azide followed by dehydrohalogenation, and their conversion to $2H$-azirines.

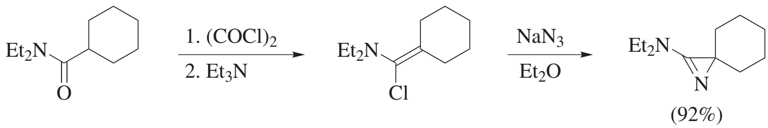


Scheme 5

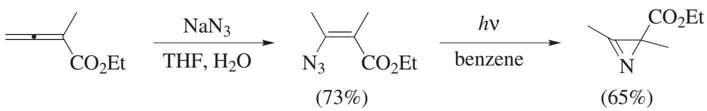


Scheme 6

3-Dialkylamino-$2H$-azirines are obtained from tertiary amides via α-chloro enamines (Scheme 7),[136] and a fully substituted $2H$-azirine-2-carboxylate is obtained via a conjugate addition of sodium azide to an allenecarboxylate, followed by photolysis (Scheme 8).[137]

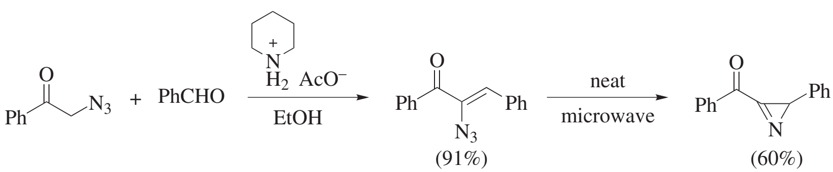


Scheme 7

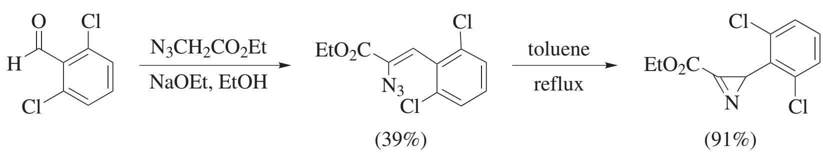


Scheme 8

Vinyl azides also form by condensation reactions of aldehydes with α-azido carbonyl compounds. Upon heating, these vinyl azides afford 2H-azirines bearing carbonyl substituents, as shown in Schemes 9[138] and 10.[139]



Scheme 9

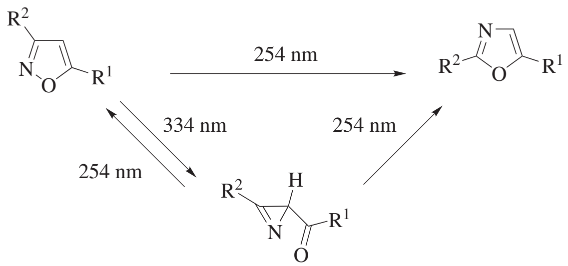


Scheme 10

Although it is versatile, the vinyl azide route is not without problems.[17,140] Different products that can form,[141] depending on the substituents and conditions,[138] include nitriles,[24] indoles,[24] and oxazoles.[130] The Neber rearrangement is the more convenient route when the precursor bears an additional activating group that controls the site of carbon–nitrogen bond formation. The efficient conversion of oximes to 2H-azirines bearing electron-withdrawing 2-substituents is illustrated in Eqs. 14 and 15. The synthesis of 3-amino-2H-azirines from amidoximes (Eq. 16) is readily achieved with the Neber rearrangement, and vinyl azide routes are also well known.[142] Unlike the Neber rearrangement, the vinyl azide route is not used to produce 2H-azirines in enantiomerically-enriched form, and although a chiral auxiliary might render such a reaction diastereoselective, no example has been reported.

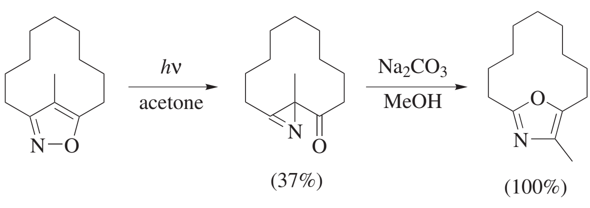
As a generalization, it is reasonable to conclude that, in the absence of interfering structural features, the choice of Neber versus vinyl azide routes may largely be predicated by the availability of the appropriate starting materials.

***2H*-Azirines from Isoxazoles.** A wide variety of substituted isoxazoles rearrange, both thermally[143–146] and photochemically,[129,147–150] to azirines and products derived from them. These rearrangements can be controlled to afford 2*H*-azirines bearing carbonyl substituents. Particularly intensive attention has been given to the structural factors involved in the thermal and photochemical interconversions of isoxazoles, azirines, and oxazoles (Scheme 11).[129]

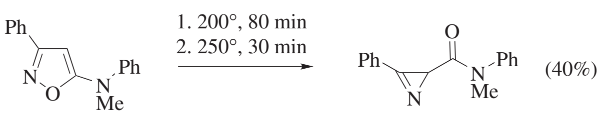


Scheme 11

The sequence in Scheme 12 shows the photochemical isomerization of an isoxazole into a 2-acyl-2*H*-azirine and the subsequent conversion of the latter substance into an oxazole by treatment with methanol and a catalytic amount of base.[150] Eq. 46 illustrates a typical, thermal rearrangement of an isoxazole into a 2*H*-azirine.[146]

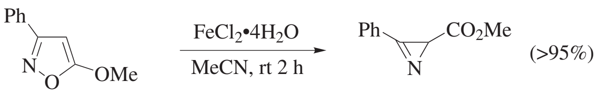


Scheme 12

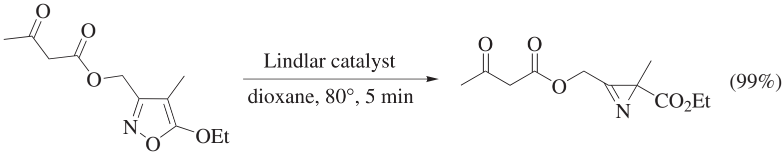


(Eq. 46)

Catalysis by metals facilitates rearrangement at much lower temperatures. A thermal reaction[143] that requires heating to 200° is accomplished at 60° in the presence of copper(I) stearate,[151] and similar rearrangements take place at room temperature in the presence of hydrated iron(II) chloride (Eq. 47).[152] An isomerization catalyzed by supported palladium is shown in Eq. 48.[153]



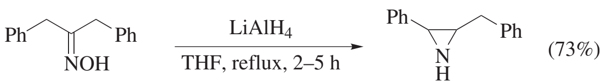
(Eq. 47)



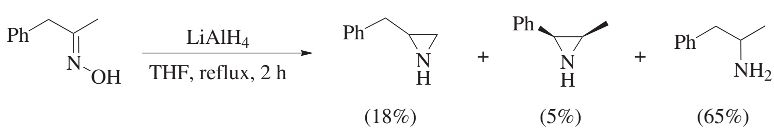
(Eq. 48)

2*H*-Azirines and Aziridines from Oximes. Reactions of oximes with either lithium aluminum hydride ($LiAlH_4$) or Grignard reagents can form aziridines.[154] 2*H*-Azirines are suggested as likely intermediates in both reactions,[155–160] and a 2*H*-azirine has been isolated from the reaction of an oxime with a Grignard reagent.[161] In these reactions, an *O*-metal species is the leaving group in the ring-closure step and the aziridine product reflects the subsequent addition of a nucleophile, either H or R, to the double bond of the intermediate 2*H*-azirine. Addition of nucleophiles to 2*H*-azirines is in fact an excellent route to aziridines.[15,17,18,121,126,162]

In $LiAlH_4$ reductions of oximes, the reaction rates and yields of the aziridine depend on the solvent;[156,158,163,164] the best yields are obtained in THF. A relatively high-yielding example is shown in Eq. 49,[156] but competing, direct reduction of the oxime to the amine can result in poorer yields (Eq. 50).[165,166] The latter example illustrates that, in contrast to the Neber rearrangement, the site selectivity of the reaction is not dominated by the acidity of the protons on the α-carbon of the oxime. When a mixture containing the isomeric *syn*-oxime is similarly treated, a larger proportion of the 2,3-disubstituted aziridine forms. This tendency for carbon–nitrogen bond formation to favor the site that is *syn* to the oxime hydroxyl is observed in other cases.[160,167–169] Reductions of 6*H*-1,2-oxazines (effectively, cyclic oxime ethers) with $LiAlH_4$ also produce aziridines via the corresponding 2*H*-azirines.[170]

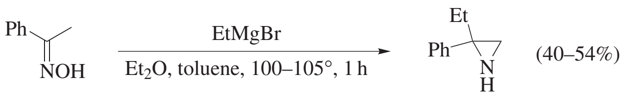


(Eq. 49)



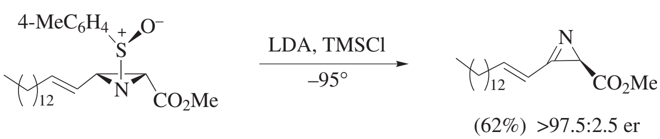
(Eq. 50)

The reaction of oximes with Grignard reagents is a convenient route to di- and trisubstituted aziridines (Eq. 51).[155] Yields are generally moderate, and byproducts have not been characterized. In the example shown, somewhat improved yields are obtained from the corresponding *O*-methyl and *O*-acetyl oximes.[155] 2*H*-Azirines are also intermediates in the formation of aziridines and pyrimidines in reactions of α,α-dibromo oxime ethers with Grignard reagents.[171]



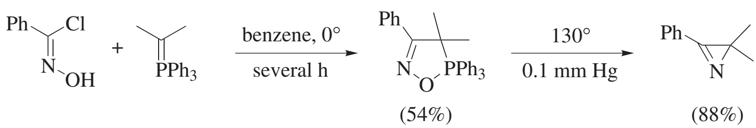
(Eq. 51)

2*H*-Azirines from Aziridines. E2 elimination of a sulfenamide,[172,173] and similar reactions involving other leaving groups attached to the nitrogen of an aziridine,[174−177] afford a 2*H*-azirine. The sulfenamide elimination, illustrated in Eq. 52, is used to form the enantiomerically enriched natural product (*R*)-(−)-dysidazirine.[172,178] Dehydrohalogenation is also used to obtain non-racemic 2*H*-azirines.[179]



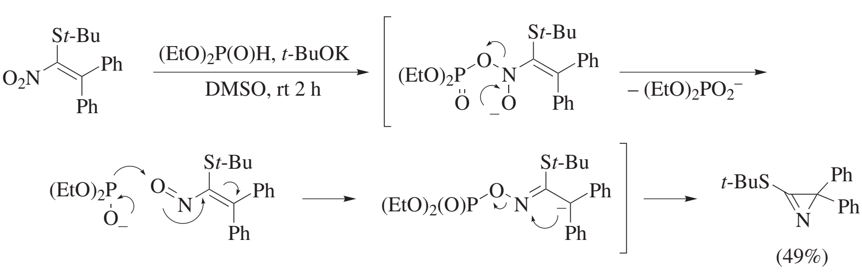
(Eq. 52)

Miscellaneous 2*H*-Azirine-Forming Reactions. 2*H*-Azirines are obtained by thermal extrusion of nitrogen from a 4*H*-triazole,[180] sulfur dioxide from a 1,5,2-oxathiazole-5-oxide,[181] or triphenylphosphine oxide from an oxazaphospholine[182−184] as shown in Scheme 13.[183]



Scheme 13

2*H*-Azirines are isolated from reactions of nitroalkenes with triphenylphosphine[185] or with diethyl phosphite anion;[186] the mechanism of the latter process is illustrated in Eq. 53.[186]



(Eq. 53)

The addition of a stabilized carbene, generated from the corresponding diazo compound, to benzonitrile also gives a 2*H*-azirine[187–189] (Eq. 54).[188]

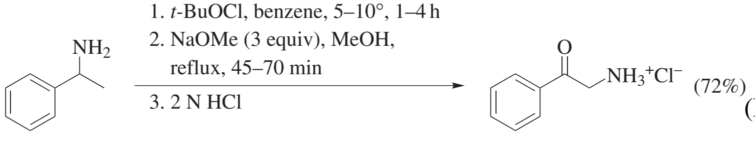
(Eq. 54)

Resolution of 2*H*-Azirines. The lipase-catalyzed kinetic resolution by acetylation of a racemic hydroxymethyl-2*H*-azirine[190,191] is effective, but the procedure has not been applied to other 2*H*-azirines bearing hydroxylated substituents. For the kinetic study described earlier (Eq. 4), the enantiomerically-enriched 2*H*-azirine is obtained from the racemate by selective destruction of one enantiomer by reaction with a substoichiometric quantity of *N*-benzyloxycarbonyl-L-leucine.[35]

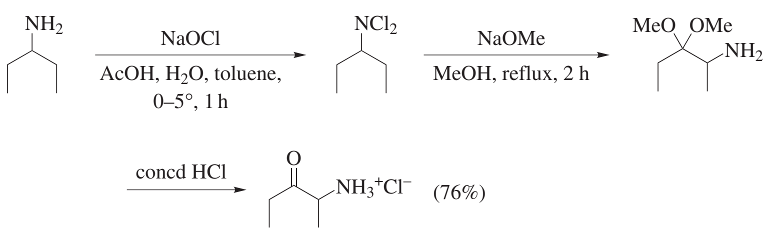
Other Routes to α-Amino Ketals and α-Amino Ketones

α-Amino ketones and their *O*- and *N*-protected forms are made by many methods.[192–195] Because of space limitations all of them cannot be summarized here, but those methods that start with a ketone and produce the primary α-amino ketone either as the salt or in a protected form are emphasized. An exception is made for the Baumgarten route to α-amino ketals from amines in view of its close mechanistic relationship with the Neber rearrangement.

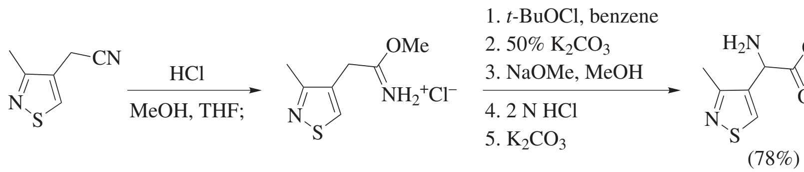
α-Amino Ketals from Amines and Imines. Mechanistically related to the Neber reactions of oxime and hydrazonium derivatives, the Baumgarten rearrangement[13,196] provides a route from amines or imines to α-amino ketals and the derived ketones. An *N*-chloroimine or, more commonly, an *N*,*N*-dichloroamine is treated with an alcohol containing the corresponding alkali metal alkoxide to afford the α-amino ketal. Although a 2*H*-azirine has never been isolated under the Baumgarten conditions, it is highly likely that 2*H*-azirines are intermediates in the reaction.[112,197,198] In the following examples, Eq. 55[196] illustrates a one-pot procedure, Scheme 14[199] shows a reaction via an isolated *N*,*N*-dichloroamine, and Scheme 15[200] exemplifies the synthesis of an amino acid from an imidate.



(Eq. 55)



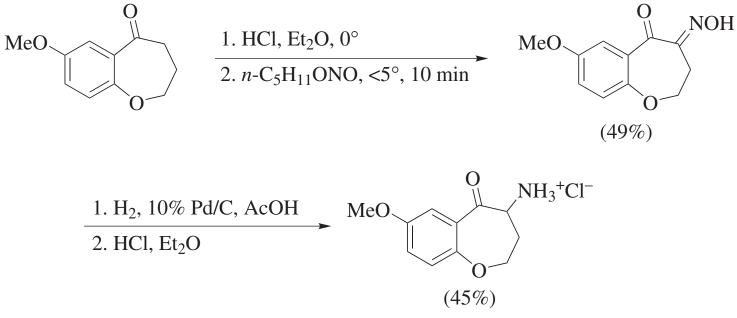
Scheme 14



Scheme 15

For the synthesis of α-amino ketals and the derived α-amino ketones, the choice between Neber and Baumgarten conditions can be made on the basis of the availability of the starting ketone or amine. The Neber rearrangement is the route of choice when the 2*H*-azirine is the desired product.

α-Amino Ketones from Ketones. *Nitrosation–Reduction.* Nitrosation of a ketone, generally with an alkyl nitrite,[192,201–203] followed by reduction of the resulting α-oximino ketone is a classical route to primary α-amino ketones. Requirements for success are enolization of the ketone in the desired direction, and selective reduction. Examples successfully use catalytic reduction,[204,205] tin(II) chloride,[206] or zinc[207] without also reducing the ketone, at times a nontrivial pursuit.[207] No asymmetric version of the reduction step is known. This method is frequently cited and employed as an alternate route to compounds appearing in the Tabular Survey. There is no consistent structural pattern that predicts which of the two methods will be the more successful. In several examples the Neber reaction succeeds[208] and the α-oximino ketone route fails,[81,82,208–211] or vice versa,[208,212] due to rearrangement, lack of formation of an intermediate, or poor conversion to the α-amino ketone product. In the specific example shown in Scheme 16,[212] the Neber route also succeeds, but in the 6,8-dimethyl analog, only the product of a Beckmann rearrangement forms on attempted Neber rearrangement of the *O*-tosyl oxime. In many examples, equivalent yields are obtained by both routes,[213–217] and in some, little or no comparative data is given.[218–220] The acid-promoted nitrosation route is not appropriate when other groups that are reactive towards the nitrosonium ion, such as alcohols, primary and secondary



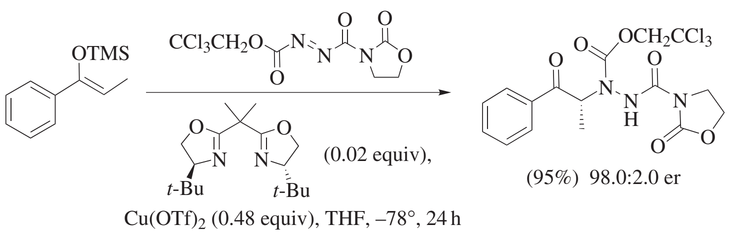
Scheme 16

amides, carbon−carbon double bonds, and highly electron-rich aromatic rings, are present.

Catalytic reduction of α-nitro ketones,[221] obtained by the related nitration of a ketone enol ether with nitronium tetrafluoroborate[222] or trifluoroacetyl nitrate[222] or by nitration of ketone enolates with alkyl nitrates,[223] is also convenient, albeit less frequently used.

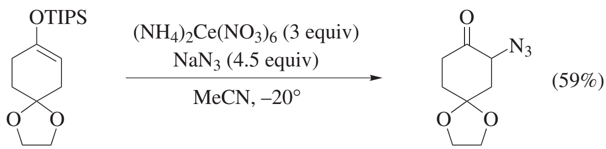
Direct, Electrophilic Amination. Introduction of a free amino group by reacting a ketone-derived enolate with a reagent such as *O*-(mesitylenesulfonyl) hydroxylamine is not a feasible approach, because of facile dimerization of the α-amino ketone under neutral or basic conditions. However, the recent, comprehensive review[192] of electrophilic amination of carbanions and their equivalents describes a variety of reagents that will convert a ketone or a derived enolate, enol ether, or enamine into an *N*-protected, primary α-amino ketone or into a related product such as an α-azido or α-hydrazino compound that can, in principle, be converted into the α-amino ketone. In contrast to nitrosation, these methods introduce a carbon−nitrogen single bond in the first step, and several will do so in an asymmetric manner. In most cases, the products are not converted to a salt of the corresponding α-amino ketone, but for the majority of the introduced groups, methodology exists that is expected to be applicable to that conversion.

Ketone-derived enolates react with esters and amides of azodicarboxylic acid to afford good yields of protected α-hydrazino ketones.[224−227] Asymmetric versions are available using a silyl enol ether[228,229] (Eq. 56)[228] or an enamine.[230]



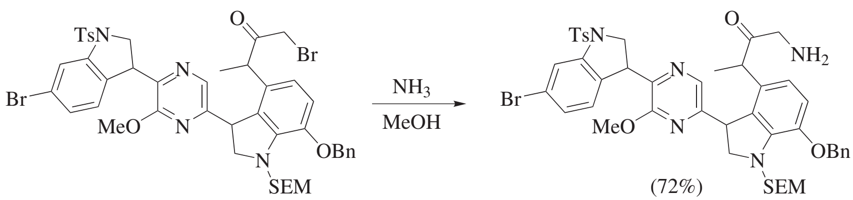
(Eq. 56)

The similar capture of enolates of esters and amides[192,203] is an efficient route to hydrazino derivatives that are easily converted into α-amino esters and α-amino acids. The analogous nitrogen−nitrogen cleavage and deprotection steps applied to an α-hydrazino ketone will afford the α-amino ketone, but examples are rare. In two instances the amine was not isolated but was converted in situ to an *N*-acetyl[225] or *N*-benzyloxycarbonyl[224] derivative, and in the third, the attempted conversion failed.[231] Direct amination of ketone enolates by *N*-(alkoxycarbonyl)oxaziridines is not efficient.[232,233] To obtain high yields of carbamate-protected α-amino ketones using these reagents, the enolate of the corresponding α-silyl ketone must be employed.[234] Aminohydroxylations of silyl enol ethers form the same products in modest yields.[235] Choramine-T plus proline,[236] the reagent "$(TsN)_2$ Se",[237] and the iodine(III) species TsN=IPh[238,239] all convert a ketone enol silyl ether to the corresponding 2-tosylamino ketone. The successful removal of the *N*-tosyl group from one product of this type, derived by a different route, is accomplished using HBr/phenol.[240] Azidation of a ketone enol silyl ether with sodium azide and cerium(IV) ammonium nitrate[231,241] is a productive route to α-azido ketones (Eq. 57).[241] One report describes the subsequent reduction of the product with Ph_3P to afford a free, sterically hindered α-amino ketone.[231] Other methods for forming and reducing α-azido ketones are described in the next section.



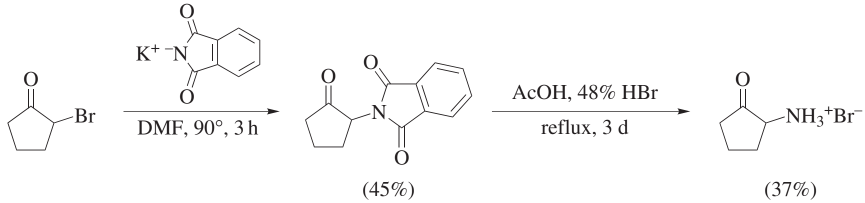
(Eq. 57)

Activation–Nucleophilic Displacement. Although *N*-substituted α-amino ketones can sometimes be prepared by direct displacement, the reaction of α-chloro- or α-bromo ketones with ammonia is not usually a satisfactory route to the primary amino compounds owing to elimination reactions[242] and the formation of pyrazines[243] and other byproducts. One successful example from a limited number[244–246] is shown in Eq. 58.[244] This free α-amino ketone is atypical in its resistance to self-condensation.



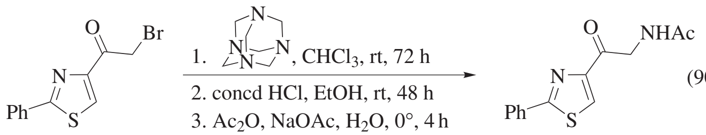
(Eq. 58)

In most cases, it is necessary to carry out the displacement step with an ammonia equivalent, followed by a deprotection, and the classical methods all succeed when applied to α-bromo ketones. An example of the Gabriel synthesis[247] is shown in Scheme 17.[248] The classical cleavage method using hydrazine obviously cannot be applied to amino ketone precursors, and the necessarily vigorous conditions for acidic hydrolysis of the phthalimido compound afford a modest yield in this instance.



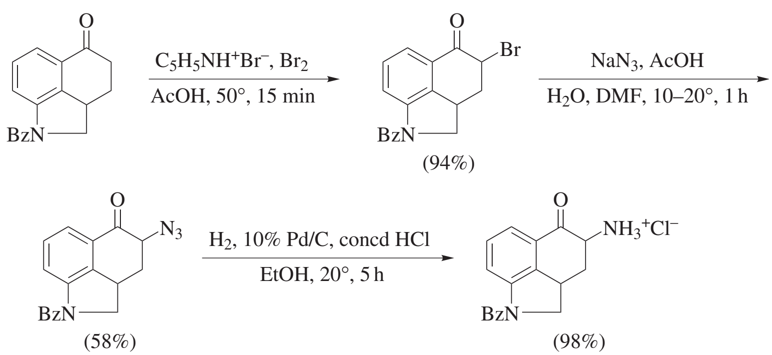
Scheme 17

A better result, especially for bromomethyl aryl ketones,[249] is obtained with the Delepine method which uses hexamethylenetetramine in the displacement step and allows milder hydrolysis conditions (Eq. 59).[250]



(Eq. 59)

A useful route to primary α-amino ketones is reduction of α-azido ketones, produced either by the electrophilic azidation described in the previous section or, more often, by reacting α-bromo ketones with sodium azide.[218,251,252] The highly nucleophilic nature of azide ion, combined with its relatively low basicity, allows successful displacements on substrates that do not give satisfactory results with more basic nitrogen nucleophiles.[252] A variety of reducing agents, used in acidic media, are effective in selectively reducing the azide.[253] Catalytic hydrogenation, reduction with phosphines, and reduction with tin(II) chloride are all employed. An example used as an alternative to a Neber rearrangement (which gives a slightly better overall yield starting from the same ketone) is given in Scheme 18.[254]



Scheme 18

EXPERIMENTAL CONDITIONS

Preparation of Starting Materials

Caution! Shock and/or thermal sensitivity of oxime tosylates has occasionally been reported.[255−257] Trimethylhydrazonium iodides have shown no such tendencies.

Oxime Derivatives. The most common method for preparing *O*-tosyl oximes for use in the Neber reaction is to react the oxime with 4-toluenesulfonyl chloride in pyridine.[3] However, due to the reactivity of *O*-tosyl oximes, in particular those prone to Beckmann rearrangement, other bases and solvents are employed, including KOH,[258] $NaNH_2$ in benzene,[259] and K_2CO_3 in THF.[74] When the starting oxime is a single isomer, the geometry is generally preserved in the oxime tosylate.[21,22,25,260]

Trimethylhydrazonium Iodides. These salts are prepared by the reaction of the corresponding ketone *N*,*N*-dimethylhydrazones with methyl iodide.[261]

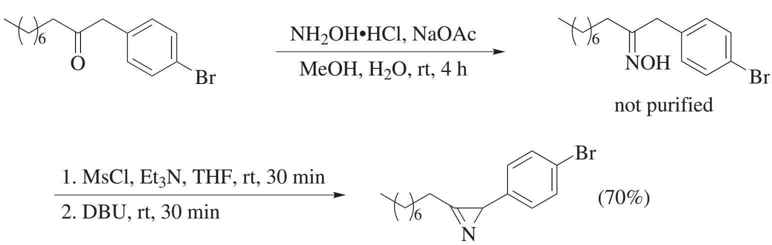
Rearrangement Conditions

Oxime Derivatives. The base most frequently used to convert an oxime tosylate to an α-amino ketone hydrochloride is KOEt in EtOH, with or without benzene or toluene as a cosolvent, at 0° to room temperature for 0.5 to 24 hours. Less frequently used, but still not unusual, are NaOEt in EtOH and NaOMe in MeOH, and occasionally KO*t*-Bu. The subsequent hydrolysis of the crude 2*H*-azirine intermediate is carried out with aqueous HCl. Acid concentrations in the 1–2 N range are typical, although higher concentrations have been used. Concentrated HCl may be needed if the α-amino ketal is the intermediate.

The preparation of azirines from oxime tosylates bearing an additional, activating ester or similar group is frequently done in aprotic solvents such as chloroform, THF, acetonitrile, or toluene with tertiary amine bases: pyridine, triethylamine, or, in pursuit of an enantiomerically enriched azirine, a chiral nonracemic heterocycle such as quinine. Polymer-bound tertiary amines have also been employed. Finally, despite the success of the less powerful amine bases, the use of DBU, NaOEt in EtOH, or KO*t*-Bu in *t*-BuOH is not unusual.

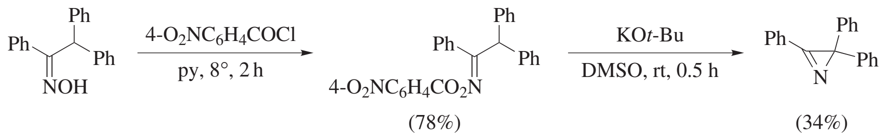
Trimethylhydrazonium Iodides. These precursors are generally converted to azirines at room temperature with NaO*i*-Pr in *i*-PrOH, or with NaH in DMSO. Conversions of hydrazonium salts to amino ketone hydrochlorides, via the amino ketals, are effected with NaOEt in EtOH at reflux followed by hydrolysis with HCl.

EXPERIMENTAL PROCEDURES



2-(4-Bromophenyl)-3-octyl-2*H*-azirine (Preparation of a 2*H*-Azirine from an *O*-Methanesulfonyl Oxime).[47] Methanol (20 mL) and water (1 mL) were added to a mixture of 1-(4-bromophenyl)decan-2-one (0.631 g, 2.03 mmol), hydroxylamine hydrochloride (0.212 g, 3.05 mmol), and sodium acetate (0.250 g, 3.05 mmol) contained in a round-bottom flask. After stirring the mixture at rt for 4 h, the solvent was removed under vacuum. The reaction mixture was partitioned between MTBE and, sequentially, water, saturated aq $NaHCO_3$, and brine. The combined organic extract was dried (Na_2SO_4). Concentration provided crude 1-(4-bromophenyl)decan-2-one oxime (0.635 g), which was used directly in the next reaction.

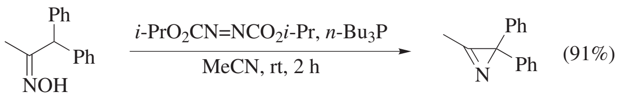
To a solution of the crude oxime (0.635 g) in THF (35 mL) was added triethylamine (296 mg, 2.93 mmol) and methanesulfonyl chloride (332 mg, 2.93 mmol) sequentially at rt. The solution became cloudy after the addition of the methanesulfonyl chloride. After 30 min, DBU (890 mg, 5.86 mmol) was added over 1 min. After 30 min, the reaction mixture was passed through a pad of silica gel, washing with MTBE. The eluate was concentrated under vacuum and the residue was chromatographed to give 3-(4-bromophenyl)-2-(1-octyl)-2*H*-azirine (437 mg, 1.42 mmol, 70% yield from the ketone) as a colorless oil: TLC R_f 0.69 (petroleum ether/MTBE 4:1); IR (film) 2927, 2855, 1765, 1487, 830 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, J = 6.8 Hz, 3H), 1.25–1.31 (m, 8H), 1.38–1.42 (m, 2H), 1.72–1.76 (m, 2H), 2.80 (t, J = 7.2 Hz, 2H), 2.82 (s, 1H), 6.92 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, solvent not given) δ 14.2, 22.8, 24.5, 27.1, 29.2, 29.3, 29.4, 31.9, 33.0, 120.5, 127.2, 131.4, 140.9, 167.5; HRMS (m/z): calcd for $C_{16}H_{22}NBr$, 307.0936; found, 307.0943.



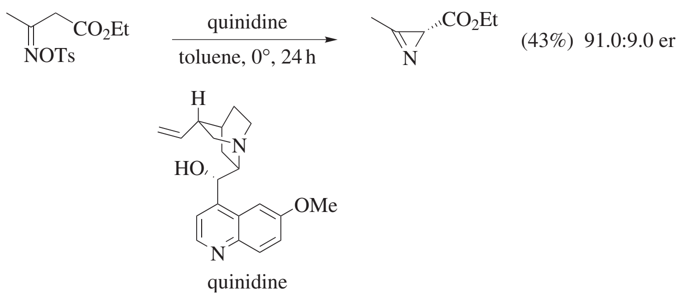
2,2,3-Triphenyl-2*H*-azirine (Preparation of a 2*H*-Azirine from an Oxime 4-Nitrobenzoate).[49] To a solution of 1,2,2-triphenylethanone oxime (3.87 g, 10 mmol) in pyridine (55 g, 0.7 mol) cooled to 8° was added 4-nitrobenzoyl chloride (3.72 g, 20 mmol). The mixture was stirred for 2 h, then was poured onto ice and was extracted with benzene. The benzene phase was washed with 2 N HCl, aq $NaHCO_3$, and water, and was concentrated under vacuum. Recrystallization of the residue from Et_2O gave crystals of *O*-(4-nitrobenzoyl)-1,2,2-triphenylethanone oxime (3.42 g, 7.8 mmol, 78%): mp 129–129.6°; IR (KBr) 1754 (C=O) cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 5.85 (s, 1H), 6.94–8.05 (m, 9H). Anal. Calcd for $C_{27}H_{20}N_2O_4$: C, 74.30; H, 4.62; N, 6.42. Found: C, 74.42; H, 4.38; N, 6.65.

To a solution of *O*-(4-nitrobenzoyl)-1,2,2-triphenylethanone oxime (500 mg, 1.15 mmol) in 5 mL of DMSO at rt was added dropwise a solution of KO*t*-Bu (350 mg, 2.86 mmol) in DMSO (5 mL). The mixture was stirred for an additional 0.5 h, then was diluted with water (20 mL), and was extracted several times with Et_2O. From the Et_2O phase was obtained 128 mg of crude product, which was recrystallized from hexane, giving pure 2,2,3-triphenyl-2*H*-azirine (105 mg, 0.390 mmol, 34%): mp 104.3–104.6°; UV (EtOH) λ_{max}, nm (ε): 250 (24,500), 285 (sh, 1,400), 310 (sh, 1,100); IR (KBr) 1735 cm^{-1}; ^1H NMR (100 MHz, CCl_4) δ 7.10–7.30 (m, 10H), 7.41–7.57 (m, 3H), 7.85–7.95 (m, 2H); MS (70 ev) m/z:

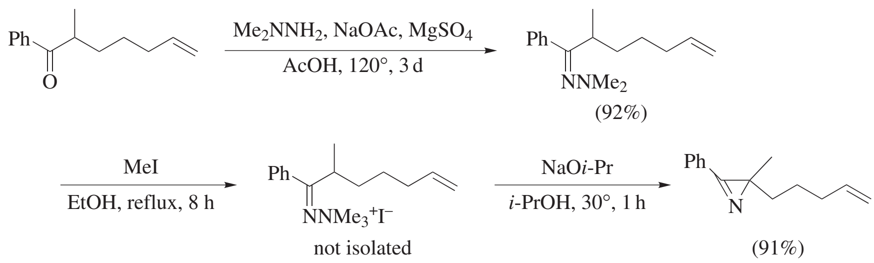
[M^+] 269 (70), 190 (1), 165 (100), 139 (5), 115 (3), 103 (4), 76 (3), 63 (3). Anal. Calcd for $C_{20}H_{15}N$: C, 89.18; H, 5.61; N, 5.20. Found: C, 89.45; H, 5.87; N, 5.48.



3-Methyl-2,2-diphenyl-2*H*-azirine (Conversion of an Oxime to a 2*H*-Azirine via a Mitsunobu Cyclization).[47] Crude 1,1-diphenylpropan-2-one oxime[262] (89 mg, 0.40 mmol) was suspended in MeCN (2 mL). While stirring the suspension, a mixture of diisopropyl azodicarboxylate (0.258 g, 1.20 mmol) and tri-*n*-butylphosphine (0.243 g, 1.20 mmol) in MeCN (1 mL) was added over 5 min at rt. After 2 h, the reaction mixture was filtered through a short pad of silica gel, washing with MTBE. The organic solution was concentrated in vacuo. The residue was chromatographed (adsorbent, solvent not given) to yield 3-methyl-2,2-diphenyl-2*H*-azirine (75 mg, 0.36 mmol, 91% yield from the ketone) as a colorless oil: TLC R_f 0.43 (petroleum ether/MTBE 4:1); ^{1}H NMR (400 MHz, solvent not given) δ 2.56 (s, 3H), 7.19–7.32 (m, 10H); ^{13}C NMR (100 MHz) δ 13.0, 42.9, 127.1, 128.1, 128.5, 142.0, 167.6.

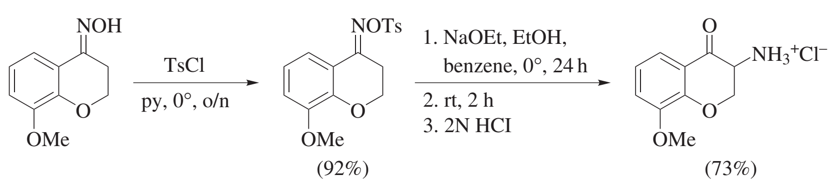


Ethyl (−)-3-Methyl-2*H*-azirine-2-carboxylate (Preparation of an Enantiomerically Enriched 2*H*-Azirine Ester Using a Chiral Alkaloid Base).[64] To a stirred solution of quinidine (162 mg, 0.449 mmol) in dry toluene (90 mL), a solution of ethyl 3-(4-toluenesulfonyloximino)butanoate (201 mg, 0.672 mmol) in dry toluene (10 mL) was added dropwise at 0°. After 24 h aq HCl (50 mL, 0.05 M) was added and the resulting mixture was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with brine, then were dried over $MgSO_4$, and concentrated under vacuum to give the crude 2*H*-azirine ester (116 mg). Purification by bulb-to-bulb distillation at 80° (1 mm Hg) yielded 37.0 mg (0.291 mmol, 43%) of ethyl (−)-3-methyl-2*H*-azirine-2-carboxylate as a colorless liquid, (100% pure by GLC, 91.0:9.0 er): $[\alpha]^{20}_D - 65.7$ (*c* 0.6, $CHCl_3$); IR (CCl_4) 1795, 1730, 1190 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26 (t, $J = 7.1$ Hz, 3H), 2.42 (s, 1H), 2.52 (s, 3H), 4.17 (q, $J = 7.1$ Hz, 2H); HRMS (m/z): [M^+] calcd for $C_6H_9NO_2$, 127.0633; found, 127.0633.



2-Methyl-2-(4-pentenyl)-3-phenyl-2*H*-azirine (Preparation of a 2*H*-Azirine from an in situ Generated Hydrazonium Iodide).[263] A mixture containing 2-methyl-1-phenylhept-6-en-l-one (20.2 g, 100 mmol), 1,1-dimethylhydrazine (20 g, 330 mmol), acetic acid (0.1 g, 2 mmol), sodium acetate (10.0 g, 122 mmol), and magnesium sulfate (10.0 g, 83 mmol) was heated at 120° for 3 d in a Carius tube. The mixture was taken up in Et_2O, and the inorganic salts were removed by filtration. Removal of the solvent under reduced pressure left a yellow oil which was distilled at 95–97° (0.4 mm) to give 2-methyl-1-phenylhept-6-en-1-one *N*,*N*-dimethylhydrazone (22.5 g, 92.1 mmol, 92%): IR (neat) 3292, 1639, 1462 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (d, $J = 7.0$ Hz, 3H), 1.2–2.1 (m, 6H), 2.32 (s, 5H), 2.50 (s, 1H), 3.67 (sextet, $J = 7.0$ Hz, 1H), 4.6–5.1 (m, 2H), 5.4–6.1 (m, 1H), 7.0–7.9 (m, 5H); MS m/z: 244, 132 (base), 105, 77.

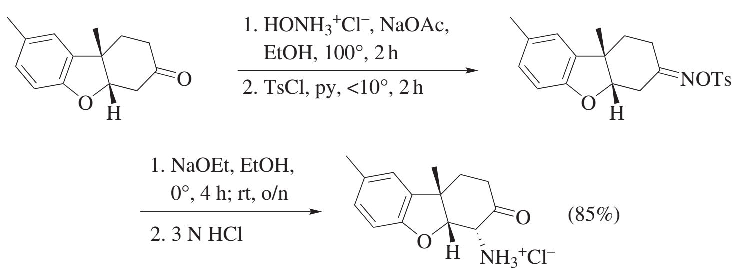
A solution containing the above hydrazone (17.5 g, 71.6 mmol), methyl iodide (32 g, 226 mmol), and absolute EtOH (10 mL) was heated at reflux for 8 h. Removal of the solvent under vacuum left a dark yellow oil that was taken up in *i*-PrOH. To this solution was added a NaO*i*-Pr solution prepared from sodium (1.63 g, 70.9 mmol) and *i*-PrOH (220 mL). The reaction mixture was stirred for 1 h at 30°, and the solvent was then removed under reduced pressure. The residue was extracted with cyclohexane and the extracts were concentrated to afford a yellow oil. Distillation of this material at 75° (0.01 mm) gave 2-methyl-2-(4-pentenyl)-3-phenyl-2*H*-azirine (13.0 g, 65.2 mmol, 91%) as a clear liquid: IR (neat) 2841, 1700, 1621, 1433, 1357, 1285, 1192, 1157, 1073, 1031, 908, 762, 687 cm^{-1}; UV (cyclohexane) λ_{max} nm (ε): 243 (15,000); ^1H NMR ($CDCl_3$) δ 1.39 (s, 3H), 1.6–2.3 (m, 6H), 4.8–5.1 (m, 2H), 5.6–5.9 (m, 1H), 7.4–7.9 (m, 5H); MS m/z: 199, 104 (base), 77. Anal. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.14; H, 8.67; N, 6.96.



3-Amino-8-methoxy-4-chromanone Hydrochloride (Preparation of an α-Amino Ketone from an *O*-(4-Toluenesulfonyl) Oxime).[264] 8-Methoxy-4-chromanone oxime (11.6 g, 60 mmol) was dissolved in dry pyridine (60 mL).

After the mixture was cooled in ice, 4-toluenesulfonyl chloride (12.4 g, 65 mmol) was added in small portions over a period of 40 min to the stirred solution, which was stirred for an additional 1.5 h at 0° and then left overnight in the refrigerator. The mixture was then poured into ice water (500 mL) and the solid product was collected by filtration and washed with water and cold EtOH. After drying, 8-methoxy-4-chromanone oxime tosylate was obtained as yellow crystals (19.24 g, 92%): mp 133–135°; IR (nujol) 1620, 1590, 1360, 1280, 1185, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 (s, 3H), 2.95 (t, 2H), 3.80 (s, 3H), 4.25 (t, 2H), 6.80 (m, 2H), 7.25 (d, m, 3H), 7.85 (d, 2H).

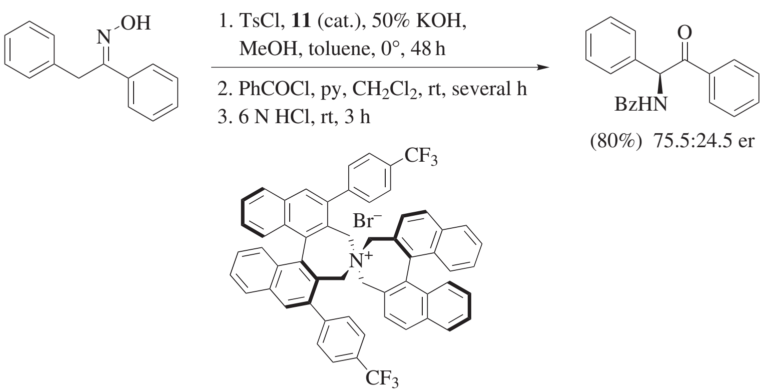
The foregoing oxime tosylate (19.0 g, 55 mmol) in dry benzene (100 mL) was added dropwise over 1 h to a stirred solution of sodium (1.30 g, 56 mmol) in dry EtOH (7.5 mL) at 0° under nitrogen. The reaction mixture was left at 0° for 24 h and for a further 2 h at rt. The solid that precipitated (sodium 4-toluenesulfonate) was removed by filtration and was washed with Et_2O. The filtrates were poured into 2 N HCl (200 mL), the mixture was stirred for 2 h, and the layers were separated. The extraction of the organic layer was repeated (2 N HCl, 2 × 20 mL). The combined, red, aqueous fractions were washed with Et_2O (3 × 50 mL) and treated with charcoal. The resulting yellow, aqueous solution was reduced in volume under vacuum to about 50 mL. On cooling, a crystalline product was obtained, which was collected by filtration and then was washed with EtOH to yield 3-amino-8-methoxy-4-chromanone hydrochloride (9.2 g, 73%) as light yellow needles: mp 212–215° (dec) (lit.[84] mp 220°, dec); IR (nujol) 2900, 1680, 1600, 1580, 1275 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.90 (s, 3H), 4.5–5.1 (m, 3H), 7.3 (m, 3H), 9.1 (br, 3H); MS m/z: [M^+] 193 (51), 151 (100), 150 (49), 122 (57).



(4*RS*),(4a*RS*),9b(*SR*)-4-Amino-8,9b-dimethyl-1,2,3,4,4a,9b-hexahydrodibenzofuran-3-one Hydrochloride (Preparation of an α-Amino Ketone from an *O*-(4-Toluenesulfonyl) Oxime).[86] Dihydro-Pummerer's ketone ((4*RS*),(4a*RS*),(9b*SR*)-8,9b-dimethyl-l,2,3,4,4a,9b-hexahydrodibenzofuran-3-one) (150 g, 0.69 mol) was dissolved in hot EtOH (375 mL) and a solution of hydroxylamine hydrochloride (60 g, 0.85 mol) and sodium acetate (75 g, 0.915 mol) in water (225 mL) was added with swirling. The solution was heated in a water bath for 2 h. TLC then indicated no starting material remained. Water (100 mL) was added and the flask was cooled in an ice bath. The crystalline oxime was collected by filtration, washed with water (0.75–1 L), and dried under vacuum over P_2O_5.

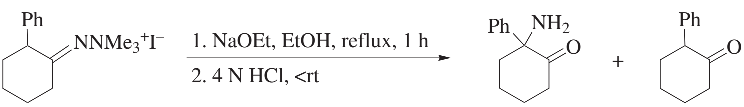
4-Toluenesulfonyl chloride (160 g, 0.84 mol) was dissolved in dry pyridine (300 mL) and the solution was stirred and cooled to <0° in an ice/salt bath. A solution of the oxime (97 g, 0.42 mol) in dry pyridine (300 mL) was then added at such a rate that the temperature of the reaction mixture remained below 10°. After 2 h, TLC indicated no starting material remained, so the mixture was poured onto ice water (4 L). The precipitated *O*-tosyl oxime was collected by filtration, washed well with water (>1 L) followed by cold MeOH (0.5 L), and dried under vacuum over P_2O_5.

Sodium metal (14.7 g, 0.64 g atom) was dissolved in dry EtOH (distilled from Mg) (1 L) and the solution was cooled in an ice bath. The oxime tosylate (230 g, 0.61 mol) was added with vigorous mechanical stirring. After 4 h of stirring at ice-bath temperature, the mixture was left overnight at rt, then was filtered, and the solid was washed with dry Et_2O (2 × 200 mL). The filtrate was concentrated to 250 mL and was then poured onto cold 3 N HCl (500 mL) in a separatory funnel along with Et_2O (750 mL). The aqueous acid layer was removed and the ether layer further extracted with 3 N HCl (2 × 125 mL). The combined acid extracts were washed once with Et_2O (200 mL) and then reduced in volume at 50° on a rotary evaporator until crystallization commenced. The mixture was cooled and the product was collected by filtration, the filtrate being further reduced in volume to obtain second and third crops. The resulting (4*RS*),(4a*RS*),(9b*SR*)-4-amino-8,9b-dimethyl-1,2,3,4,4a,9b-hexahydodibenzofuran-3-one hydrochloride was obtained as colorless needles (158 g, 0.59 mol, 85%), which were washed with a little acetone and dried over P_2O_5: IR (KBr disk) 1738 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.59 (s, 3H), 1.5–2.5 (m, 4H), 2.31 (s, 3H), 4.94, 5.13 (dd, J = 4 Hz, 4H), 6.71, 7.05 (ABq, J = 8 Hz, 2H), 7.13 (br s, 1H), 8.8–9.2 (br s, 3H, exch. by D_2O).



7

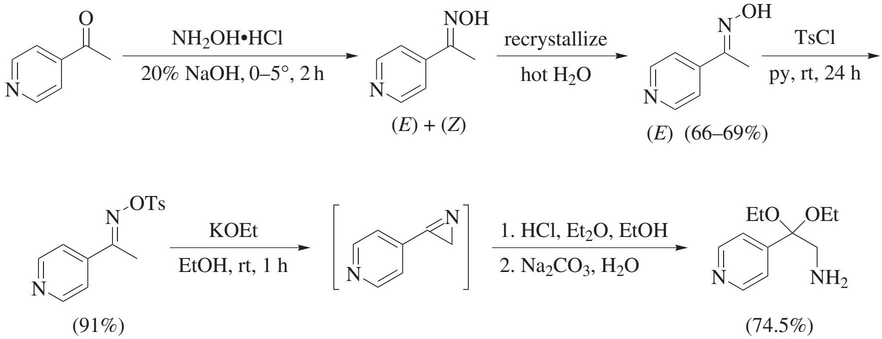
(1*S*)-*N*-(2-Oxo-1,2-diphenylethyl)benzamide (Preparation of an Enantiomerically Enriched α-Amino Ketone Derivative Using a Chiral Phase-Transfer Catalyst).[25] (*Z*)-1,2-Diphenylethanone oxime (63 mg, 0.30 mmol), 4-toluenesulfonyl chloride (69 mg, 0.36 mmol), catalyst **11** (14 mg, 0.015 mmol, 5 mol %), and MeOH (123 μL, 3 mmol, 10 equiv) were dissolved in toluene (3 mL). Aqueous KOH (50%, 1 mL) was added dropwise to this solution at 0°. Stirring at 0° was continued for 48 h. The resulting mixture was diluted with cooled water, the organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined organic phases were dried over $MgSO_4$. The solvents were evaporated and the residue was dissolved in CH_2Cl_2 (3 mL). Pyridine (485 μL, 6 mmol) and benzoyl chloride (174 μL, 1.5 mmol) were added sequentially and the mixture was stirred at rt. After several h, 6 N HCl (ca. 6 mL) was added, and the biphasic mixture was stirred vigorously for 3 h. The mixture was extracted with Et_2O and the extracts were dried over Na_2SO_4. Removal of solvents and purification of the residue by silica gel column chromatography (CH_2Cl_2/hexane/Et_2O 30:20:1) afforded (1*S*)-*N*-(2-oxo-1,2-diphenylethyl)benzamide (76 mg, 0.24 mmol, 80%, 75.5:24.5 er): $[\alpha]^{28.8}{}_D + 121.47$ (*c* 1.14, $CHCl_3$); IR (KBr) 3387, 1688, 1643, 1597, 1580, 1483, 1448, 1352, 1331, 1300, 1254, 1175, 1072, 989, 762, 710, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.76 (d, $J = 7.2$ Hz, 1H), 7.23–7.37 (m, 3H), 7.40–7.58 (m, 8H), 7.75 (d, $J = 7.2$ Hz, 1H), 7.83–7.88 (m, 2H), 8.01–8.06 (m, 2H); MS m/z: $[M+H]^+$ 316, 256, 226, 210, 195, 167, 105 (100), 77, 69; HRMS (m/z): $[M+H]^+$ calcd for $C_{21}H_{17}NO_2$, 316.1338; found, 316.1342. Anal. Calcd for $C_{21}H_{17}NO_2$: C, 79.98; H 5.43; N, 4.44. Found: C, 79.14; H, 5.54; N, 4.26. The er of the product was determined by HPLC analysis [DAICEL Chiral Pak AD, hexane/*i*-PrOH 2:1, 0.5 mL/min flow rate, retention time = 22.7 min (*S*), and 28.3 min (*R*)].



(74%) (14%)

2-Amino-2-phenylcyclohexanone (Preparation of an α-Amino Ketone from a Hydrazonium Iodide).[261] To a solution of NaOEt (52 g, 0.66 mol) in EtOH (500 mL) at 80° was added the dry, powdered *N*,*N*,*N*-trimethylhydrazonium iodide of 2-phenylcyclohexanone (209 g, 0.58 mol) in portions. The mixture was refluxed for 1 h, cooled to 15°, and 4 N HCl (250 mL, 1.0 mol) was added in portions while keeping the temperature below rt. The reaction mixture was concentrated under vacuum, and the residue diluted with water and extracted with Et_2O. The Et_2O layer was dried, filtered, and evaporated, and the residue was recrystallized from petroleum ether to give 2-phenylcyclohexanone (15.8 g, 83 mmol, 14%), mp 54–55°. The aqueous acidic layer was made basic with 50% NaOH and extracted with Et_2O (2 × 500 mL). The combined Et_2O layers were washed with water, dried, filtered, and concentrated, and the residue was distilled to give 2-amino-2-phenylcyclohexanone (82 g, 0.433 mol, 74%): bp 107–110° (1.3 mm); IR (film) 3360, 3300, 1716 cm^{-1}; ^1H NMR ($CDC1_3$) δ 1.44–2.17 (m, 5H), 1.87 (s, 2H), 2.26–2.59 (m, 2H) 2.65–3.06 (m, 1H), 7.14–7.58 (m, 5H).

A sample of the hydrochloride salt, prepared using HCl/*i*-PrOH and recrystallized from *i*-PrOH/MeOH, had a melting point of 233–234°. Anal. Calcd for $C_{12}H_{16}NOCl$: C, 63.85; H, 7.15. Found: C, 63.56; H, 6.96.



2,2-Diethoxy-2-(4-pyridyl)ethylamine (Preparation of an α-Amino Ketal from an *O*-(4-Toluenesulfonyl) Oxime) This preparation is described in *Organic Syntheses*.[256]

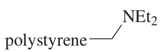
TABULAR SURVEY

Tables 1–5 contain all examples of the classical Neber rearrangement (oxime derivatives), and the "modified" Neber rearrangement (hydrazonium iodides) found in the literature through December, 2009. The ordering of the tables follows the ordering of the text discussion, and compounds are displayed in order of increasing carbon-count of the starting material, which does not include the carbon-count of standard protecting groups, the OR of esters or phosphonates, or the activating group on the oxime or hydrazonium iodide. Aryl ethers are included in the carbon-count; alkyl ethers, unless they are a reacting partner in a subsequent reaction, are not included in the carbon-count. In the large majority of the examples shown, the reference given contains the actual experimental conditions or a reference to the procedure used for that specific compound; in a few cases only the conversion is shown, with a yield and a reference to the general procedure used. All yields are for the isolated product. In addition to the standard abbreviations used in the *Journal of Organic Chemistry*, the following abbreviations are also used in the tables:

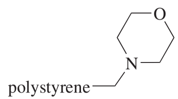
DIAD	diisopropyl azodicarboxylate
EDCI	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride
hν	irradiation by UV light
ia	inverse addition

o/n	overnight
Phth	phthaloyl
SEM	trimethylsilylethoxymethyl
TBDPS	*tert*-butyldiphenylsilyl

Chart 1. Polymer-Bound Amines and Chiral Catalysts Used in Tables



1



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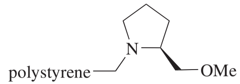

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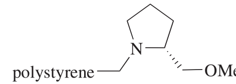

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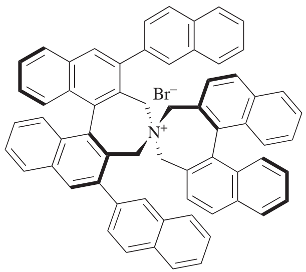

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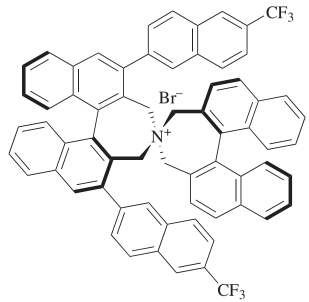

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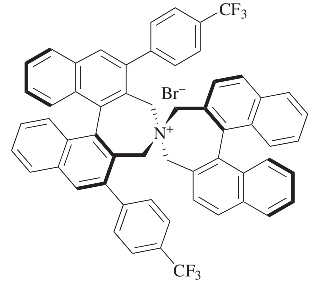

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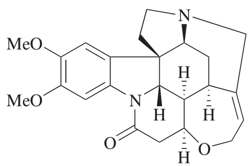
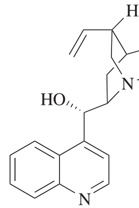
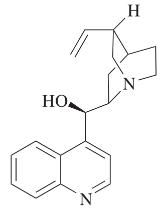
Chart 2. Chiral Amine Bases Used In Tables



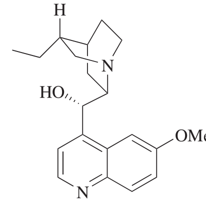
brucine



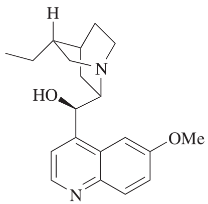
cinchonine



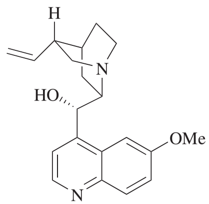
cinchonidine



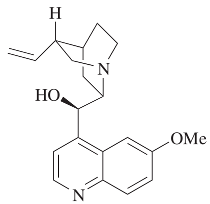
hydroquinidine



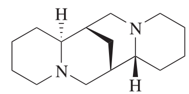
hydroquinine



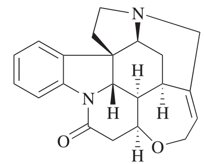
quinidine



quinine

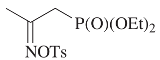
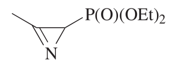


(–)-sparteine

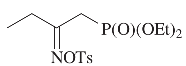


strychnine

TABLE 1. 2*H*-AZIRINES FROM OXIME DERIVATIVES

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	Amine (x eq), K_2CO_3 (y eq), benzene		

Amine	x	y	Dilution[a]	Temp	Time		er		Refs.
Et_3N	1.1	0	1/5	rt	8 h	(70)	—	—	59, 60
(–)-sparteine	1.1	0	1/5	rt	8 h	(87)	51.0:49.0	(*S*)	59, 60
hydroquinidine	1.1	0	1/5	rt	8 h	(97)	55.5:44.5	(*S*)	60
quinine	1.1	0	1/5	rt	8 h	(93)	54.0:46.0	(*R*)	60
quinidine	1.1	0	1/5	rt	8 h	(94)	60.0:40.0	(*S*)	59, 60
quinidine	1.1	0	1/10	rt	8 h	(84)	66.5:33.5	(*S*)	60
quinidine	1.1	0	1/20	rt	8 h	(72)	71.0:29.0	(*S*)	60
quinidine	0.25	10	1/20	rt	8 h	(69)	68.5:31.5	(*S*)	60
quinidine	0.1	5	1/20	rt	24 h	(63)	51.0:49.0	(*S*)[b]	60
1	1.1	0	1/7	50º	5–6 d	(82)	—	—	60
3	1.1	0	1/7	50º	5–6 d	(83)	53.5:46.5	(*S*)	60

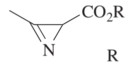
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	Amine, benzene, rt, 8 h	 **I**	

Amine		er		Refs.
Et_3N	(79)	—	—	60
quinidine	(95)	62.0:38.0	(*S*)	59
hydroquinidine	(92)	61.0:39.0	(*S*)	59
quinine	(94)	55.0:45.0	(*R*)	59

Resin-bound amine, benzene, 50°, 5–6 d — **I**

Amine		er		Refs.
1	(87)	—	—	60
2	(98)	—	—	59
3	(30)	57.5:42.5	(*R*)	59
4	(43)	55.5:44.5	(*S*)	59

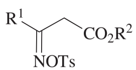
Amine (1 eq), rt, 24 h



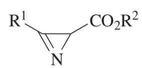
64

R	Amine	Solvent		er	
Me	quinidine	toluene	(40)	72.5:27.5	(*R*)
Et	sparteine	CH_2Cl_2	(53)	0	—
Et	brucine	CH_2Cl_2	(38)	52.5:47.5	(*S*)
Et	strychnine	CH_2Cl_2	(37)	52.0:48.0	(*S*)
Et	cinchonine	CH_2Cl_2	(52)	66.0:34.0	(*R*)
Et	cinchonidine	CH_2Cl_2	(43)	62.0:38.0	(*S*)
Et	quinine	CH_2Cl_2	(34)	62.0:38.0	(*S*)
Et	quinine	toluene	(38)	77.5:22.5	(*S*)
Et	hydroquinine	CH_2Cl_2	(41)	61.0:39.0	(*S*)
Et	hydroquinidine	CH_2Cl_2	(47)	73.5:26.5	(*R*)
Et	hydroquinidine	ethanol	(75)	0	—
Et	hydroquinidine	acetonitrile	(47)	54.0:46.0	(*R*)
Et	hydroquinidine	ether	(48)	72.5:27.5	(*R*)
Et	hydroquinidine	hexane	(59)	73.5:26.5	(*R*)
Et	hydroquinidine	CS_2	(77)	81.5:18.5	(*R*)
Et	hydroquinidine	toluene	(74)	85.0:15.0	(*R*)
Et	quinidine[c]	toluene	(70)	85.5:14.5	(*R*)
Et	quinidine	CH_2Cl_2	(37)	90.5:9.5	(*R*)
Et	quinidine	toluene	(43)	91.0:9.0	(*R*)
t-Bu	quinidine	toluene	(29)	72.0:28.0	(*R*)

C_{4-10}



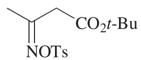
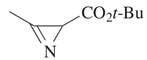
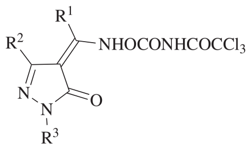
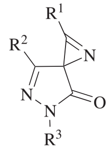
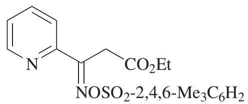
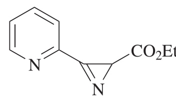
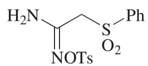
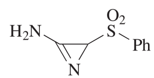
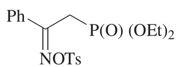
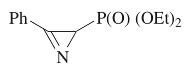
Amine (1 eq), toluene,[d] 0°, 24 h



R^1	R^2	Amine		er	
Me	Me	quinidine	(40)	90.5:9.5	(*R*)
Me	Et	quinidine	(43)	91.0:9.0	(*R*)
Me	Et	quinine	(38)	77.5:22.5	(*S*)
Me	*t*-Bu	quinidine	(29)	72.0:28.0	(*R*)
n-Pr	Et	quinidine	(72)	90.0:10.0	(*R*)
Bn	Et	quinidine	(85)	90.0:10.0	(*R*)
Bn	Et	quinine	(58)	78.5:21.5	(*S*)

64

TABLE 1. 2*H*-AZIRINES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4 	Et_3N, CH_2Cl_2, 0°, 6.5 h	 (66)	265
C_{6-17} 	Et_2O, K_2CO_3, reflux, 2 h	 (see table below)	58
C_8 	NaOMe, MeOH, rt, 0.5 h	 (94)	46
	Et_3N, K_2CO_3, toluene, 55°, 16 h	 (74)	62
	Amine (*x* eq), K_2CO_3 (*y* eq), benzene, rt, 8 h	 **I** (see table below)	59, 60

R^1	R^2	R^3	
Me	Me	Bn	(39)
2-C_4H_3S	Me	Me	(54)
Ph	Me	Bn	(64)
Ph	Me	Me	(61)
Me	Me	Ph	(50)
Ph	H	Ph	(38)
Ph	Me	Ph	(59)

Amine	*x*	*y*	Dilution[a]		er	
Et_3N	1.1	0	1/5	(69)	—	—
quinine	1.1	0	1/5	(79)	69.5:30.5	(*R*)
hydroquinidine	1.1	0	1/5	(81)	76.5:23.5	(*S*)
quinidine	1.1	0	1/5	(85)	82.5:17.5	(*S*)
quinidine	1.1	0	1/20	(77)	86.0:14.0	(*S*)
quinidine	1.1	0	1/100	(77)	81.5:18.5	(*S*)
quinidine	0.25	5	1/20	(69)	83.0:17.0	(*S*)
quinidine	0.05	5	1/20	(49)	84.5:15.5	(*S*)[b]

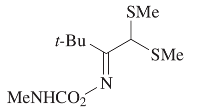
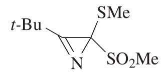
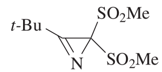
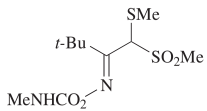
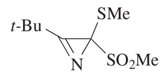
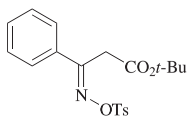
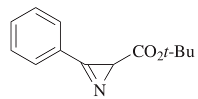
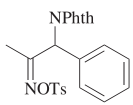
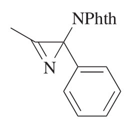
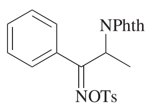
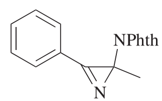
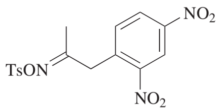
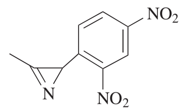
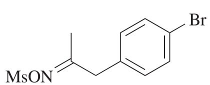
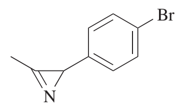
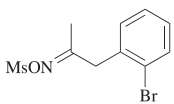
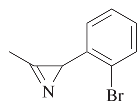
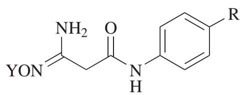
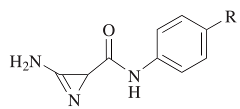
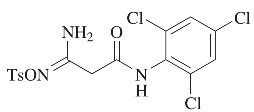
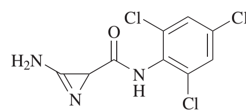
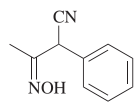
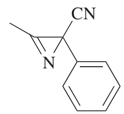
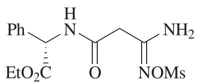
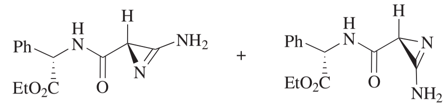
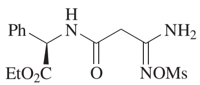
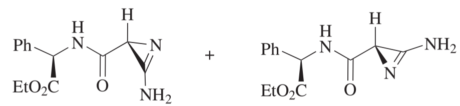
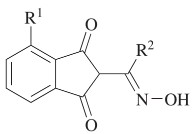
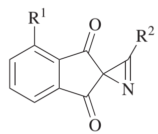
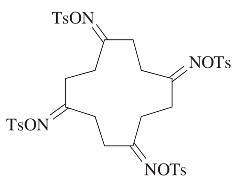
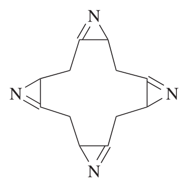
	Resin-bound amine, benzene, 50°, 5–6 d	**I**	Amine: **3** (60), er 51.5:48.5 (*S*); **4** (88), er 54.0:46.0 (*R*)		60
	$KMnO_4$, $MgSO_4$, acetone, H_2O, 0°, 0.5 h; rt, 20 h		(81)		50
	m-CPBA, CH_2Cl_2, 0°, 16 h		(55)		50
	Thick-layer chromatography on silica gel		(—)		50
C_9 	Et_3N, 0° to rt, 6.5 h		(>70)		265
	KO*t*-Bu, benzene, reflux, 6 h		(10)		100
	KO*t*-Bu, benzene, 80°, 4 h		(0.3)		100

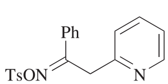
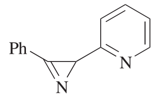
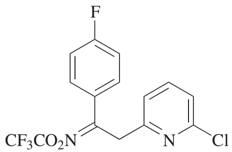
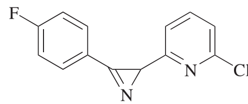
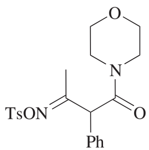
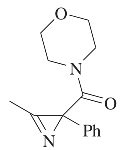
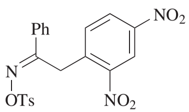
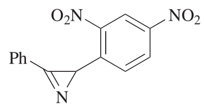
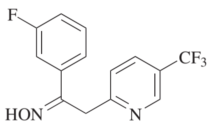
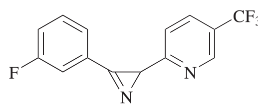
TABLE 1. 2*H*-AZIRINES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	1. Py, 0°, 36 h 2. Na_2CO_3, H_2O, 0°, 18 h	 (74) **I**	4
	Brucine, $CHCl_3$, 0°, 2 h	**I** (71) 1:1 er	7
	1. Py, 0°, 2 h 2. Na_2CO_3, H_2O	**I** (59)	7
	DBU, THF, rt, 0.5 h	 (78)	47
	DBU, THF, rt, 0.5 h	 (78)	47
	NaOMe, EtOH, rt, 1 h	 R Y H Ts (73) H Ms (~73) Cl Ts (~73) Cl Ms (~73)	48
	NaOMe, MeOH, rt, 20 min	 (88)	62

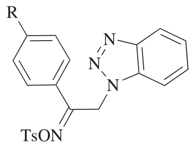
C_{10}		TsCl, Et_3N, 0°, 1 h	 (48)	266
C_{11}		NaOMe, EtOH, 22°, 2 h	 **I** **I + II** (82), **I**:**II** = 96:4 **II**	63
		NaOMe, EtOH, 22°, 2 h	 **I** **I + II** (82), **I**:**II** = 96:4 **II**	63
C_{11-13}		A: AcOH, Ac_2O, HCl, heat B: Ac_2O, py, heat C: TsCl, py, acetone, heat; H_2O D: AcCl, Et_3N, acetone		51
C_{12}		Py, rt, 16 h	 (54)	55

R^1	R^2	A	B	C	D
H	Me	(81)	(65)	(79)	(55)
O_2N	Me	(—)	(72)	(99)	(—)
H	Et	(80)	(—)	(70)	(52)
H	*n*-Pr	(81)	(—)	(—)	(—)

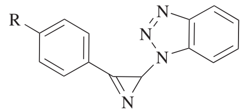
TABLE 1. 2*H*-AZIRINES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	Et_3N, CH_2Cl_2, rt, 1 d	 (31)	267
	Et_3N, CH_2Cl_2, rt, 1 d	 (—)	52
C_{14} 	DBU, CH_2Cl_2, 0°, 1 h	 (73)	266
	TsCl, py, refrigerate, 12 h	 (78)	5
	$(CF_3CO)_2O$, Et_3N, 0°, 0.7 h	 **I** (81)	53
	$(CF_3CO)_2O$, Et_3N, CH_2Cl_2, 0°, 0.5 h	**I** (82)	54

C_{14-15}



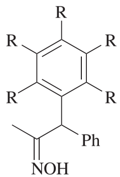
KOH, H_2O, Et_2O, $CHCl_3$, 0°, 0.5 h



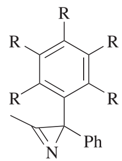
R	
H	(40)
Cl	(58)
Me	(66)

26

C_{15}

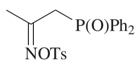


DIAD, $(n\text{-Bu})_3P$, acetonitrile, rt, 3 h



R	
H	(91)
D	(73)

47

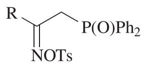


Et_3N, THF, 0°, 10 h

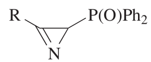
(92)

268

C_{15-16}



Amine, benzene, 0–5°; rt, 1–2 h



I

R	Amine		er	
Me	Et_3N	(89)	—	—
Me	quinidine	(99)	91.0:9.0	(*R*)
Me	hydroquinidine	(94)	62.0:38.0	(*R*)
Et	quinidine	(95)	65.0:35.0	(*R*)

61

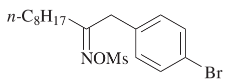
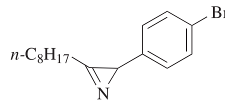
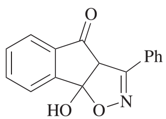
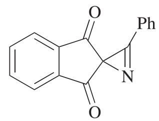
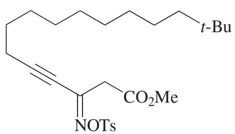
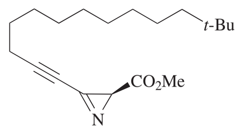
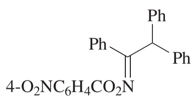
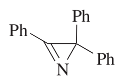
Resin-bound amine, benzene, 50°, 3–4 d

I

R	Amine		er	
Me	**1**	(70)	—	—
Me	**2**	(66)	—	—
Me	**3**	(74)	58.0:42.0	(*R*)
Me	**4**	(60)	58.5:41.5	(*S*)
Et	**1**	(88)	—	—
Et	**2**	(66)	—	—
Et	**3**	(65)	82.5:17.5	(*R*)
Et	**4**	(89)	57.5:42.5	(*S*)

65

TABLE 1. 2*H*-AZIRINES FROM OXIME DERIVATIVES (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}		DBU, THF, rt, 0.5 h	 (70)	47
		AcOH, Ac_2O, HCl, heat	 **I** (87)	51
		Ac_2O, py, heat	**I** (48)	51
C_{18}		Quinidine, toluene, 0°, 40 h; 10°, 2.5 h	 (80) 79.5:20.5 er	113
C_{20}		KO*n*-Bu, DMSO, rt, 0.5 h	 (30)	49

[a] A dilution reported as 1/*x* refers to 1 mmol of substrate in *x* mL of solvent.
[b] This was a one-pot reaction using the crude *O*-tosyl oxime.
[c] In this reaction, 0.1 equivalent of quinidine and 10 equivalents of K_2CO_3 were used.
[d] The substrate concentration was 0.5 mg/mL.

TABLE 2. 2*H*-AZIRINES FROM HYDRAZONIUM IODIDES

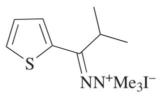
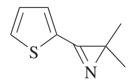
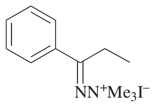
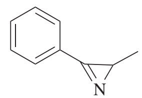
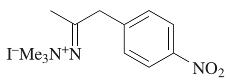
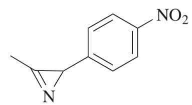
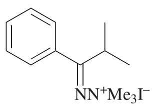
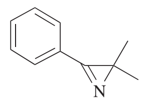
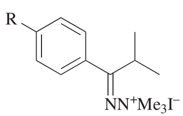
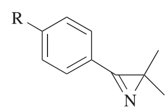
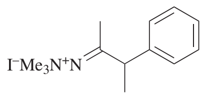
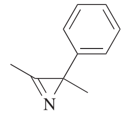
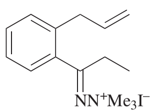
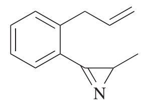
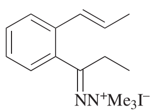
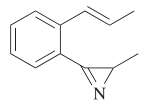
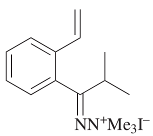
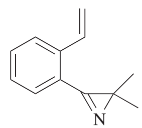
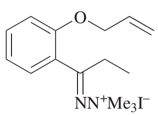
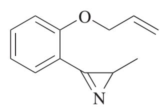
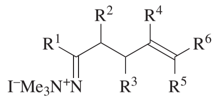
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	NaO*i*-Pr, *i*-PrOH, 50°, 1 h	 (69–74)	269
C_9 	NaH, DMSO, rt, 3 h	 **I** (63)	270, 77
	KO*t*-Bu, *t*-BuOH, 50–55°, 1.5 h	**I** (50)	76
	NaH, DMSO, rt, 4 h	 (—)	271
C_{10} 	NaO*i*-Pr, *i*-PrOH, 35–40°, 1.5 h	 **I** (80)	56
	NaO*i*-Pr, *i*-PrOH, 35–40°, 2 h	**I** (88)	272
	NaO*i*-Pr (<1 eq), *i*-PrOH, "short period"	**I** (85)	273
	NaH, DMSO, <20°	**I** (87)	77
	NaOMe, *i*-PrOH, rt, 2 h	 R: F (61); MeO (52)	274

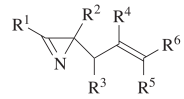
TABLE 2. 2*H*-AZIRINES FROM HYDRAZONIUM IODIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	NaH, DMSO, <20°, 3 h	 **I** (90)	77
	NaO*i*-Pr, *i*-PrOH, 35–40°, 1.5 h	**I** (30)	99
	NaO*i*-Pr, benzene, rt, 24 h; reflux, 7 h	**I** (15)	275
C_{12} 	NaH, DMSO, rt, 6 h	 (64)	57
	NaH, DMSO, rt, 6 h	 (81)	57
	NaH, DMSO, rt, 5 h	 (50)	57
	NaH, DMSO, rt, 6 h	 (100)	276

C_{12-14}

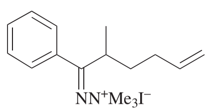


NaH

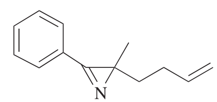


R^1	R^2	R^3	R^4	R^5	R^6	Solvent	Temp (°)	Time (h)		
Me	Ph	H	H	H	H	DMSO	rt	6	(83)	277
Me	Ph	H	H	H	H	DMF	0	1	(—)	266
Ph	Me	H	H	H	H	*i*-PrOH	rt	6	(80)	277
Ph	Me	H	H	H	H	*i*-PrOH	rt	15	(51)	278
Me	Ph	H	Me	H	H	DMSO	rt	6	(82)	277
Me	Ph	H	H	H	Me	DMSO	rt	6	(95)	277
Me	Ph	Me	H	H	H	DMSO	rt	6	(82)	277
Ph	Me	H	Me	H	H	*i*-PrOH	rt	6	(93)	277
Ph	Me	Me	H	H	H	*i*-PrOH	rt	6	(68)	277
Ph	Me	H	H	H	Me	*i*-PrOH	rt	6	(98)	277
Ph	Me	H	H	Me	H	*i*-PrOH	rt	6	(65)	277
Ph	Me	H	H	Me	Me	*i*-PrOH	rt	6	(94)	277

C_{13}



NaO*i*-Pr, *i*-PrOH, rt, 15 h

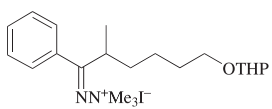


I

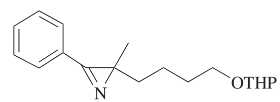
(51) 278

NaO*i*-Pr, *i*-PrOH, rt, 1.25 h

I (23) 263

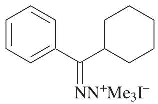
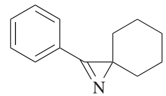
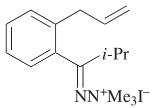
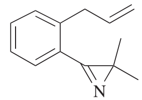
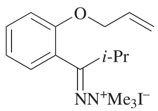
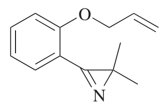
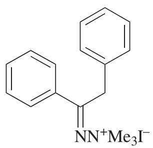
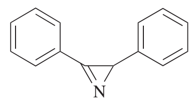
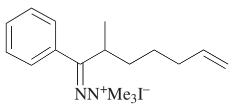
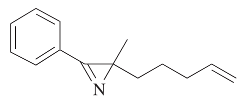


NaO*i*-Pr, *i*-PrOH, rt, 15.5 h



(87) 278

TABLE 2. 2*H*-AZIRINES FROM HYDRAZONIUM IODIDES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	NaO*i*-Pr, *i*-PrOH, 40°, 1 h	 **I** (80)	76
	NaH, DMSO, 20°, 3 h	**I** (94)	77
	NaH, DMSO, rt, 6 h	 (65)	57
	NaH, DMSO, rt, 6 h	 (95)	276
C_{14} 	NaH, DMSO, <20°, 3 h	 (56)	77
	NaO*i*-Pr, *i*-PrOH, 20°, 15 h	 **I** (87)	279
	NaO*i*-Pr, *i*-PrOH, 30°, 1 h	**I** (91)	263

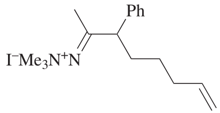
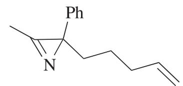
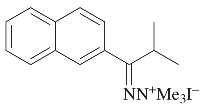
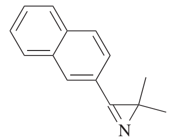
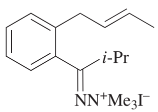
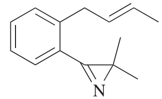
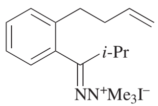
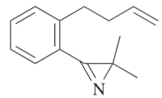
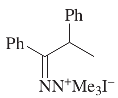
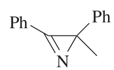
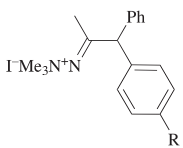
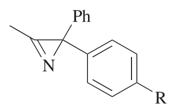
		NaH, *i*-PrOH, rt, 15 h	 (98)	279
		NaO*i*-Pr, *i*-PrOH, 35°, 1 h	 (84)	280
		NaO*i*-Pr, *i*-PrOH, rt, 6 h	 (86)	57
C_{15}		NaH, DMSO, rt, 6.5 h	 (62)	57
		NaH, DMSO, rt, 4 h	 (15)	262
		NaH, DMF, 0°, 1 h	 **I** — R: H (78); F (—)	266
		NaH, DMSO, rt, 4 h	**I** R=H (55)	262

TABLE 2. 2H-AZIRINES FROM HYDRAZONIUM IODIDES (*Continued*)

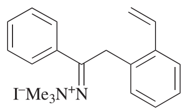
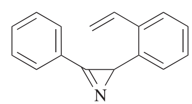
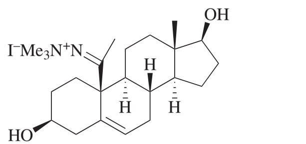
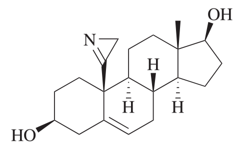
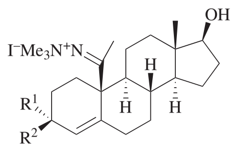
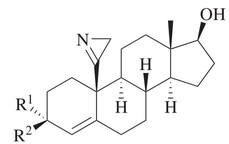
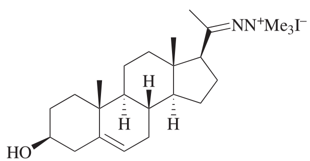
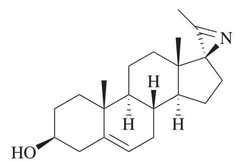
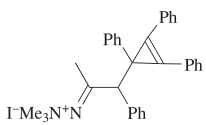
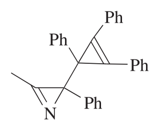
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}		NaH, DMSO, rt, 6.5 h	 (—)	57
C_{20}		NaH, DMSO, rt, 24 h	 (56)	281
		NaH, DMSO, rt, 3 h	 R^1 / R^2: H / HO (37); HO / H (25)	281
		NaH, DMSO, rt, 3 h	 (67)	79
C_{30}		NaO*i*-Pr, *i*-PrOH, rt, o/n	 (81)	282

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES

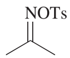
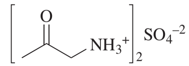
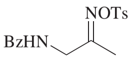
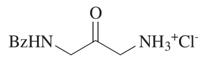
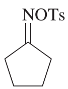
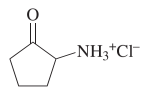
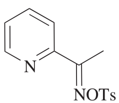
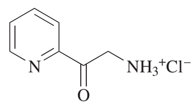
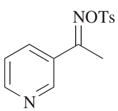
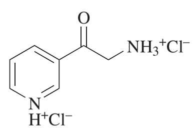
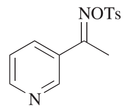
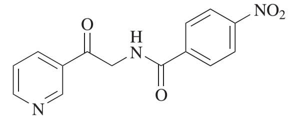
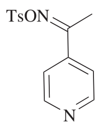
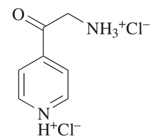
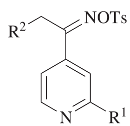
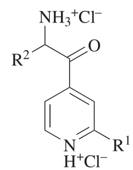
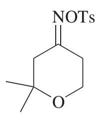
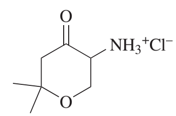
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3		1. KOEt, EtOH, refrigerate, 2 h 2. H_2SO_4	 (68–79)	5
		1. KOEt, EtOH, rt, 0.5 h 2. 2 N HCl	 (61)	6
C_5		1. KOEt, EtOH, 0°, 2 h; rt, 12 h 2. 2 N HCl	 (15)	248
C_7		1. KOEt, EtOH, rt, 1 h 2. 2 N HCl	 **I** (>100 crude)	9
		1. KOEt, EtOH, rt, 1 h 2. 2 N HCl	**I** (45)	283
		1. KOEt, EtOH, rt, 1 h 2. 2 N HCl	 **I** (76)	9
		1. KOEt, EtOH, rt, 1 h 2. 2 N HCl	**I** (45)	283

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. KOEt, EtOH, 10–30° 2. HCl, MTBE to pH 1–2; isolate ketal as di-HCl salt 3. 4-$O_2NC_6H_4CO_2H$, EDCI, THF, H_2O 4. HCl, H_2O	 (76)	255
	1. KOEt, EtOH, 0° to rt, 1.5 h 2. 2 N HCl, Et_2O	 (100) **I**	90
	1. KOMe, MeOH, rt; isolate ketal 2. Concd HCl, 50°, 4 h	**I** (85)	284
	1. KOEt, EtOH, rt, 1 h 2. 2 N HCl	**I** (60)	285, 283
C_{7-9}			
	1. KOEt, EtOH, rt, 0.5–1 h 2. 2 N HCl	 R^1 / R^2 H_2N / H (>55) H_2N / Me (>56) EtHN / H (>64) Me_2N / H (>71)	286, 287
C_7			
	1. KOEt, EtOH, 20–22°, 12 h; isolate ketal 2. Concd HCl	 (28)	78

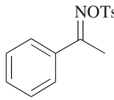
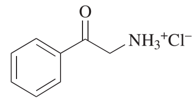
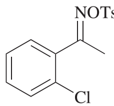
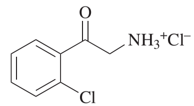
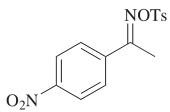
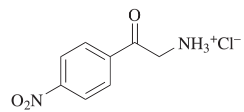
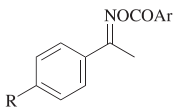
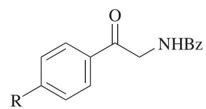
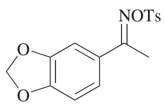
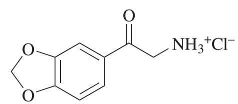
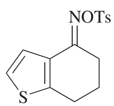
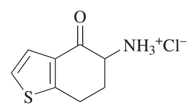
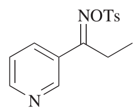
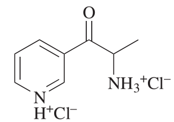
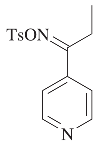
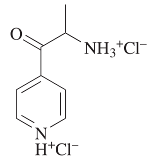
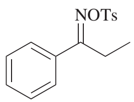
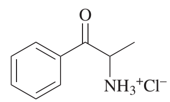
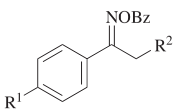
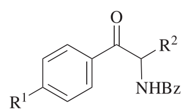
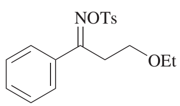
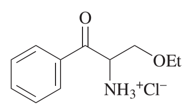
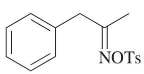
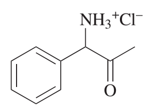
C_8 	1. KOEt, EtOH 2. 2 N HCl	 (69) **I**	5
	1. NaOEt, EtOH, 0°; rt, 2 h 2. 5% HCl	**I** (76)	11
	1. NaOEt, EtOH, 0°; rt, 2 h 2. 5% HCl	 (41)	67
	1. NaOEt, EtOH, 0°; rt, 2 h 2. 5% HCl	 (74)	10
	1. NaH, toluene, 115–120°, 1.5 h 2. BzCl, 1 M Na_2CO_3	 R / Ar: H / Ph (4) H / 4-ClC_6H_4 (3) H / 4-MeC_6H_4 (6) H / 2,4,6-$Me_3C_6H_2$ (16) Cl / Ph (7) Cl / 4-ClC_6H_4 (5) Cl / 4-MeC_6H_4 (6)	68
	1. KOEt, EtOH, rt; 50–60° 2. 2 N HCl	 (80)	6
	1. KO*t*-Bu, toluene, 0–5°, 2 h 2. Concd HCl	 (71)	288

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			
	1. KOEt, EtOH, rt, 3 h 2. 2 N HCl	 (46)	70
	1. KOEt, EtOH, rt, 1 h 2. 2 N HCl	 (<49)	287
C_9			
	1. KOEt, EtOH 2. 2 N HCl	 (78)	5
	1. NaH, toluene, 115–120°, 1.5 h 2. 3 N HCl 3. BzCl, 1 M Na_2CO_3	 R^1 R^2 Me H (3) H Me (16)	68
	1. NaOEt, EtOH, 0°, 30 min; rt, 2 h 2. 2 N HCl	 (43)	215
	1. KOEt, KOH, EtOH, <35°, 15–30 min 2. AcOH 3. Dilute HCl, 100°	 (31)	2

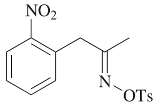
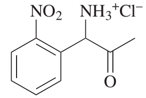
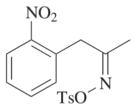
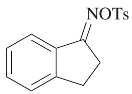
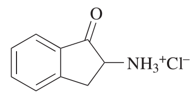
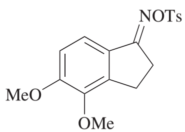
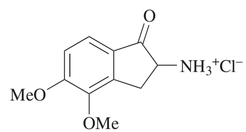
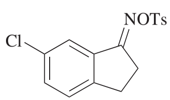
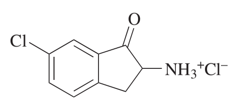
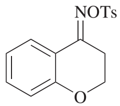
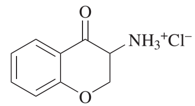
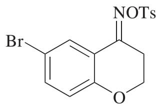
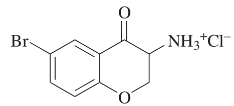
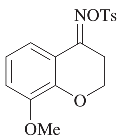
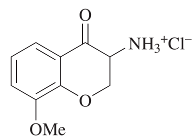
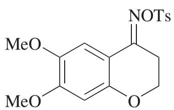
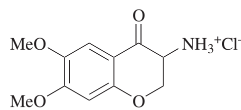
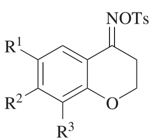
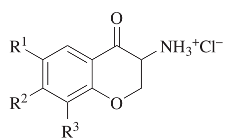
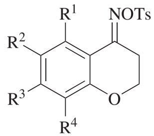
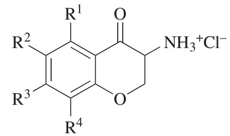
	1. KOEt, KOH, EtOH, <35°, 15–30 min 2. AcOH 3. Dilute HCl, 100°	 (36) **I**	2
	1. KOEt, EtOH, rt, 3 h 2. 2 N HCl	**I** (92)	5
	1. KOEt, EtOH, 0°, 2–3 h; rt, 4 h 2. 2 N HCl	 (73) **I**	6
	1. NaOEt, EtOH, toluene, 0°, 40 h 2. 1 N HCl	**I** (25)	289
	1. NaOEt, EtOH, toluene, –10 to 0°, o/n 2. 1 N HCl	**I** (17)	290
	1. KOEt, EtOH, benzene, 0°, 0.25 h; 4°, 22 h 2. 10% HCl	 (56)	291
	1. NaOEt, EtOH, toluene, 0°, 15 h 2. 1 N HCl	 (28)	289

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	1. NaOEt, EtOH, rt, 18 h 2. 10% HCl	 (58)	69
	1. KOEt, EtOH, benzene, rt, 12 h 2. Concd HCl	 (74)	242
	1. NaOEt, EtOH, "cold", 21 h 2. 1 N HCl	 **I** (73)	84
	1. NaOEt, EtOH, benzene, rt, 21 h 2. 2 N HCl	**I** (33)	264
	1. NaOEt, EtOH, benzene, 0°, 24 h 2. 4 N HCl	 (48)	292
	1. KOEt, EtOH, benzene, 5°, 5 d 2. Concd HCl	 R^1 R^2 R^3 Cl Cl H (56) H Cl Cl (30)	293

	Substrate	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{9-11}		1. NaOEt, EtOH, benzene, rt, 21 h 2. 1 N HCl			84

R^1	R^2	R^3	R^4	
H	H	H	H	(77)
H	HO	H	H	(53)
H	Cl	H	H	(38)
H	H	H	Cl	(60)
H	O_2N	H	H	(44)
H	H	O_2N	H	(43)
H	H	H	O_2N	(42)
H	MeO	H	H	(53)
H	H	MeO	H	(40)
H	H	H	MeO	(33)
Cl	H	H	Cl	(74)
H	Cl	H	Cl	(23)
H	Me	H	H	(55)
H	H	Me	H	(58)
H	H	H	Me	(79)
Me	H	Me	H	(60)[a]

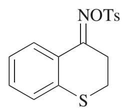
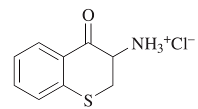
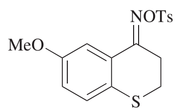
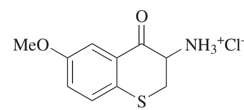
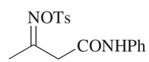
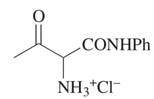
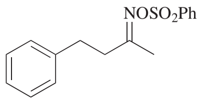
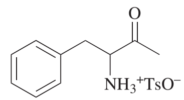
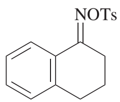
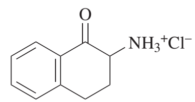
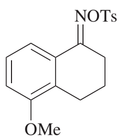
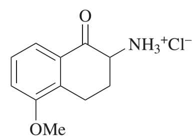
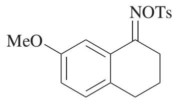
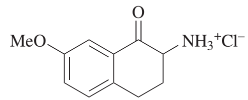
	Substrate	Conditions	Product(s) and Yield(s) (%)		Refs.
C_9		1. NaOEt, EtOH, rt, 18 h 2. 10% HCl		(58)	69
		1. KO*t*-Bu, EtOH, toluene, 0°, 1 h; rt, 1.5 h; 35°, 0.5 h 2. 1 N HCl		(80)	294
C_{10}		1. KOEt, EtOH, 0°; rt, 0.75 h 2. 2 N HCl		(—)	6

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

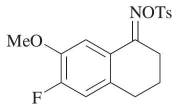
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}			
	1. KOEt, EtOH, rt, 3 h 2. TsOH, EtOH, Et_2O	 (—)	3
	1. KOEt, EtOH, rt, 0.5 h 2. 0.5 M HCl	 (72) **I**	6
	1. KOEt, EtOH, "cold", 1 h 2. 1 M HCl	**I** (45)	295
	1. KOEt, EtOH, benzene, rt, 24 h 2. 5 N HCl	**I** (35)	208
	1. KOEt, EtOH, rt, 24 h 2. 5 N HCl	**I** (35)	217
	1. KOEt, EtOH, benzene, 0°, 5 h; rt, 2 d 2. Concd HCl	 (71) **I**	210
	1. KOEt, EtOH, rt, 24 h 2. 5 N HCl	**I** (54)	216
	1. KOEt, EtOH, benzene, 0°, 24 h 2. 2 N HCl	**I** (54)	208



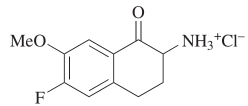
1. KOEt, EtOH, benzene, 0°, 5 h; rt, 2 d
2. Concd HCl



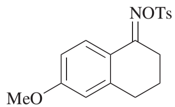
(71) 210



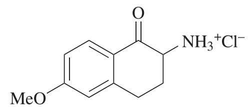
1. KOt-Bu, EtOH, CH_2Cl_2, 20°, 24 h
2. 6 N HCl



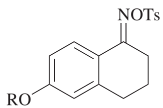
(55) 296



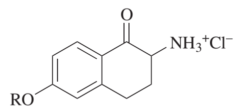
1. KOEt, EtOH, benzene, refrigerate, o/n
2. Concd HCl



(48) 297

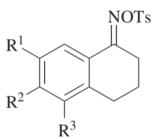


1. KOEt, EtOH, benzene, "cold", 1 wk
2. Concd HCl

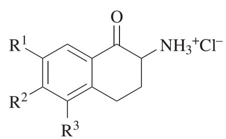


R	
Et	(28)
n-Pr	(47)
i-Pr	(24)
CH_2=$CHCH_2$	(47)
$EtOCH_2CH_2$	(32)
MeO_2CCH_2	(57)
Bn	(45)
2-$ClC_6H_4CH_2$	(40)
3-$ClC_6H_4CH_2$	(23)
4-$ClC_6H_4CH_2$	(38)
$PhCH_2CH_2$	(50)
c-$C_6H_{11}CH_2CH_2$	(—)

298



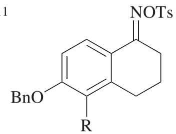
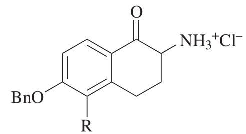
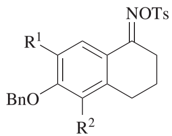
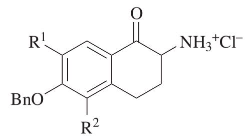
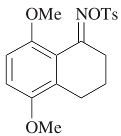
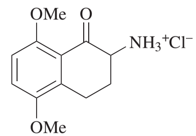
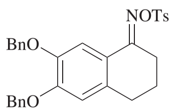
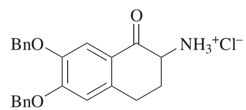
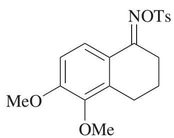
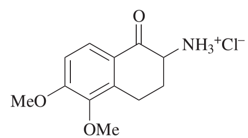
1. KOEt, EtOH, benzene, 0°, 24 h
2. 2 N HCl

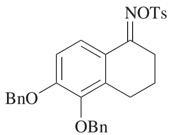
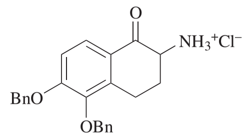
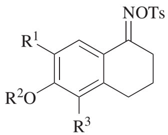
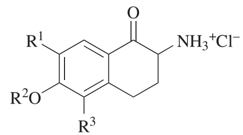
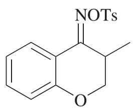
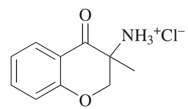
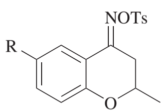
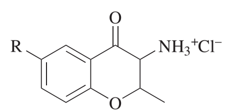
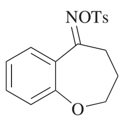
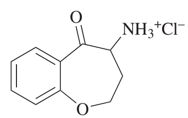


R^1	R^2	R^3	
H	H	BnO	(75)
H	BnO	H	(65)
BnO	H	H	(60)

208

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

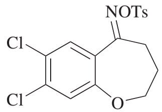
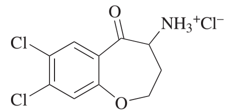
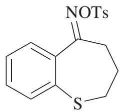
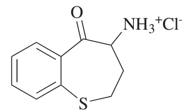
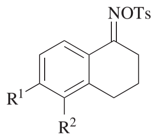
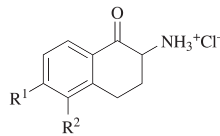
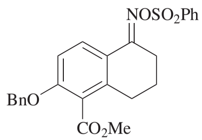
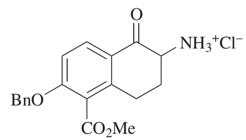
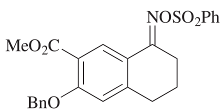
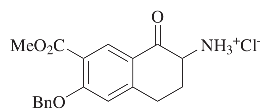
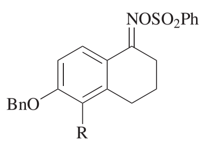
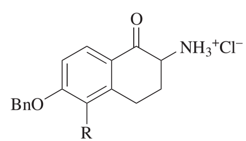
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10-11} 	1. KOEt, EtOH, benzene, "cold", 1 wk 2. 10% HCl	 R: Cl (26); Bn(Ms)N (31); Bn(Me)N (>17); Cbz(Me)N (>28)	299
C_{10} 	1. KOEt, EtOH, benzene, "cold", o/n 2. Concd HCl	 R^1 / R^2: H / O_2N (83); O_2N / H (53)	44
	1. KOEt, EtOH, benzene, 0–5°, 17 d 2. Concd HCl	 **I** (73)	71
	1. KOEt, EtOH, rt, 24 h 2. 2 N HCl	**I** (75)	217
	1. KOEt, EtOH, benzene, 5°, 5 d 2. HCl, Et_2O	 (44)	300
	1. KOEt, EtOH, cold, 6 h; rt, 12 h 2. 10% HCl	 **I** (54)	211

	1. KOEt, EtOH, benzene, 0°, 0.25 h; 4°, 22 h 2. 10% HCl	**I** (46–53)		301, 291
	1. KOEt, EtOH, benzene, "cold", o/n 2. 10% HCl		(35)	302
C_{10-11}				
	1. KOEt, EtOH, benzene, "cold", 1 wk 2. Concd HCl		see table below	298
C_{10}				
	1. NaO*i*-Pr, *i*-PrOH, reflux, 2 h 2. 10% HCl		(28)	69
	1. KOEt, EtOH, benzene, rt, 21 h 2. 1 N HCl		R: H (62)[b]; Cl (42)[b]	84
	1. KOEt, EtOH, benzene, 0°; rt, 12 h 2. Concd HCl		(80)	212

R^1	R^2	R^3	
H	Me	O_2N	(64)
O_2N	Me	H	(34)
H	Me	Cl	(67)
H	Me	NC–	(77)
H	Bn	H_2NCO	(48)

R	
H	(62)[b]
Cl	(42)[b]

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	1. KOEt, EtOH, 0°, 5 h; "cold", o/n 2. 3 N HCl	 (80)	303
	1. NaOEt, EtOH, rt, 18 h 2. 10% HCl	 (72)	69
C_{11} 	1. KOEt, EtOH, benzene, 0–5°, 17 d 2. Concd HCl	 R^1 / R^2 H / EtO_2C (62) NC– / H (84) EtO_2C / H (76)	71
	1. KOEt, EtOH, toluene, 0–5°, 1.5 h; refrigerate, o/n 2. HCl, MeOH	 (57)	43
	1. KOEt, EtOH, toluene, 0–5°, 1.5 h; refrigerate, o/n 2. HCl, MeOH	 (30)	304, 43
	1. KOEt, EtOH, benzene, 5–10°, 8–16 h 2. Concd HCl	 R CHO (35) NC– (85) MeO_2C (63) $MeOCH_2$ (15)	45

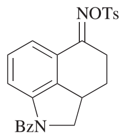
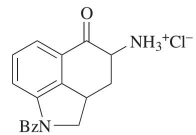
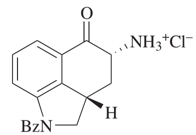
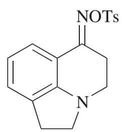
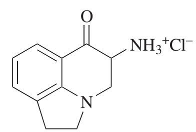
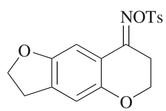
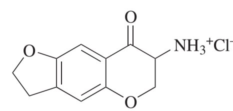
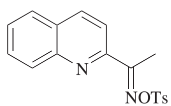
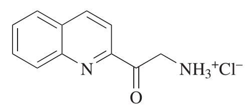
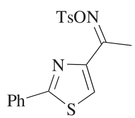
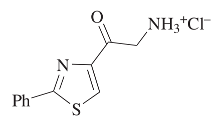
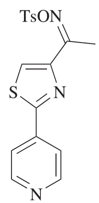
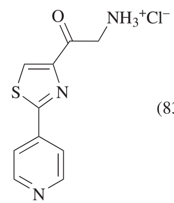
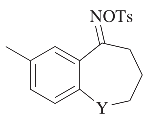
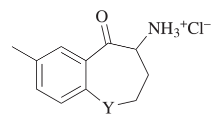
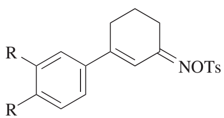
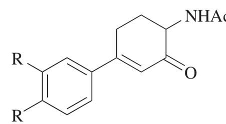
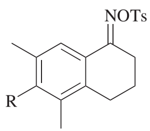
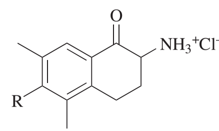
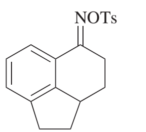
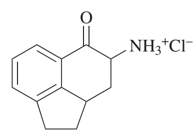
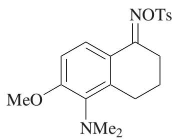
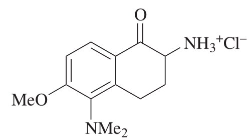
	1. KOEt, EtOH, "cold", 3 d 2. 6 N HCl	 (60)	209
	1. KO*t*-Bu, EtOH, $CHCl_3$, 0°, 15 h 2. 2 N HCl	 (>75)[c]	254
	1. NaOEt, EtOH, benzene, rt, o/n 2. 2 N HCl	 (100)	305
	1. NaOEt, EtOH, benzene, rt, 6 h; 5°, o/n 2. 4 N HCl	 (78)	306, 307
	1. KOEt, EtOH, rt, 18 h 2. 1.5 N HCl	 (>100, crude)	308
	1. KOEt, EtOH, 50–60°, 5–7 min 2. Concd HCl, 55°	 (76)	250

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

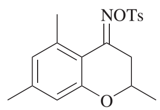
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}		1. KOEt, EtOH, 50–60°, 10 min 2. Concd HCl, rt, 5 h	 (83)	66
		1. KOEt, EtOH, benzene, rt, 12 h 2. Concd HCl	 Y: O (70); S (72); O_2S (61)	212
C_{12}		1. KOEt, EtOH, benzene, "cold", 1 wk 2. Concd HCl 3. Ac_2O	 R: H (18); MeO (18)	73
		1. KOEt, EtOH, benzene, 0–5°, 17 d 2. Concd HCl	 R: H (40); O_2N (49)	71
		1. NaOEt, EtOH, benzene, rt, 23 h 2. 2 N HCl	 (64)	218



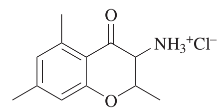
1. KOEt, EtOH, benzene, "cold", 1 wk
2. Concd HCl



(—) 298



1. NaOEt, EtOH, benzene, rt, 21 h; 100°, 1 h
2. 1 N HCl

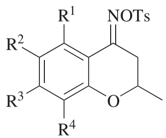


I

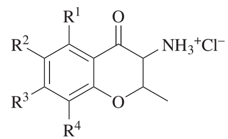
$(42)^b$ 84

1. KOEt, EtOH, rt, 12 h
2. 1 N HCl

I $(42)^b$ 84

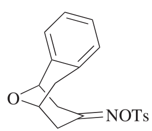


1. KOEt, EtOH, rt, 16 h
2. 1 N HCl

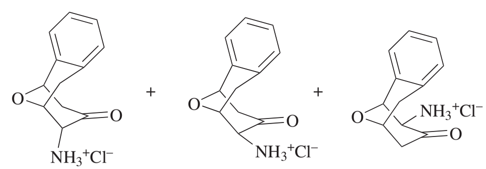


R^1	R^2	R^3	R^4	
H	Me	H	Me	(27–64)
H	Me	Me	H	(27–64)
Me	H	Me	H	(27–64)

309



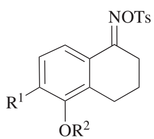
1. NaOEt, EtOH, benzene, 0°, 17 h
2. 1 N HCl



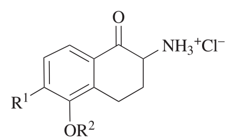
(49) (24) (24)

80

C_{13}



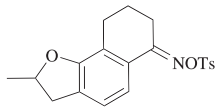
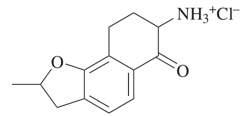
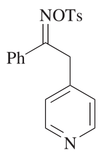
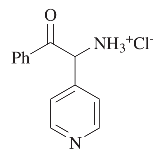
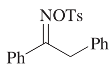
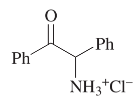
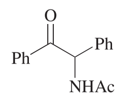
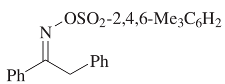
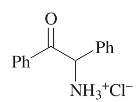
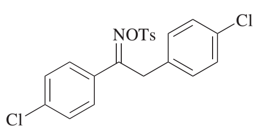
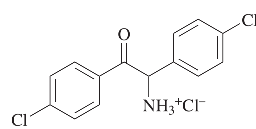
1. KOEt, EtOH, benzene, 0–5°, 17 d
2. Concd HCl



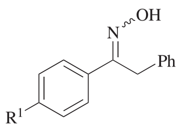
R^1	R^2	
CH_2=CHCH$_2$	Me	(59)
MeCH=CH	*n*-Pr	(53)
MeCH=CH	Bn	(46)

71

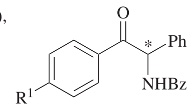
TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 	1. KOEt, EtOH, benzene, 0–5°, 17 d 2. Concd HCl	 (51)	71
	1. KOEt, EtOH, 5°, 30 min 2. 5% HCl	 (>100, crude)	310
C_{14} 	1. KOEt, EtOH, "cold", 2 h 2. 2 N HCl	 (75)	5
	1. KOEt, EtOH, –3 to 0°, 15 h 2. Ac_2O	 (64)	22
	1. NaOEt, EtOH, rt, 1 h 2. 10% HCl	 (34)	311
	1. KOEt, EtOH, "cold", 2 h 2. 2 N HCl	 (56)	8

C_{14}

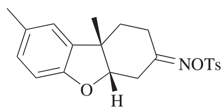


1. R^2SO_2Cl (1.2 eq), catalyst (0.05 eq), MeOH (10 eq), solvent, KOH–H_2O (1:1), 0°
2. BzCl, pyr, CH_2Cl_2
3. 6 N HCl

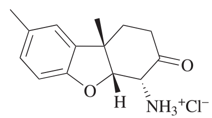


R^1		R^2	Solvent	Catalyst	Time (h)		er	*
H	(*Z*)	4-MeC_6H_4	toluene	$Bu_4N^+Br^-$	2	(80)	—	—
H	(*Z*)	4-MeC_6H_4	toluene	**5**	72	(60)	65.0:35.0	(*S*)
H	(*Z*)	4-MeC_6H_4	toluene	**6**	19	(86)	67.5:32.5	(*S*)
H	(*Z*)	4-MeC_6H_4	mesitylene	**7**	68	(81)	85.0:15.0	—
H	(*Z*)	4-MeC_6H_4	toluene	**7**	48	(80)	75.5:24.5	(*S*)
H	(*E*)	4-MeC_6H_4	toluene	**7**	48	(61)	racemic	—
F	(*Z*)	4-MeC_6H_4	toluene	**6**	19	(95)	75.0:25.0	—
F	(*Z*)	4-MeC_6H_4	toluene	**7**	43	(90)	81.5:18.5	—
F	(*Z*)	4-$MeOC_6H_4$	mesitylene	**7**	48	(80)	85.0:15.0	—
F	(*Z*)	Me	toluene	**7**	48	(73)	56.5:43.5	—

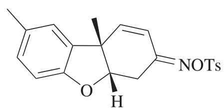
25



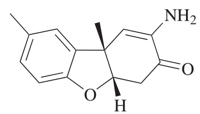
1. NaOEt, EtOH, 0°, 4 h; rt, o/n
2. 10% HCl



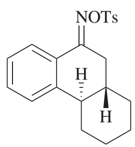
(85) 86



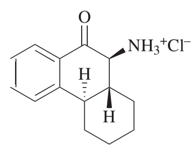
1. NaOEt, EtOH, 0°, 4 h; rt, o/n
2. 10% HCl
3. Na_2CO_3



(—)[d] 86

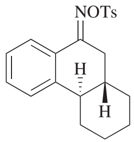
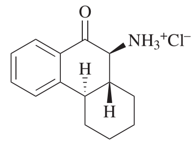
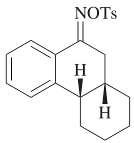
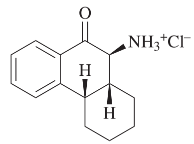
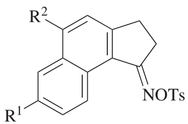
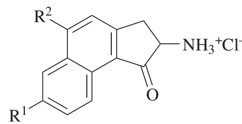
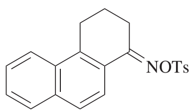
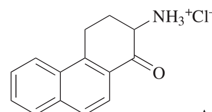
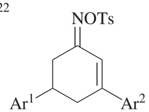
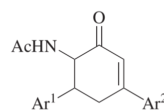


1. KOEt, EtOH, benzene, 10°, 10 h; rt, 24 h
2. 10% HCl



(1) 219

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	1. KOEt, EtOH, 60° to rt, 2 h 2. 0.5 N HCl	 (24)	214
	1. KOEt, EtOH, 60° to rt, 2 h 2. 0.5 N HCl	 (27)	214
	1. KOEt, EtOH, benzene, rt, o/n 2. 1 N HCl	 R^1 / R^2 Me / H (40–45) H / Me (40–45)	312
	1. KOEt, EtOH, benzene, rt, 24 h 2. 2 N HCl	 (20)	295
C_{14-22} 	1. NaOEt, EtOH, rt, 8 h 2. 10% HCl 3. NaOAc, Ac_2O, 70°, 0.5 h	 Ar^1 / Ar^2 2-C_4H_3O / 2-C_4H_3S (59) 2-C_4H_3O / Ph (58) 2-C_4H_3S / 4-$MeOC_6H_4$ (62) 4-MeC_6H_4 / 2-C_4H_3S (61) Ph / Ph (61) Ph / 4-ClC_6H_4 (60) 4-$MeOC_6H_4$ / Ph (65) 4-$MeOC_6H_4$ / 4-ClC_6H_4 (65) 4-MeC_6H_4 / Ph (61) Ph / 2-$C_{10}H_7$ (62)	72

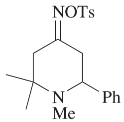
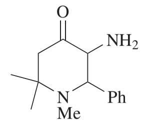
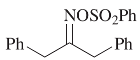
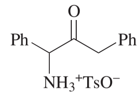
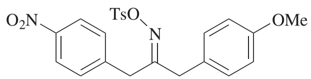
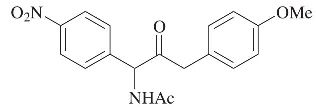
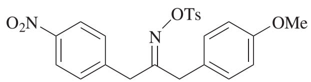
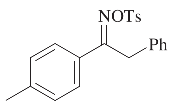
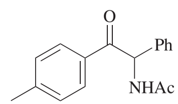
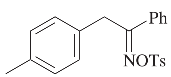
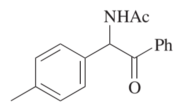
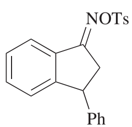
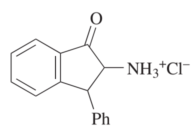
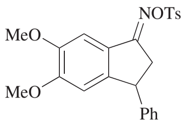
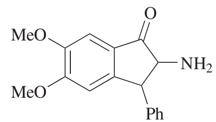
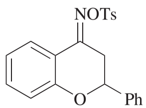
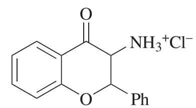
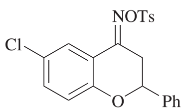
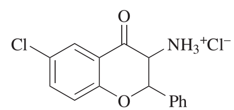
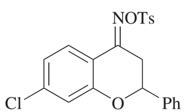
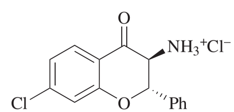
C_{14}				
	1. KOEt, EtOH, 40–60°, 0.25 h 2. 2 N HCl 3. NaOH, H_2O		(86)	6
C_{15}				
	1. KOEt, EtOH, rt, 1 h 2. TsOH, Et_2O		(65)	3
	1. KOEt, EtOH, –5 to 0°, 15 h 2. HCl 3. Ac_2O, py	 **I**	(61)	21
	1. KOEt, EtOH, –5 to 0°, 15 h 2. HCl 3. Ac_2O, py	**I** (63)		21
	1. KOEt, EtOH, 5°, 4 h 2. 4 N HCl 3. Ac_2O, py		(37)	22
	1. KOEt, EtOH, 0–5°, 4.5 h 2. 4 N HCl 3. Ac_2O, py		(31)	22
	1. NaOEt, EtOH, toluene, rt, 24 h 2. 1 N HCl		(27)	313

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	1. NaOEt, EtOH, toluene, rt, 3 h 2. HCl, 40°, 2 h	 (76)	314
	1. KOEt, EtOH, 0–5°, 8 h 2. HCl	 (82) **I** *trans*	81
	1. KOEt, EtOH, 0°, 12 h 2. 1 N HCl	**I** (55)	82, 83
	1. NaOEt, EtOH, toluene, rt, 4 h 2. 1 N HCl	**I** (50)	315
	1. NaOEt, EtOH, benzene, rt, 21 h; 100°, 1 h 2. 1 N HCl	**I** (19)	84
	1. KOEt, EtOH, 0°, 12 h 2. 1 N HCl	 (—)	82
	1. KOEt, EtOH, benzene, rt, o/n 2. 2 N HCl	 (45)	220

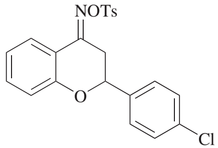
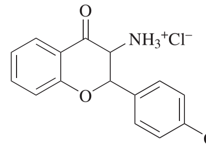
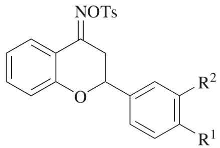
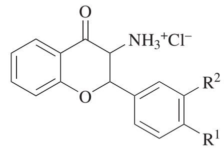
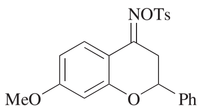
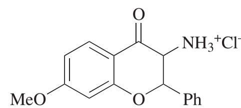
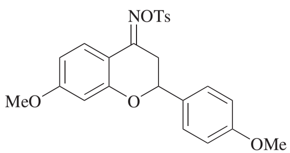
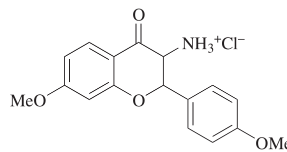
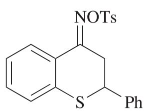
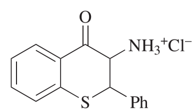
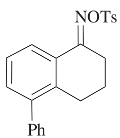
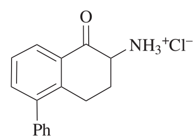
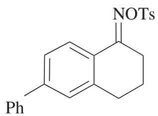
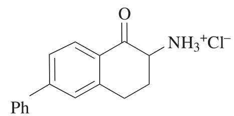
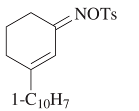
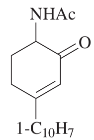
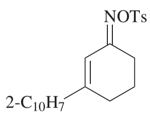
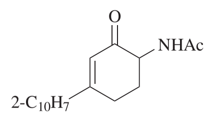
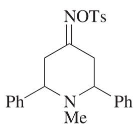
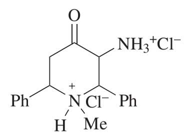
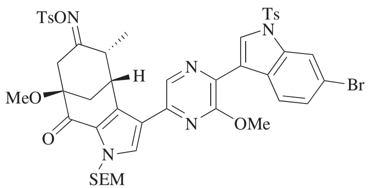
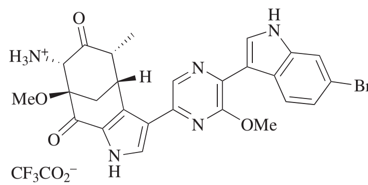
		1. KOEt, EtOH, 0°, 12 h 2. 2 N HCl	 (60)	220
		1. KOEt, EtOH, 0°, 12 h 2. 1 N HCl	 (—) R^1 / R^2: H / MeO; MeO / H; MeO / MeO; $-OCH_2O-$	82
		1. KOEt, EtOH, benzene, 0°; rt, o/n 2. 2 N HCl	 (45)	220
		1. KOEt, EtOH, benzene, 10°, 5.5 h 2. 12% HCl	 (65)	316
		1. KOEt, EtOH, benzene, rt, 24 h 2. 1 N HCl	 (66)	213, 317
C_{16}		1. KOEt, EtOH, benzene, "cold", 1 wk 2. Concd HCl	 (59)	71

TABLE 3. α-AMINO KETONES FROM OXIME DERIVATIVES (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{16}		1. KOEt, EtOH, benzene, "cold", 1 wk 2. Concd HCl	 (50)	71
		1. KOEt, EtOH, benzene, "cold", 1 wk 2. Concd HCl 3. Ac_2O	 (23)	73
		1. KOEt, EtOH, benzene, "cold", 1 wk 2. Concd HCl 3. Ac_2O	 (19)	73
C_{18}		1. KOEt, EtOH, rt, 1.5 h 2. 2 N HCl	 (94)	6
C_{24}		1. KOEt, EtOH, 0°, 3 h 2. 6 N HCl, 60°, 10 h 3. K_2CO_3, H_2O, THF, rt, 10 min 4. TFA	 (96)	114, 115

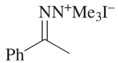
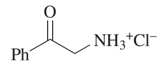
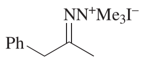
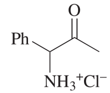
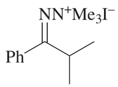
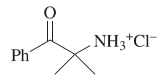
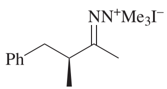
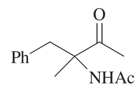
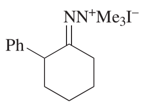
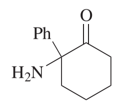
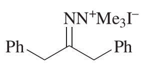
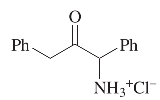
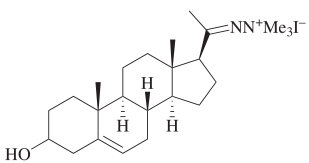
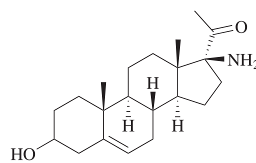
[a] After 21 hours at room temperature, the reaction mixture was heated on a steam bath for 1 hour prior to the hydrolysis step.

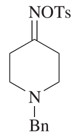
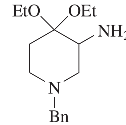
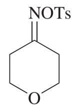
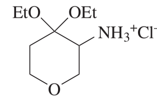
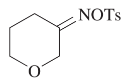
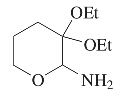
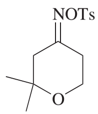
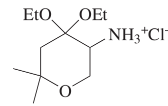
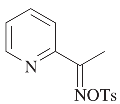
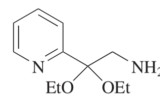
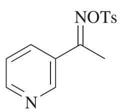
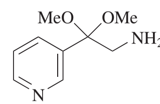
[b] A mixture of stereoisomers in unspecified proportions was obtained.

[c] The relative stereochemistry was determined by X-ray crystallography on the amino alcohol obtained by reduction with $NaBH_4$.

[d] The yield was reported as "good".

TABLE 4. α-AMINO KETONES FROM HYDRAZONIUM IODIDES

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8		1. NaOEt, EtOH, reflux, 22 h 2. HCl, Et_2O	 (67)	12
C_9		1. NaOEt, EtOH, reflux, 1.5–4 h 2. HCl, Et_2O	 (20–22)	12
C_{10}		1. NaO*i*-Pr, *i*-PrOH, reflux, several h; isolate hemiaminal 2. HCl	 (78)	273
C_{11}	 73.0:27.0 er	1. NaH, EtOH, DMSO, reflux, 6 h 2. Concd HCl 3. Ac_2O, py	 (28, crude) 51.5:48.5 er	39
C_{12}		1. NaOEt, EtOH, reflux, 1 h 2. 4 N HCl 3. 50% NaOH	 (74)	261
C_{15}		1. NaOEt, reflux, 18 h 2. HCl, Et_2O	 (29)	12
C_{21}		1. NaH, DMSO, 20°, 2 h 2. 6 N HCl, EtOH, 100°, 30 min 3. NaOH	 (40)	79

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5 	KOEt, EtOH, Na_2SO_4, rt, 1 h; 60°, 1 h	 (63)	74
	1. KOEt, EtOH, benzene, rt, o/n 2. HCl	 (78)	318
	KOEt, EtOH, benzene, rt, o/n	 (85)	318
C_7 	1. KOEt, EtOH, 20–22°, 12 h 2. HCl	 (50)	78
	1. KOEt, EtOH, 0°, 1–3 h 2. HCl, Et_2O 3. Na_2CO_3, H_2O	 (58)	75
	NaOH, MeOH, toluene, 20–40°, 5–10 h	 (85) **I**	319

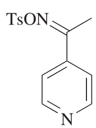
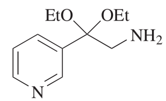
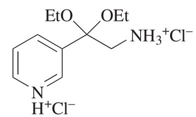
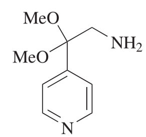
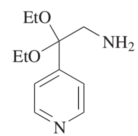
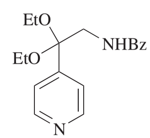
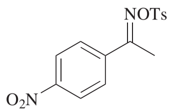
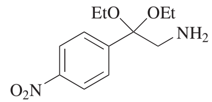
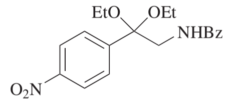
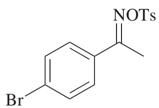
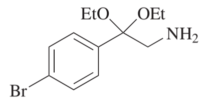
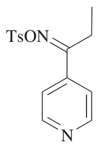
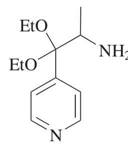
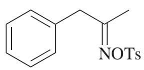
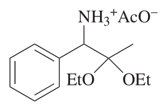
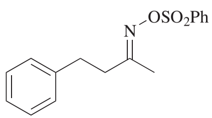
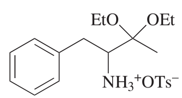
	NaOMe, MeOH, 20–22°, 2 h; $(CO_2H)_2$, MeOH	**I** (—)	320
	1. KOEt, EtOH, 0°, 1–3 h 2. HCl, Et_2O 3. Na_2CO_3, H_2O	 (53)	75
	1. KOEt, EtOH, 10–30° 2. HCl	 (82) **I**	255
	1. KOEt, EtOH, 20°, 2.5 h 2. 1 M HCl, MTBE, Et_2O, 20°, 15 h	**I** (95–99)	321
	KOMe, MeOH, rt, 1 h	 (90)	284
	1. KOEt, EtOH, 0°, 1–3 h 2. Et_2O, HCl 3. Na_2CO_3, H_2O	 (75–76)	75, 256, 255
	1. KOEt, EtOH, 0° to rt, 1.5 h 2. Bz_2O, Et_2O, rt, 19 h	 (51)	90

TABLE 5. α-AMINO KETALS FROM OXIME DERIVATIVES (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8		1. KOEt, EtOH, 0°, 1–3 h 2. HCl, Et_2O 3. Na_2CO_3, H_2O	 (78)	75
		1. KOEt, EtOH, –10°; rt, 3 h 2. Bz_2O, Et_2O, rt, 24 h	 (69)	322
		1. KOEt, EtOH, 0°, 1–3 h 2. HCl, Et_2O 3. Na_2CO_3, H_2O	 (92)	75
		1. KOEt, EtOH, 0°, 1–3 h 2. HCl, Et_2O 3. Na_2CO_3, H_2O	 (40)	75
C_9		1. KOEt, EtOH, <35°, 0.25–0.5 h 2. AcOH	 (32)	2
C_{10}		1. KOEt, EtOH, rt, 3 h 2. TsOH, Et_2O	 (25)	3

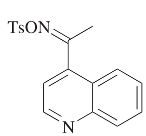
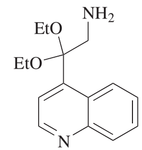
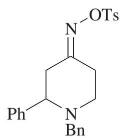
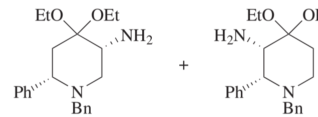
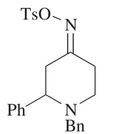
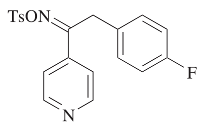
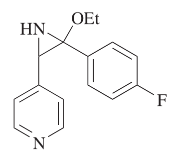
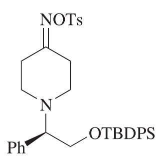
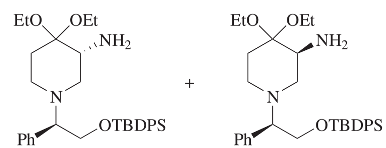
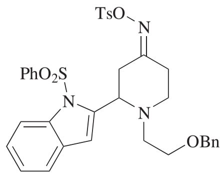
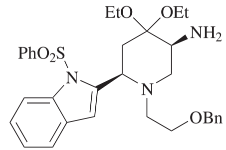
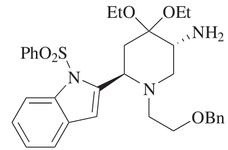
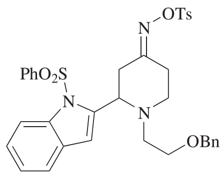
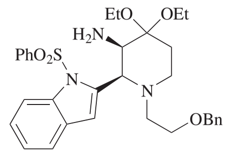
C_{11} 	NaOEt, EtOH	 (—)		323
	KOEt, EtOH, anhydrous MgSO$_4$, 0° to rt, 1 h; 60°, 1 h	 **I** **II**	**I** + **II** (60), **I**:**II** = 1:4	74
	KOEt, EtOH, anhydrous MgSO$_4$, 0° to rt, 1 h; 60°, 1 h	**I** + **II** (52), **I**:**II** = 5:1		74
C_{13} 	KOEt, EtOH, Et$_2$O, rt, 1 h	 (86)		324, 325
	KOEt, EtOH, anhydrous MgSO$_4$, 0° to rt, 1 h; 60°, 1 h	 **I** **II**	**I** + **II** (36) **I**:**II** = 1:1.7	74

TABLE 5. α-AMINO KETALS FROM OXIME DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}			
	KOEt, EtOH, Na_2SO_4, rt, 2 h	 **I** +  **II** **I + II** (51), **I**:**II** = 4:1	85
	KOEt, EtOH, Na_2SO_4, rt, 2 h	 (58)	85

REFERENCES

[1] Neber, P. W.; Hartung, K.; Ruopp, W. *Chem. Ber.* **1925**, *58*, 1234.
[2] Neber, P. W.; Friedolsheim, A. V. *Liebigs Ann. Chem.* **1926**, *449*, 109.
[3] Neber, P. W.; Uber, A. *Liebigs Ann. Chem.* **1928**, *467*, 52.
[4] Neber, P. W.; Burgard, A. *Liebigs Ann. Chem.* **1932**, *493*, 281.
[5] Neber, P. W.; Huh, G. *Liebigs Ann. Chem.* **1935**, *515*, 283.
[6] Neber, P. W.; Burgard, A.; Thier, W. *Liebigs Ann. Chem.* **1936**, *526*, 277.
[7] Cram, D. J.; Hatch, M. J. *J. Am. Chem. Soc.* **1953**, *75*, 33.
[8] Hatch, M. J.; Cram, D. J. *J. Am. Chem. Soc*. **1953**, *75*, 38.
[9] Clemo, G. R.; Holmes, T.; Leitch, G. C. *J. Chem. Soc*. **1938**, 753.
[10] Tatsuoka, S.; Osugi, K.; Morimoto, A.; Miyake, A.; Ueyanagi, J.; Miyamoto, M.; Honjo, M.; Miyazaki, H.; Shimada, T.; Nakamori, R. *Yakugaku Zasshi* **1951**, *71*, 604.
[11] Tatsuoka, S.; Osugi, K.; Miyake, A.; Honjo, M.; Nakamori, R. *Yakugaku Zasshi* **1951**, *71*, 777.
[12] Smith, P. A. S.; Most, E. E., Jr. *J. Org. Chem*. **1957**, *22*, 358.
[13] O'Brien, C. *Chem. Rev*. **1964**, *64*, 81.
[14] Conley, R. T.; Ghosh, S. In *Mechanisms of Molecular Migrations*; Wiley: New York, 1971; Vol. 4, pp 289–308.
[15] Nair, V.; Kim, K. H. *Heterocycles* **1977**, *7*, 353.
[16] Mikhaleva, A. I.; Zaitsev, A. B.; Trofimov, B. A. *Russ. Chem. Rev. (Engl. Transl.)* **2006**, *75*, 797; *Uspekhi Khimii* **2006**, *75*, 884.
[17] Palacios, F.; Ochoa de Retana, A. M.; Martinez de Marigorta, E.; de los Santos, J. M. *Eur. J. Org. Chem.* **2001**, 2401.
[18] Zwanenburg, B.; ten Holte, P. *Top. Curr. Chem.* **2001**, *216*, 93.
[19] Palacios, F.; Ochoa de Retana, A. M.; Martínez de Marigorta, E.; De los Santos, J. M. *Org. Prep. Proced. Int.* **2002**, *34*, 219.
[20] Mangelinckx, S.; Giubellina, N.; De Kimpe, N. *Chem. Rev*. **2004**, *104*, 2353.
[21] House, H. O.; Berkowitz, W. F. *J. Org. Chem*. **1963**, *28*, 2271.
[22] House, H. O.; Berkowitz, W. F. *J. Org. Chem*. **1963**, *28*, 307.
[23] Abramovitch, R. A.; Davis, B. A. *Chem. Rev*. **1964**, *64*, 149.
[24] Hassner, A.; Wiegand, N. H.; Gottlieb, H. E. *J. Org. Chem*. **1986**, *51*, 3176.
[25] Ooi, T.; Takahashi, M.; Doda, K.; Maruoka, K. *J. Am. Chem. Soc*. **2002**, *124*, 7640.
[26] Katritzky, A. R.; Wang, M.; Wilkerson, C. R.; Yang, H. *J. Org. Chem*. **2003**, *68*, 9105.
[27] Narasaka, K.; Kitamura, M. *Eur. J. Org. Chem*. **2005**, 4505.
[28] Friis, P.; Larsen, P. O.; Olsen, C. E. *J. Chem. Soc., Perkin Trans. 1* **1977**, 661.
[29] Waser, J.; Watson, W. H. *Nature* **1963**, *198*, 1297.
[30] Smith, M. B.; March, J. In *March's Advanced Organic Chemistry; Reactions, Mechanisms, and Structure*, 5th ed.; Wiley: New York, 2001; p 1308 ff.
[31] Jordan, D. *J. Org. Chem*. **1989**, *54*, 3584.
[32] Yamabe, T.; Kaminoyama, M.; Minato, T.; Hori, K.; Isomura, K.; Taniguchi, H. *Tetrahedron* **1984**, *40*, 2095.
[33] Bock, H.; Dammel, R.; Aygen, S. *J. Am. Chem. Soc*. **1983**, *105*, 7681.
[34] Lohr, L. L., Jr.; Hanamura, H.; Morokuma, K. *J. Am. Chem. Soc*. **1983**, *105*, 5541.
[35] Isomura, K.; Ayabe, G.-I.; Hatano, S.; Taniguchi, H. *J. Chem. Soc., Chem. Commun.* **1980**, 1252.
[36] L'abbé, G.; Mathys, G. *J. Org. Chem.* **1974**, *39*, 1778.
[37] Nishiwaki, T.; Fujiyama, F. *J. Chem. Soc. Perkin Trans.* **1973**, *1*, 817.
[38] Suárez, D.; Sordo, T. L. *J. Am. Chem. Soc.* **1997**, *119*, 10291.
[39] Yamada, S.-I.; Terashima, S. *Chem. Pharm. Bull.* **1968**, *16*, 1816.
[40] Sato, S.; Kato, H.; Ohta, M. J. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2936.
[41] Partch, R. E.; Andrews, R. R.; Luellen, P.; Forsyth, D. A. *Tetrahedron Lett.* **1982**, *23*, 4447.
[42] Smith, R. F.; Walker, L. E. *J. Org. Chem.* **1962**, *27*, 4372.
[43] Bach, N. J.; Kornfeld, E. C.; Titus, R. D. U.S. Patent 4,500,545, 1985.
[44] Miyake, A; Kuriki, H.; Tada, N.; Nishikawa, M.; Oka, Y. *Chem. Pharm. Bull.* **1977**, *25*, 3066.
[45] Sugihara, H.; Ukawa, K.; Kuriki, H.; Nishikawa, M.; Sanno, Y. *Chem. Pharm. Bull.* **1977**, *25*, 2988.

[46] Alves, M. J.; Fortes, A. G.; Lemos, A.; Martins, C. *Synthesis* **2005**, 555.
[47] Taber, D. F.; Tian, W. *J. Am. Chem. Soc*. **2006**, *128*, 1058.
[48] Eremeev, A. V.; Piskunova, I. P.; Él'kinson, R. S. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1985**, *21*, 998; *Khim. Geterotsikl. Soedin.* **1985**, 1202.
[49] Sieber, W.; Gilgen, P.; Chaloupka, S.; Hansen, H; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 1679.
[50] Corkins, H. G.; Storace, L.; Osgood, E. *J. Org. Chem*. **1980**, *45*, 3156.
[51] Geita, L. S.; Dalberga, L. E.; Grinvalde, A. K.; Yankovska, I. S. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1976**, *12*, 60; *Khim. Geterotsikl. Soedin.* **1976**, 65.
[52] Johns, B. A.; Gudmundsson, K. S.; Turner, E. M.; Allen, S. H.; Jung, D. K.; Sexton, C. J.; Boyd, F. L., Jr.; Peel, M. R. *Tetrahedron* **2003**, *59*, 9001.
[53] Fitzgerald, R. N.; Jung, D. K.; Eaddy, J. F. U.S. Patent 6,756,498 B2, 2004.
[54] Stevens, K. L.; Jung, D. K.; Alberti, M. J.; Badiang, J. G.; Peckham, G. E.; Veal, J. M.; Cheung, M.; Harris, P. A.; Chamberlain, S. D.; Peel, M. R. *Org. Lett.* **2005**, *7*, 4753.
[55] Müller, F.; Karwe, A.; Mattay, J. *J. Org. Chem* **1992**, *57*, 6080.
[56] Leonard, N. J.; Zwanenburg, B. *J. Am. Chem. Soc.* **1967**, *89*, 4456.
[57] Padwa, A.; Ku, A. *J. Am. Chem. Soc.* **1978**, *100*, 2181.
[58] Holzer, W.; Claramunt, R. M.; Pérez-Torralba, M.; Guggi, D.; Brehmer, T. H. *J. Org. Chem*. **2003**, *68*, 7943.
[59] Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I. *Tetrahedron Lett*. **2000**, *41*, 5363.
[60] Palacios, F.; Aparicio, D.; Ochoa de Retana, A. M.; de los Santos, J. M.; Gil, J. I.; de Munain, R. U. *Tetrahedron: Asymmetry* **2003**, *14*, 689.
[61] Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I; Ezpeleta, J. M. *J. Org. Chem.* **2000**, *65*, 3213.
[62] Hyatt, J. A. *J. Org. Chem*. **1981**, *46*, 3953.
[63] Piskunova, P.; Eremeev, A. V.; Mishnev, A. F.; Vosekalna, I. A. *Tetrahedron* **1993**, *49*, 4671.
[64] Verstappen, M. M. H.; Ariaans, G. J. A.; Zwanenburg, B. *J. Am. Chem. Soc.* **1996**, *118*, 8491.
[65] Palacios, F.; Aparicio, D.; Ochoa de Retana, A. M.; de los Santos, J. M.; Gil, J. I.; Alonso, J. L. *J. Org. Chem*. **2002**, *67*, 7283.
[66] Benkö, A.; Levente, A. *Liebigs Ann. Chem*. **1968**, *717*, 148.
[67] Santilli, A. A.; Osdene, T. S. U.S. Patent 3,336,300, 1967.
[68] Renfrow, W. B.; Witte, J. F.; Wolf, R. A.; Bohl, W. R. *J. Org. Chem.* **1968**, *33*, 150.
[69] Dudykina, N. V.; Zagorevskii, V. A. *Zh. Org. Khim. (Engl. Transl.)* **1966**, *2*, 2179; *Zh. Org. Khim.* **1966**, *2*, 2222.
[70] Stout, D. M.; Yamamoto, D. M. U.S. Patent 4,532,250, 1985.
[71] Itoh, K.; Miyake, A.; Tada, N.; Hirata, M.; Oka, Y. *Chem. Pharm. Bull.* **1984**, *32*, 130.
[72] Sridharan, V.; Muthusubramanian, S.; Sivasubramanian, S. *J. Heterocycl. Chem.* **2005**, *42*, 1321.
[73] Itoh, K.; Oka, Y. *Chem. Pharm. Bull.*, **1983**, *31*, 2016.
[74] Diez, A.; Voldoire, A.; López, I.; Rubiralta, M.; Segarra, V.; Pagès, L.; Palacios, J. M. *Tetrahedron* **1995**, *51*, 5143.
[75] LaMattina, J. L.; Suleske, R. T. *Synthesis* **1980**, 329.
[76] Sato, S. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1440.
[77] Laurent, A.; Mison, P.; Nafti, A.; Pellissier, N. *Tetrahedron* **1979**, *35*, 2285.
[78] Paronikyan, E. G.; Noravyan, A. S. *Khim. Zh. Armenii* **2000**, *53*, 69.
[79] Morrow, D. F.; Butler, M. E.; Huang, E. C. Y. *J. Org. Chem.* **1965**, *30*, 579.
[80] Wünsch, B.; Zott, M.; Höfner, G. *Liebigs Ann. Chem.* **1992**, 1225.
[81] Kasahara, A. J. *Nippon Kagaku Zasshi* **1959**, *80*, 416.
[82] O'Brien, C.; Philbin, E. M.; Ushioda, S.; Wheeler, T. S. *Tetrahedron* **1963**, *19*, 373.
[83] Bognár, R.; Clark-Lewis, J. W.; Liptákné-Tökés, A.; Rákosi, M. *Aust. J. Chem*. **1970**, *23*, 2015.
[84] Huckle, D; Lockhart, I. M.; Wright, M. *J. Med. Chem*. **1969**, *12*, 277.
[85] López, I.; Diez, A.; Rubiralta, M. *Tetrahedron* **1996**, *52*, 8581.
[86] Matharu, S. S; Rowlands, D. A.; Taylor, J. B.; Westwood, R. *J. Med. Chem.* **1977**, *20*, 197.
[87] Krems, I. J.; Spoerri, P. E. *Chem. Rev*. **1947**, *40*, 279.
[88] Sato, N. *Science of Synthesis* **2003**, *16*, 768.
[89] Barlin, G.B. *The Chemistry of Heterocyclic Compounds: The Pyrazines*; Weissberger, A., Taylor, E. C., Eds.; Wiley: New York, 1982; Vol. 41, pp 11–58.

[90] Vandermeer, S; Kofman, H; Veldstra, H. *Recl. Trav. Chim. Pays-Bas* **1953**, *72*, 236.
[91] Tsubomura, T.; Enoto, S.; Endo, S.; Tamane, T.; Matsumoto, K.; Tsukuda, T. *Inorg. Chem.* **2005**, *44*, 6373.
[92] Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I.; Lopez de Munain, R. *Org. Lett.* **2002**, *4*, 2405.
[93] Perosa, A.; Selva, M.; Tundo, P. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1033.
[94] Isomura, K.; Sakurai, M.; Komura, T.; Saruwatari, M.; Taniguchi, H. *Chem. Lett.* **1987**, 883.
[95] Hickey, D. M. B.; Moody, C. J.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1113.
[96] Knittel, D. *Synthesis* **1985**, 186.
[97] Padwa, A.; Carlsen, P. H. J. *Tetrahedron Lett.* **1976**, *19*, 433.
[98] Padwa, A.; Carlsen, P. H. J. *J. Org. Chem.* **1978**, *43*, 2029.
[99] Wendling, L. A.; Bergman, R. G. *J. Org. Chem.* **1976**, *41*, 831.
[100] Gilchrist, T. L.; Gymer, G. E.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1973**, 555.
[101] Isomura, K.; Kobayashi, S.; Taniguchi, H. *Tetrahedron Lett.* **1968**, *9*, 3499.
[102] Garst, M. E.; Cox, D. D.; Harper, R. W.; Kemp, D. S. *J. Org. Chem.* **1975**, *40*, 1169.
[103] Kemp, D. S.; Garst, M. E.; Harper, R. W.; Cox, D. D.; Carlson, D.; Denmark, S. *J. Org. Chem.* **1979**, *44*, 4469.
[104] Scopton, A.; Kelly, T. R. *J. Org. Chem.* **2005**, *70*, 10004.
[105] Mphahlele, M. J.; Gheevarghese, O.; Makhubela, N. F. H. *Phosphorus, Sulfur Silicon Relat. Elem.* **2000**, *166*, 303.
[106] El-Sheikh, M. I.; Cook, J. M. *J. Org. Chem.* **1980**, *45*, 2585.
[107] Tamura, Y.; Yoshimoto, Y.; Sakai, K.; Kita, Y. *Synthesis* **1980**, 483.
[108] Mphahlele, M. J.; Modro, T. A. *Phosphorus, Sulfur, Silicon, Relat. Elem.* **1997**, *127*, 131.
[109] Newkome, G. R.; Fishel, D. L. *J. Org. Chem.* **1972**, *37*, 1329.
[110] Padwa, A.; Kulkarni, Y. *Tetrahedron Lett.* **1979**, *20*, 107.
[111] Moldvai, I.; Szántay, C., Jr.; Szántay, C. *Heterocycles* **1996**, *43*, 2377.
[112] Oae, S.; Furukawa, N. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 62.
[113] Skepper, C. K.; Dalisay, D. S.; Molinski, T. F. *Org. Lett.* **2008**, *10*, 5269.
[114] Garg, N. K.; Caspi, D. D.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 9552.
[115] Garg, N. K.; Caspi, D. D.; Stoltz, B. M. *J. Am. Chem. Soc.* **2005**, *127*, 5970.
[116] Smolinsky, G. *J. Org. Chem.* **1962**, *27*, 3557.
[117] Horner, L.; Christmann, A.; Gross, A. *Chem. Ber.* **1963**, *96*, 399.
[118] Bräse, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188.
[119] Hassner, A. In *Azides and Nitrenes. 2. Reactivity and Utility;* Scriven, E. F. V., Ed.; Academic Press: Orlando, 1984; pp 35–94.
[120] L'abbé, G.; Hassner, A. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 98.
[121] Yeremeyev, A. V.; Elkinson, R. S. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1984**, *20*, 723.
[122] Laurent, A. *Bull. Soc. Chim. Belg.* **1983**, *92*, 797.
[123] Hassner, A. *Heterocycles* **1980**, *14*, 1517.
[124] Gilgen, P.; Heimgartner, H.; Schmid, H. *Heterocycles* **1977**, *6*, 143.
[125] Heimgartner, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 238.
[126] Singh, G. S.; D'hooghe, M.; De Kimpe, N. *Chem. Rev.* **2007**, *107*, 2080.
[127] Osborn, H. M. I.; Sweeney, J. *Tetrahedron: Asymmetry* **1997**, *8*, 1693.
[128] Söderberg, B. C. G. *Curr. Org. Chem.* **2000**, *4*, 727.
[129] Sauers, R. R.; Hadel, L. M.; Scimone, A. A.; Stevenson, T. A. *J. Org. Chem.* **1990**, *55*, 4011.
[130] Saalfrank, R. W.; Ackermann, E.; Fischer, M.; Wirth, U.; Zimmermann, H. *Chem. Ber.* **1990**, *123*, 115.
[131] Trofimov, B. A.; Mikhaleva, A. I. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1988**, 1037; *Khim. Geterotsikl. Soedin.* **1987**, 1299.
[132] Fowler, F. W.; Hassner, A.; Levy, L. A. *J. Am. Chem. Soc.* **1967**, *89*, 2077.
[133] Hassner, H.; Fowler, F. W. *J. Org. Chem.* **1968**, *33*, 2686.
[134] Hassner, H.; Fowler, F. W. *J. Am. Chem. Soc.* **1968**, *90*, 2869.
[135] Hortmann, A. G.; Robertson, D. A.; Gillard, B. K. *J. Org. Chem.* **1972**, *37*, 322.
[136] Rens, M.; Ghosez, L. *Tetrahedron Lett.* **1970**, *11*, 3765.
[137] Harvey, G. R.; Ratts, K. W. *J. Org. Chem.* **1966**, *31*, 3907.

[138] Singh, P. N. D.; Carter, C. L.; Gudmundsdottir, A. D. *Tetrahedron Lett.* **2003**, 6763.
[139] Henn, L.; Hickey, D. M. B.; Moody, C. J.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2189.
[140] L'abbé, G. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 775.
[141] L'abbé, G. *Chem. Rev.* **1969**, *69*, 345.
[142] Villalgordo, J. M.; Heimgartner, H. *Helv. Chim. Acta* **1993**, *76*, 2830.
[143] Nishiwaki, T. *Tetrahedron Lett.* **1969**, *10*, 2049.
[144] Ballabio, M.; Destro, R.; Franzoi, L.; Gelmi, M. L.; Pocar, D.; Trimarco, P. *Chem. Ber.* **1987**, *120*, 1797.
[145] Lipshutz, B. H.; Reuter, D. C. *Tetrahedron Lett.* **1988**, *29*, 6067.
[146] Himbert, G.; Kuhn, H.; Barz, M. *Liebigs Ann. Chem.* **1990**, 403.
[147] Ullman, E. F.; Singh, B. *J. Am. Chem. Soc.* **1966**, *88*, 1844.
[148] Singh, B.; Ullman, E. F. *J. Am. Chem. Soc.* **1967**, *89*, 6911.
[149] Singh, B.; Zweig, A.; Gallivam, J. B. *J. Am. Chem. Soc.* **1972**, *94*, 1199.
[150] Beccalli, E. M.; Majori, L.; Marchesini, A.; Torricelli, C. *Chem. Lett.* **1980**, 659.
[151] Komendantov, M. I.; Bekmukhametov, R. R. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1975**, *11*, 1127; *Khim. Geterotsikl. Soedin.* **1975**, 1292.
[152] Auricchio, S.; Bini, A.; Pastormerlo, E.; Truscello, A. M. *Tetrahedron* **1997**, *53*, 10911.
[153] Auricchio, S.; Vajna de Pava, O. *J. Chem. Res. (S)* **1983**, 132.
[154] Deyrup, J. A. In *The Chemistry of Heterocyclic Compounds: Small Ring Heterocycles, Part 1*; Hassner, A., Ed.; Wiley: New York, 1983; Vol. 42, pp 1–214.
[155] Eguchi, S.; Ishii, Y. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 1434.
[156] Kitahonoki, K.; Kotera, K.; Matsukawa, Y.; Miyazaki, S. *Tetrahedron Lett.* **1965**, *6*, 1059.
[157] Kotera, K.; Takano, Y. T.; Matsuura, A.; Kitahonoki, K. *Tetrahedron* **1970**, *26*, 539.
[158] Tanida, H.; Okada, T.; Kotera, K. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 934.
[159] Ferrero, L.; Rouillard, M.; Decouzon, M.; Azzaro, M. *Tetrahedron Lett.* **1974**, *15*, 131.
[160] Bartnik, R.; Laurent, A. *Bull. Soc. Chim. Fr.* **1975**, 173.
[161] Alvernhe, G.; Laurent, A. *J. Chem. Res. (S)* **1978**, 28.
[162] Taniguchi, H, Isomura, K. *J. Synth. Org. Chem. Jpn.* **1972**, *30*, 280.
[163] Kitahonoki, K.; Takano, T.; Takahashi, H. *Tetrahedron* **1968**, *24*, 4605.
[164] Ricart, G.; Couturier, D. *C. R. Hebd. Séance Acad. Sci.* **1977**, *284*, 941.
[165] Kotera, K.; Okada, T.; Miyazaki, S. *Tetrahedron Lett.* **1967**, *8*, 841.
[166] Kotera, K.; Okada, T.; Miyazaki, S. *Tetrahedron* **1968**, *24*, 5677.
[167] Laurent, A.; Muller, A. *Tetrahedron Lett.* **1969**, *10*, 759.
[168] Kitahonoki, K.; Takano, Y. T.; Matsuura, A.; Kotera, K. *Tetrahedron* **1969**, *25*, 335.
[169] Alvernhe, G.; Laurent, A. *Bull. Soc. Chim. Fr.* **1970**, 3003.
[170] Zimmer, R.; Homann, K.; Reissig H.-U. *Liebigs Ann. Chem.* **1993**, 1155.
[171] Kakiya, H.; Yagi, K.; Shinokubo, H.; Oshima, K. *J. Am. Chem. Soc.* **2002**, *124*, 9032.
[172] Davis, F. A.; Liu, H.; Liang, C.-H.; Reddy, G. V.; Zhang, Y.; Fang, T.; Titus, D. D. *J. Org. Chem.* **1999**, *64*, 8929.
[173] Davis, F. A.; Liu, H.; Zhou, P.; Fang, T.; Reddy, G. V.; Zhang, Y. *J. Org. Chem.* **1999**, *64*, 7559.
[174] Atkinson, R. S.; Kelly, B. J. *Tetrahedron Lett.* **1989**, *30*, 2703.
[175] Atkinson, R. S.; Kelly, B. J. *J. Chem. Soc., Chem. Commun.* **1989**, 836.
[176] Legters, J.; Thijs, L.; Zwanenburg, B. *Recl. Trav. Chim. Pays-Bas* **1992**, *111*, 75.
[177] Gentilucci, L; Grijzen, Y.; Thijs, L.; Zwanenburg, B. *Tetrahedron Lett.* **1995**, *36*, 4665.
[178] Davis, F. A.; Reddy, G. V.; Liu, H. *J. Am. Chem. Soc.* **1995**, *117*, 3651.
[179] Davis, F. A.; Deng, J. *Org. Lett.* **2007**, *9*, 1707.
[180] Bernard, C.; Ghosez, L. *J. Chem. Soc., Chem. Commun.* **1980**, 940.
[181] Bonini, B. F.; Maccagnani, G.; Mazzanti, G.; Pedrini, P.; Lammerink, B. H. M.; Zwanenburg, B. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2097.
[182] Bestmann, H. J.; Kunstmann, R. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 1039.
[183] Bestmann, H. J.; Kunstmann, R. *Chem. Ber.* **1969**, *102*, 1816.
[184] Hassner, A.; Alexanian, V. *J. Org. Chem.* **1979**, *44*, 3861.
[185] Devlin, C. J.; Walker, B. J. *J. Chem. Soc., Perkin Trans. 1* **1974**, 453.

[186] Russell, G. A.; Yao, C.-F.; Tashtoush, H. I.; Russell, J. E.; Dedolph, D. F. *J. Org. Chem.* **1991**, *56*, 663.
[187] Chan, T. H.; Massuda, D. *J. Am. Chem. Soc*. **1977**, *99*, 936.
[188] Piquet, V.; Baceiredo, A.; Gornitzka, H.; Dahan, F.; Bertrand, G. *Chem.—Eur. J.* **1997**, *3*, 1757.
[189] Alcaraz, G.; Wecker, U.; Baceiredo, A.; Dahan, F.; Bertrand, G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1246.
[190] Sakai, T.; Matsuda, A.; Korenaga, T.; Ema, T. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1819.
[191] Sakai, T.; Kawabata, I.; Kishimoto, T.; Ema, T.; Utaka, M. *J. Org. Chem.* **1997**, *62*, 4906.
[192] Ciganek, E. *Org. React.* **2008**, *72*, 1.
[193] Suffert, J. *Science of Synthesis* **2004**, *26*, 953.
[194] Fisher, L. E.; Muchowski, J. M. *Org. Prep. Proced. Int*. **1990**, *22*, 399.
[195] Mayer, H. In *Methoden der Organischen Chemie* (*Houben-Weyl),* 4th ed.; Müller, E., Bayer, O., Meerwein, H., Ziegler, K., Kropf, H., Padeken, H.-G., Eds.; Thieme: Stuttgart, 1977; pp 2253–2295.
[196] Baumgarten, H. E.; Petersen, J. M. *Organic Syntheses Coll. Vol. 5*; Wiley: New York, **1973**, 909.
[197] Nakai, M.; Furukawa, N.; Oae, S. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2917.
[198] Alt, G. H.; Knowles, W. S. *J. Org. Chem.* **1960**, *25*, 2047.
[199] Coffen, D. L.; Hengartner, U.; Katonak, D. A.; Mulligan, M. E.; Burdick, D. C.; Olson, G. L.; Todaro, L. J. *J. Org. Chem*. **1984**, *49*, 5109.
[200] Hatanaka, M.; Ishimaru, T. *J. Med. Chem.* **1973**, *16*, 978.
[201] Touster, O. *Org. React.* **1953**, *7*, 327.
[202] Landais, Y.; Vincent, J. M. *Science of Synthesis* **2004**, *26*, 718.
[203] Greck, C.; Drouillat, B.; Thomassigny, C. *Eur. J. Org. Chem*. **2004**, 1377.
[204] Laufer, S. A.; Liedtke, A. J. *Tetrahedron Lett.* **2006**, *47*, 7199.
[205] Tandon, V. K.; Singh, K. A.; Awasthi, A. K.; Khanna, J. M.; Lal, B.; Anand, N. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 2867.
[206] Edwards, O. E.; Dixon, J.; Elder, J. W.; Kolt, R. J.; Lesage, M. *Can. J. Chem.* **1981**, *59*, 2096.
[207] Laufer, S. A.; Wagner, G. K.; Kotschenreuther, D. A.; Albrecht, W. *J. Med. Chem.* **2003**, *46*, 3230.
[208] Delgado, A.; Garcia, J. M.; Mauleon, D.; Minguillon, C.; Subirats, J. R.; Feliz, M.; Lopez, F.; Velasco, D. *Can. J. Chem*. **1988**, *66*, 517.
[209] Kornfeld, E. C.; Fornefeld, E. J.; Kline, G. B.; Mann, M. J.; Morrison, D. E.; Jones, R. G.; Woodward, R. B. *J. Am. Chem. Soc*. **1956**, *78*, 3087.
[210] Perrone, R.; Berardi, F.; Bettoni, G.; Tortorella, V. *Il Farmaco* **1985**, *40*, 422.
[211] Sprenger, W. G.; Cannon, J. G.; Barman, B. K.; Burkman, A. M. *J. Med. Chem*. **1969**, *12*, 487.
[212] Huckle, D.; Lockhart, I. M.; Webb, N. E. *J. Chem. Soc. (C*) **1971**, 2252.
[213] Bognár, R.; Rákosi, M. *Liebigs Ann. Chem*. **1966**, *693*, 225.
[214] Drefahl, G.; Martin, D. *Chem. Ber*. **1960**, *93*, 2497.
[215] Matsumoto, T; Nishida, T; Shirahama, H. *J. Org. Chem*. **1962**, *27*, 79.
[216] Delgado, A.; Mauleon, D.; Rosell, Y. G. *Anal. Química* **1987**, *83*, 322.
[217] Delgado, A.; Mauleon, D.; Rosell, Y. G.; Granados, R. *Eur. J. Med. Chem.* **1988**, *23*, 31.
[218] Bowman, R. E.; Evans, D. D.; Guyett, J.; Nagy, H.; Weale, J.; Weyell, D. J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 438.
[219] Nelson, W. L.; Miller, D. D. *J. Med Chem*. **1970**, *13*, 807.
[220] Sarda, N.; Grouiller, A.; Pacheco, H.; Gier, A; Genin, D. *Bull. Soc. Chim. Fr*. **1972**, 3183.
[221] Tamura, R.; Oda, D.; Kurokawa, H. *Tetrahedron Lett*. **1986**, *27*, 5759, and references cited therein.
[222] Dampawan, P.; Zajac, W. W., Jr. *J. Org. Chem*. **1982**, *47*, 1176.
[223] Hassner, A.; Larkin, J. M.; Dowd, J. E. *J. Org. Chem*. **1968**, *33*, 1733.
[224] Udodong, U. E.; Fraser-Reid, B. *J. Org. Chem.* **1988**, *53*, 2131.
[225] Udodong, U. E.; Fraser-Reid, B. *J. Org. Chem*. **1989**, *54*, 2103.
[226] Dessole, G.; Bernardi, L.; Bonini, B. F.; Capitò, E.; Fochi, M.; Herrera, R. P.; Ricci, A.; Cahiez, G. *J. Org. Chem.* **2004**, *69*, 8525.
[227] Nair, V.; Biju, A. T.; Mathew, S. C.; Babu, B. P. *Chem. Asian J.* **2008**, *3*, 810.

[228] Evans, D. A.; Johnson, D. S. *Org. Lett.* **1999**, *1*, 595.
[229] Yamashita, Y.; Ishitani, H.; Kobayashi, S. *Can. J. Chem.* **2000**, *78*, 666.
[230] Kumaragurubaran, N.; Juhl, K.; Bogevig, A.; Jorgensen, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 6254.
[231] Battaglia, A.; Baldelli, E.; Bombardelli, E.; Carenzi, G.; Fontana, G.; Gelmi, M. L.; Guerrini, A.; Pocar, D. *Tetrahedron* **2005**, *61*, 7727.
[232] Armstrong, A.; Edmonds, I. D.; Swarbrick, M. E.; Treweeke, N. R. *Tetrahedron* **2005**, *61*, 8423.
[233] Vidal, J.; Guy, L.; Stérin, S.; Collet, A. *J. Org. Chem.* **1993**, *58*, 4791.
[234] Enders, D.; Poiesz, C.; Joseph, R. *Tetrahedron: Asymmetry* **1998**, *9*, 3709.
[235] Phukan, P; Sudelai, A. *Tetrahedron: Asymmetry* **1998**, *9*, 1001.
[236] Baumann, T.; Bächle, M.; Bräse, S. *Org. Lett.* **2006**, *8*, 3797.
[237] Magnus, P. D.; Lacour, J.; Coldham, I.; Mugrage, B.; Bauta, W. B. *Tetrahedron* **1995**, *51*, 11087.
[238] Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742.
[239] Anada, M.; Tanaka, M.; Washio, T.; Yamawaki, M.; Abe, T.; Hashimoto, S. *Org. Lett.* **2007**, *9*, 4559.
[240] Sharma, A. K.; Hergenrother, P. J. *Org. Lett.* **2003**, *5*, 2107.
[241] Magnus, P. D.; Barth, L. *Tetrahedron* **1995**, *51*, 11075.
[242] Lap, B. V.; Williams, L. R. *Aust. J. Chem.* **1976**, *29*, 1791.
[243] Utsukihara, T.; Nakamura, H.; Watanabe, M.; Horiuchi, C. A. *Tetrahedron Lett.* **2006**, *47*, 9359.
[244] Garg, N. K.; Sarpong, R.; Stoltz, B. M. *J. Am. Chem. Soc.* **2002**, *124*, 13179.
[245] Yelekci, K. *Doga, Turk. J. Chem.* **1992**, *16*, 18.
[246] Joshi, U. R.; Limaye, P. A. *Indian J. Chem., Sect. B* **1986**, *B25*, 1176.
[247] Gibson, M. S.; Bradshaw, R. W. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 919.
[248] Schubert, H.; Ruhberg, B.; Fiedrich, G. *J. Prakt. Chem.* **1966**, *32*, 249.
[249] Loughlin, W. A.; Henderson, L. C.; Elson, K. E.; Murphy, M. E. *Synthesis* **2006**, 1975.
[250] Silberg, A.; Benkö, A. *Chem. Ber.* **1964**, *97*, 1915.
[251] Bretschneider, H.; Hormann, H. *Monatsh. Chem.* **1953**, *84*, 1021.
[252] Bowman, R. E.; Evans, D. D.; Guyett, J.; Nagy, H.; Weale, J.; Weyell, D. J.; White, A. C. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1926.
[253] Patonay, T.; Micskei, K.; Juhász-Tóth, É.; Fekete, S.; Pardi-Tóth, V. C. *ARKIVOC* **2009**, *vi*, 270, and references cited therein.
[254] Nedelec, L.; Pierdet, J. A.; Fauveau, P.; Euvrard, C.; Proulx-Fedand, L.; Dumont, C.; Labrie, F.; Boissiert, J. R. *J. Med. Chem.* **1983**, *26*, 522.
[255] Chung, J. Y. L.; Ho, G. J.; Chartrain, M.; Roberge, C.; Zhao, D.; Leazer, J.; Farr, R.; Robbins, M.; Emerson, K.; Mathre, D. J.; McNamara, J. M.; Hughes, D. L.; Grabowski, E. J. J.; Reider, P. J. *Tetrahedron Lett.* **1999**, *40*, 6739.
[256] LaMattina, J. L.; Suleske, R. T. *Org. Synth.* **1986**, *64*, 19.
[257] Ripin, D. H. B.; Am Ende, D. J.; Weston, N. P. *Chem. Eng. News* **2001**, *79* (40), 8.
[258] Oxley, P.; Short, W. F. *J. Chem. Soc.* **1948**, 1514.
[259] Heldt, W. Z. *J. Am. Chem.* Soc. **1958**, *80*, 5880.
[260] Wakabayashi, N.; Waters, R. M.; Law, M. W. *Org. Prep. Proced. Int.* **1974**, *6*, 203.
[261] Parcel1, R. F.; Sanchez, J. P. *J. Org. Chem.* **1981**, *46*, 5229.
[262] Padwa, A.; Rosenthal, R. J.; Dent, W.; Filho, P.; Turro, N. J.; Hrovat, D. A.; Gould, I. R. *J. Org. Chem.* **1984**, *49*, 3174.
[263] Padwa, A.; Kamigata, N. *J. Am. Chem. Soc.* **1977**, *99*, 1871.
[264] Horn, A. S.; Kaptein, B.; Vermue, N. A.; de Vries, J. B.; Mulder, T. B. A. *Eur. J. Med. Chem.* **1988**, *23*, 325.
[265] Sakai, T.; Liu, Y.; Ohta, H.; Korenaga, T.; Ema, T. *J. Org. Chem.* **2005**, *70*, 1369.
[266] Chiba, S.; Hattori, G.; Narasaka, K. *Chem. Lett.* **2007**, *36*, 52.
[267] Benincori, T.; Brenna, E.; Sannicolo, F. *J. Chem. Soc., Perkin Trans. 1* **1993**, 675.
[268] González-Nogal, A. M.; Cuadrado, P.; Sarmentero, M. A. *Eur. J. Org. Chem.* **2009**, 850.
[269] Pfoertner, K.-H.; Zell, R. *Helv. Chim. Acta* **1980**, *63*, 645.
[270] Nair, N. *J. Org. Chem.* **1968**, *33*, 2121.
[271] Inui, H.; Murata, S. *J. Chem. Soc., Chem. Commun.* **2001**, 1036.
[272] Anderson, W. K.; Milowsky, A. S. *J. Med. Chem.* **1986**, *29*, 2241.

[273] Parcell, R. F. *Chem. Ind. (London)*, **1963**, 1396.
[274] Gerber, U.; Heimgartner, H.; Schmid, H.; Heinzelmann, W. *Helv. Chim. Acta* **1977**, *60*, 687.
[275] Arséniyadis, S.; Laurent, A.; Mison, P. *Bull. Soc. Chim. Fr.* **1980**, 246.
[276] Padwa, A.; Carlsen, P. H. J.; Ku, A. *J. Am. Chem. Soc.* **1978**, *100*, 3494.
[277] Padwa, A.; Carlsen, P. H. J. *J. Am. Chem. Soc.* **1977**, *99*, 1514.
[278] Abbas, S. A.; Laurent, A.; Mison, P.; Pellissier, N. *Bull. Soc. Chim. Fr.* **1986**, 288.
[279] Eddaïf, A.; Laurent, A.; Mison, P.; Pellissier, N.; Carrupt, P.-A.; Vogel, P. *J. Org. Chem.* **1987**, *52*, 5548.
[280] Padwa, A.; Wetmore, S. I., Jr. *J. Org. Chem.* **1974**, *39*, 1396.
[281] Njar, V. C. O.; Düerkop, J.; Hartmann, R. W. *Steroids* **1996**, *61*, 138.
[282] Padwa, A.; Cohen, L. A.; Gingrich, H. L. *J. Am. Chem. Soc.* **1984**, *106*, 1065.
[283] Nuriev, V. N.; Zyk, N. V.; Vatsadze, S. Z. ARKIVOC **2005**, *iv*, 208.
[284] Ganellin, C. R.; Hosseini, S. K.; Khalaf, Y. S.; Tertiuk, W.; Arrang, J.-M.; Garbarg, M.; Ligneau, X.; Schwartz, J.-C. *J. Med. Chem.* **1995**, *38*, 3342.
[285] Cymerman-Craig, J.; Willis, D. *J. Chem. Soc.* **1955**, 4315.
[286] LaMattina, J. L. *J. Heterocycl. Chem.* **1983**, *20*, 533.
[287] Lipinski, C. A.; LaMattina, J. L.; Oates, P. J. *J. Med. Chem.* **1986**, *29*, 2154.
[288] Dijkstra, D.; Rodenhuis, N.; Vermeulen, E. S.; Pugsley, T. A.; Wise, L. D.; Wikström, H. V. *J. Med. Chem.* **2002**, *45*, 3022.
[289] Aloup, J.-C.; Audiau, F.; Barreau, M.; Damour, D.; Jimonet, P.; Mignani, S.; Ribeill, Y. U.S. Patent 5,922,716, 1999.
[290] Ribeill, Y.; Genevois-Borella, A.; Vuilhorgne, M.; Mignani, S. *Heterocycles* **1999**, *51*, 2977.
[291] Cannon, J. G.; Kim, J. C.; Aleem, M. A.; Long, J. P. *J. Med. Chem.* **1972**, *15*, 348.
[292] Horn, A. S.; Kaptein, B.; Mulder, T. B. A.; de Vries, J. B.; Wynberg, H. *J. Med. Chem.* **1984**, *27*, 1340.
[293] Balsamo, A.; Breschi, M. C.; Giannaccini, G.; Lapucci, A.; Lucacchini, A.; Macchia, C. B.; Manera, C.; Martin, C.; Martinotti, E.; Nencetti, S.; Rossello, A.; Scatizzi, R. *Eur. J. Med. Chem.* **1993**, *28*, 735.
[294] van Vliet, L. A.; Rodenhuis, N.; Dijkstra, D.; Wikström, H.; Pugsley, T. A.; Serpa, K. A.; Meltzer, L. T.; Heffner, T. G.; Wise, L. D.; Lajiness, M. E.; Huff, R. M.; Svensson, K.; Sundell, S.; Lundmark, M. *J. Med. Chem.* **2000**, *43*, 2871.
[295] Pandit, U. K.; Huisman, H. O. *Recl. Trav. Chim. Pays-Bas* **1966**, *85*, 311.
[296] Weinstock, J.; Gaitanopoulos, D. E.; Oh, H.-J.; Pfeiffer, F. R.; Karash, C. B.; Venslavsky, J. W.; Sarau, H. M.; Flaim, K. E.; Hieble, J. P.; Kaiser, C. *J. Med. Chem.* **1986**, *29*, 1615.
[297] Callahan, J. F.; Keenan, R. M.; Kwon, C.; Samanen, J. M. U.S. Patent 6,117,910, 2000.
[298] Miyake, A.; Itoh, K.; Tada, N.; Tanabe, M.; Hirata, M.; Oka, Y. *Chem. Pharm. Bull.* **1983**, *31*, 2329.
[299] Miyake, A.; Kuriki, H.; Itoh, K.; Nishikawa, M.; Oka, Y. *Chem. Pharm. Bull.* **1977**, *25*, 3289.
[300] Macchia, M.; Balsamo, A.; Breschi, M. C.; Lapucci, A.; Lucacchini, A.; Macchia, F.; Manera, C.; Martinelli, A.; Martini, C.; Martinotti, E.; Nencettit, S. *J. Med. Chem.* **1992**, *35*, 1009.
[301] Kim, J. C.; Lee, S.-K.; Kim, C.-B.; Han, S.-K.; Choi, S.-K.; Lee, K.-H. *J. Korean Chem. Soc. (Taehan Hwahakhoe Chi)* **1977**, *21*, 187.
[302] Itoh, K.; Motohashi, M.; Kuriki, H.; Sugihara, H.; Inatomi, N.; Nishikawa, M.; Oka, Y. *Chem. Pharm. Bull.* **1977**, *25*, 2917.
[303] Tandon, V. K.; Khanna, J. M.; Anand, N. *Indian J. Chem., Sect. B* **1977**, *15B*, 264.
[304] Bach, N. J.; Kornfeld, E. C.; Titus, R. D. U.S. Patent 4,448,990, 1984.
[305] Evans, D. D.; Peters, D. J. *J. Chem. Soc., Perkin Trans. 1* **1974**, 285.
[306] Peglion, J.-L.; Vian, J.; Goument, B.; Millan, M.; Audinot, V.; Schwartz, J.-C.; Sokoloff, P. European Patent Application EP 0 686637; A1 19951213, 1995.
[307] Peglion, J.-L.; Vian, J.; Goument, B.; Despaux, N.; Audinot, V.; Millan, M. J. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 881.
[308] Jordaan, A.; Joynt, V. P.; Arndt, R. R. *J. Chem. Soc.* **1965**, 3001.
[309] Joshi, V.; Merchant, J. R. *Indian J. Chem., Sect. B* **1976**, *B14*, 724.

[310] Shilcrat, S. C.; Hill, D. T.; Bender, P. E.; Griswold, D. E.; Baures, P. W.; Eggleston, D. S.; Lantos, I.; Pridgen, L. N. *J. Heterocycl. Chem.* **1991**, *28*, 1181.
[311] Tamura, Y.; Fujiwara, H.; Sumoto, K.; Ikeda, M.; Kita, Y. *Synthesis* **1973**, 215.
[312] Roveri, P.; Gatti, R.; Cavrini, V.; Baserga, M. *Boll. Chim. Farm.* **1979**, *118*, 102.
[313] Finizio, M. U.S. Patent 4,548,946, 1985.
[314] Bertolini, G.; Vecchietti, V.; Mabilia, M.; Norcini, G.; Restelli, A.; Santangelo, F.; Villa, A. M.; Casagrande, C. *Eur. J. Med. Chem.* **1992**, *27*, 663.
[315] Finizio, M. U.S. Patent 4,371,541, 1983.
[316] Kidd, D. *J. Chem. Soc.* **1962**, 5121.
[317] Bognár, R.; Rákosi, M.; Bálint, J. *Tetrahedron Lett.* **1964**, *5*, 137.
[318] Grouiller, A.; Pacheco, H.; Carret, G. *J. Heterocycl. Chem.* **1976**, *13*, 853.
[319] Flemming, H. W.; Korb, G.; Mueller-Lehar, J.; Weber, W. U.S. Patent 6,916,934 B2, 2005.
[320] Bouchet, R.; Lagouardat, J.; Scholl, J. U.S. Patent 6,353,108 B1, 2002.
[321] Chartrain, M. M.; Roberge, C.; Chung, J. Y. L.; Zhao, D. U.S. Patent 5,792,871, 1998.
[322] Tricerri, S.; Pedrazzoli, A.; Treu, T. *Gazz. Chim. Ital.* **1954**, *84*, 701.
[323] Stadler, H.; Vieira, E.; Wostl, W. European Patent 0 543 245 A1, 1993.
[324] Lantos, I.; Gombatz, K.; McGuire, M.; Pridgen, L.; Remich, J.; Shilcrat, S. *J. Org. Chem.* **1988**, *53*, 4223.
[325] Koch, P.; Bäuerlein, C.; Jank, H.; Laufer, S. *J. Med. Chem.* **2008**, *51*, 5630.

CHAPTER 3

TWOFOLD EXTRUSION REACTIONS

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CONTENTS

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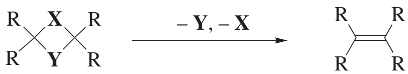
INTRODUCTION

Extrusion reactions are defined as chemical reactions in which an atomic or molecular fragment **Y**, connected to two other atoms **X** and **Z**, is lost, leading to a product in which **X** becomes directly bonded to **Z** (Eq. 1).[1–5] Typically, the fragments lost are small, stable, inorganic molecules or atoms. Twofold extrusion reactions involve tandem loss of two such species, **X** and **Y**, affording multiple bonds (Eq. 2), and are particularly useful for the preparation of sterically hindered alkenes and imines. The most common species liberated in twofold extrusion reactions are molecular nitrogen, sulfur, selenium, sulfur dioxide, sulfur monoxide, and carbon dioxide. Extrusions of carbon monoxide and tellurium are also known.

$$\mathrm{X{-}\mathbf{Y}{-}Z} \xrightarrow{-\,\mathbf{Y}} \mathrm{X{-}Z} \qquad \text{(Eq. 1)}$$

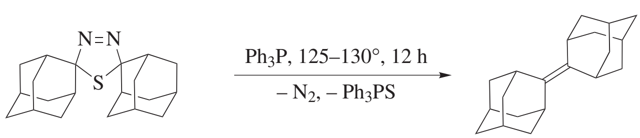


(Eq. 2)

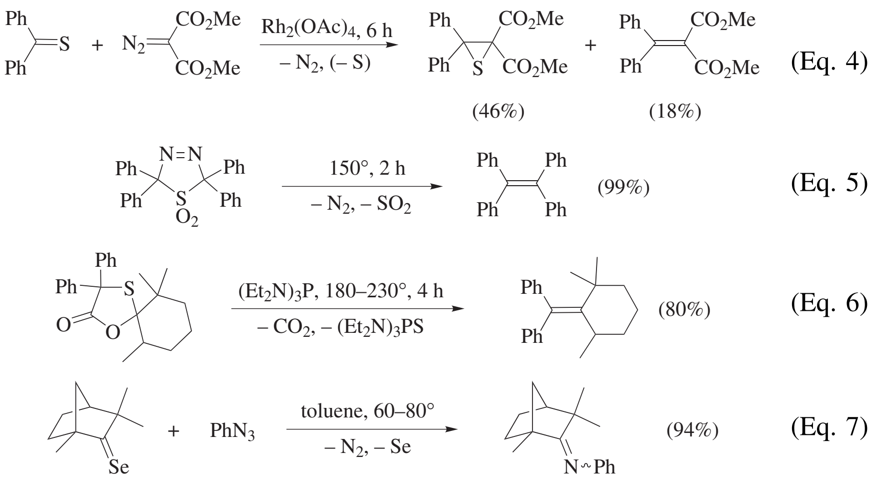
This chapter discusses the preparation of alkenes, imines, and other doubly bonded species via twofold extrusions. A number of closely related reactions that also afford alkenes and imines by extrusion of two fragments, but do not involve discrete, cyclic intermediates such as those indicated in Eq. 2, are also included in this chapter. The mechanism section will show that these reactions frequently proceed in a stepwise manner and are often metal-catalyzed transformations.

No comprehensive reviews of these reactions are found in the literature, although the topic has been covered within the context of general extrusion reactions.[3,5] Two related, alkene-forming reactions that involve a displacement step followed by a single fragment extrusion are not treated in this chapter: the Ramberg-Bäcklund reaction, the preparation of alkenes via sulfur dioxide extrusion from base-generated thiirane-1,1-dioxides, which has been extensively reviewed;[6,7] and the Eschenmoser sulfide contraction reaction.[8] The wider topic of single extrusion reactions, which most frequently involve the loss of a single, stable inorganic species, will be covered in a subsequent chapter.

Representative twofold extrusion processes include: the preparation of a moderately hindered alkene via an isolated thiadiazoline (Eq. 3);[9] the transition-metal-promoted reaction of dimethyl diazomalonate with a thione (Eq. 4);[10] the preparation of alkenes via extrusion of molecular nitrogen and sulfur dioxide (Eq. 5)[11] or extrusions of sulfur and carbon dioxide (Eq. 6);[12] and the preparation of an extremely sterically hindered imine via extrusion of molecular nitrogen and selenium (Eq. 7).[13] From these examples it should be clear that the key to the overall extrusion process is the ability to assemble the required precursors for the reactions. This prerequisite will be discussed in detail in the Scope and Limitations section.



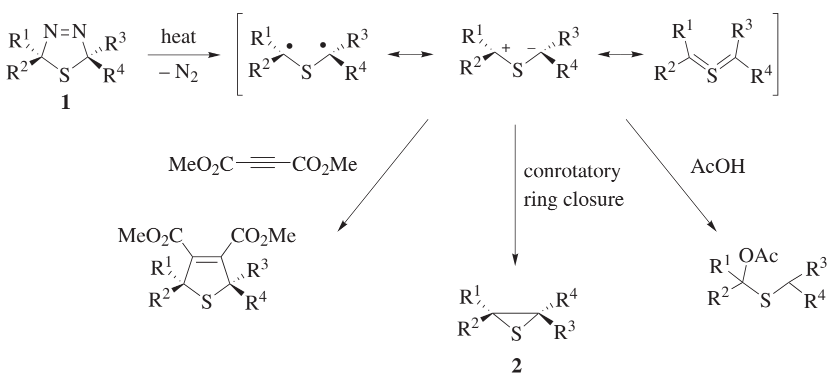
(74%) (Eq. 3)



MECHANISM AND STEREOCHEMISTRY

A key feature of all extrusion reactions is the thermal or photochemical liberation of one or more small, stable molecules or atoms. For related substrates with similar extrusion mechanisms the ease of extrusion of a number of fragments is as follows: $N_2 > CO_2 > CO > SO > SO_2 > O_2 > S > O$.[5] This order of reactivity has been confirmed in a quantitative manner using thermodynamic considerations.[4] At the elevated temperatures quite often needed in extrusion processes, such losses of small molecular or atomic fragments are also entropically favorable.

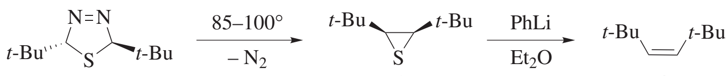
The mechanism of some twofold extrusion reactions, particularly the initial step of nitrogen extrusion from a thiadiazoline **1**, has been investigated in detail (Scheme 1).[14–16] Thermal decomposition of a thiadiazoline leads to loss of molecular nitrogen and formation of a thiocarbonyl ylide. This intermediate, which can



Scheme 1

be described in terms of biradical, dipolar, and "tetravalent sulfur" resonance structures, can close to a thiirane **2**, be intercepted by protonation, or be trapped by an added reagent.[16,17] With stereochemically defined thiadiazolines, the reactions proceed by the expected 4π electron conrotatory ring closure with nearly complete stereospecificity in both simple cyclization and trapping experiments.

A specific example (Scheme 2) is the conversion of a *trans*-thiadiazoline into the very hindered *cis*-2,3-di-*tert*-butylthiirane (**3**) in quantitative yield.[15] This thiirane is desulfurized with retention of configuration to (*Z*)-1,2-di-*tert*-butylethylene (**4**) using phenyllithium.



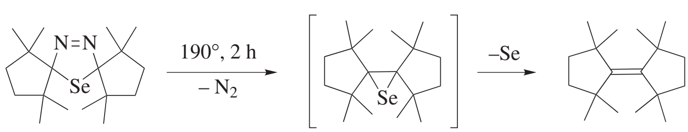
3 (100%) **4** (100%)

Scheme 2

Similar retention of configuration is also seen in the reaction of an initially formed thiirane with a tertiary phosphine or phosphite, or with copper bronze. The stereochemical utility of this reaction is therefore limited only by the availability of stereo-defined thiadiazoline precursors. The preparation of thia- and selenadiazoline precursors will be discussed in the "Scope and Limitations" section.

In a number of cases, reactions of diazo compounds with thiones are catalyzed by metal species. For example, dimethyl diazomalonate does not react with thiobenzophenone except in the presence of rhodium(II) acetate [$Rh_2(OAc)_4$].[10] This reaction presumably involves the formation of the metal carbenoid with loss of nitrogen, followed by reaction with the thione to afford a thiocarbonyl ylide, which closes to the thiirane. Copper reagents, which are often used in the desulfurization step of the twofold extrusion reaction, may also play a part in promoting diazo compound additions to less reactive thiones.

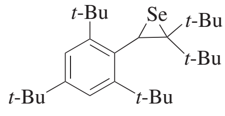
Extrusion of nitrogen from selenadiazoline **5** (Eq. 8) is assumed to occur in a stepwise manner similar to that observed in the thiadiazoline reactions, but stereochemical aspects of the initial nitrogen loss in these reactions have not been determined because the intermediate selenirane **6** loses selenium at a faster rate than the loss of nitrogen that forms it.[18]



(Eq. 8)

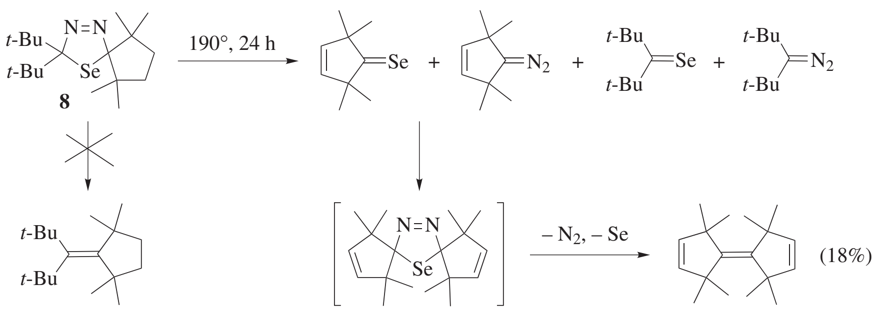
5 **6** (70%)

In two cases, seleniranes such as **7** have been detected by ^1H and ^{13}C NMR spectroscopy and are stable at−40°. They are generated at low temperature by metal-catalyzed reactions of an extremely hindered selenal with hindered diazo compounds such as di-*tert*-butyldiazomethane or 2-diazo-1,1,3,3-tetramethyl-indane.[19] As in the thione reactions discussed above, it is likely that metal carbenoid complexes are involved in these selenirane-forming reactions.



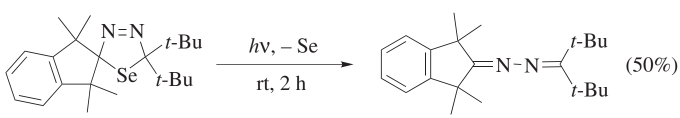
7

Extremely sterically hindered thia- and selenadiazolines such as **8** (Scheme 3) are particularly prone to retrocyclization. Pyrolysis of such unsymmetrical compounds leads to the formation of the symmetrical alkenes as the only isolable olefinic products, along with the more hindered thione or selone. This process occurs by retrocyclization followed by recombination of the resulting, less hindered, thione or selone and the diazo compound, affording the less hindered, symmetrical thia- or selenadiazoline **9**.[18] These heterocycles in turn undergo normal extrusions, affording the less sterically hindered alkene **10**.[18] In these cases, it is likely that unfavorable steric interactions prevent the formation of the desired, unsymmetrical thio- or selenocarbonyl ylide via extrusion of nitrogen.



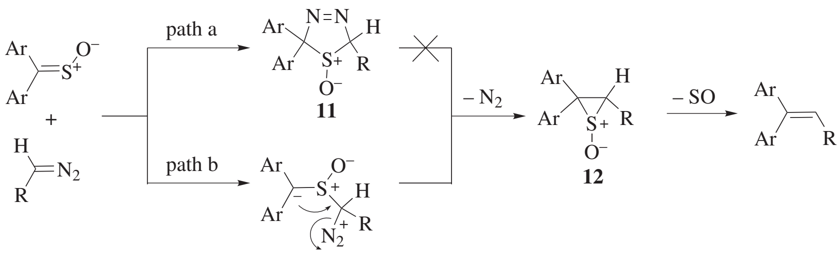
Scheme 3

In contrast to thermally induced extrusion, irradiation of a thiadiazoline or selenadiazoline leads to clean extrusion of sulfur or selenium, affording the azine as the only identifiable organic product (Eq. 9).[14,18] In this photochemical transformation the cheleotropic loss of selenium or sulfur is a Woodward-Hoffmann allowed process.[20]



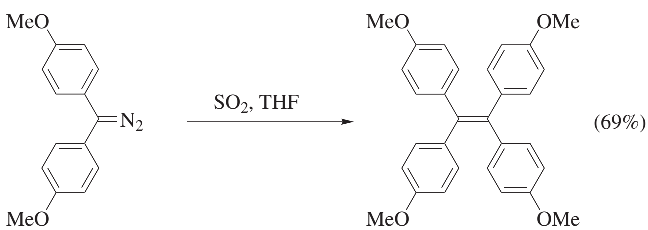
(Eq. 9)

The mechanism for alkene formation from the reactions of diazo compounds with sulfines, a reaction that is limited in almost all examples to sulfines with two aromatic substituents, is more controversial. One obvious mechanism for the formation of the intermediate would be the initial formation of the thiadiazoline-1-oxide **11** followed by extrusion of nitrogen to give the thiirane oxide **12** (Scheme 4, path a). However, this does not seem to be the case.[21–23] The dominant mechanism involves the formation and cyclization of a dipolar intermediate (Scheme 4, path b) analogous to the mechanism proposed for the formation of oxiranes in the reactions of diazo compounds with ketones.[24] Thermolysis of isolated 1,3,4-thiadiazoline-1-oxides leads predominantly to retrocyclization, and not alkene formation,[25] clearly favoring the second mechanism. The fact that thiirane oxide formation is not stereospecific also favors the dipolar mechanism.[21,22] The resulting thiirane oxides can occasionally be isolated, but they are thermally labile and extrude SO upon heating at reflux in dichloromethane affording the corresponding alkenes in nearly quantitative yield.[26]

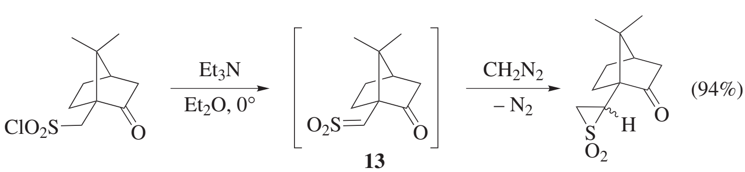


Scheme 4

Similar mechanistic considerations apply to the formation of alkenes and other products in the reactions of diazo compounds with SO_2 (the Staudinger-Pfenninger Reaction, Eq. 10),[27] and to the reactions of diazo compounds with in situ generated sulfenes such as **13** (Eq. 11).[28]

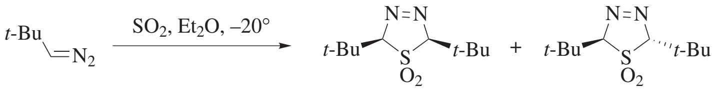


(Eq. 10)



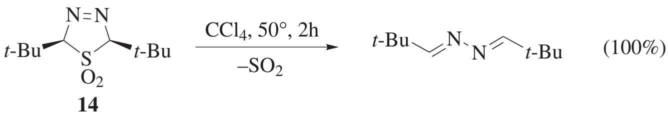
(Eq. 11)

Although 1,3,4-thiadiazoline-1,1-dioxide can be isolated from some of these reactions (Eq. 12), it is unlikely that these compounds are intermediates on the direct pathway to thiirane dioxides and alkenes under normal thermal conditions.[29] The stereoisomeric thiadiazoline 1,1-dioxides **14** and **15** (Eq. 12) exhibit different behavior on heating, and neither affords the alkene.[30] Upon mild heating the *cis*-isomer extrudes SO_2, affording the (E,E) azine (Eq. 13).



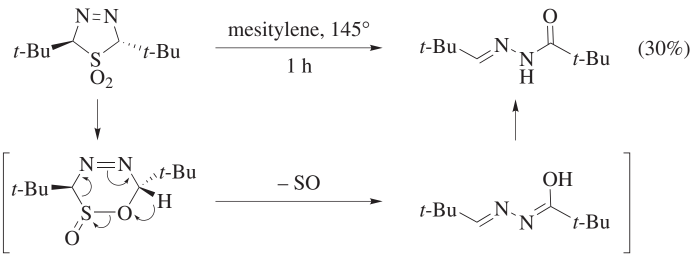
14 (14%) **15** (61%)

(Eq. 12)



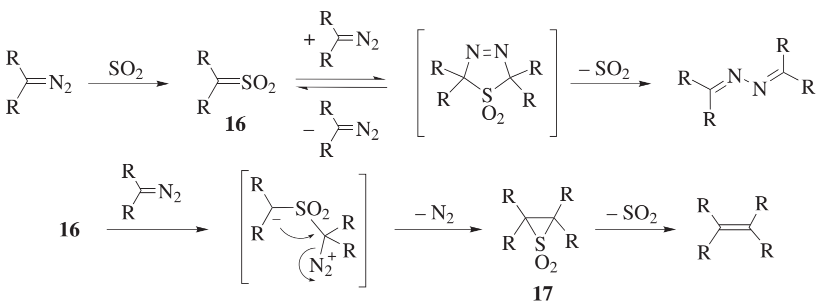
(Eq. 13)

In the *trans*-isomer, severe steric interactions prevent the normal, thermal cheleotropic extrusion, and the reaction takes a completely different course (Eq. 14).[30] A reasonable mechanism for the formation of the acylhydrazone product would involve the formation and collapse of a 6-membered-ring intermediate.



(Eq. 14)

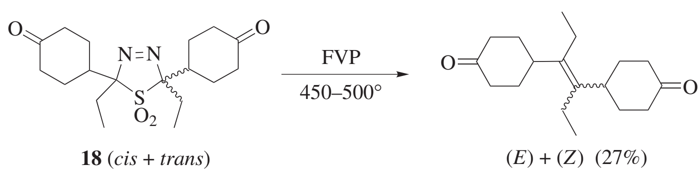
Therefore, the mechanism of the Staudinger-Pfenninger reaction probably parallels that of the previously discussed reaction of sulfines with diazo compounds, and does not involve 1,3,4-thiadiazoline-1,1-dioxides as the major intermediates in the alkene-forming process (Scheme 5). The diazo compound reacts with sulfur dioxide to afford the corresponding sulfene **16**, which reacts with additional diazo compound via a dipolar intermediate to afford the thiirane dioxide **17**. Extrusion of sulfur dioxide from **17** affords the alkene.



Scheme 5

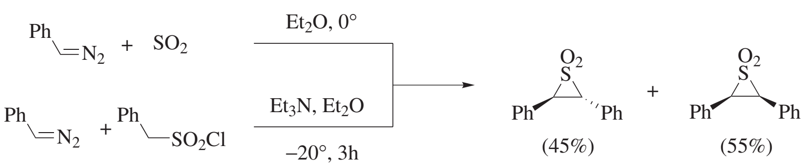
A detailed study of the effect of solvent on product distributions in the Staudinger-Pfenninger reaction shows that increased solvent polarity favors thiirane dioxide formation relative to azine formation; when the reaction shown in Eq. 12 is carried out in methanol, a 78% yield of the thiirane dioxide is obtained.[31] Aryl substitution also favors the formation of thiirane dioxides.[31] Both of these solvent and substituent effects are consistent with stabilization of the zwitterionic intermediate, favoring that route over the alternative cycloaddition reaction. Solvent and substituent effects on product distributions in additions of sulfenes with diazo compounds are attributed to "the existence of two low-lying sulfene MO's, only one of which exhibits π-symmetry."[31] Kinetic studies of the reactions of diazo compounds with SO_2 have also been reported.[32]

As shown earlier (Eq. 5), 1,3,4-thiadiazoline-1,1-dioxides bearing multiple aryl substituents behave differently from those bearing aliphatic substituents (Eq. 12) and do extrude molecular nitrogen and sulfur dioxide on moderate heating to give high yields of alkenes.[11] Flash vacuum pyrolysis (FVP) of thiadiazoline-1,1-dioxides such as **18** (Eq. 15) to afford a non-conjugated alkene may also involve direct extrusions of molecular nitrogen and sulfur dioxide; however, yields in these cases are only modest.[33]



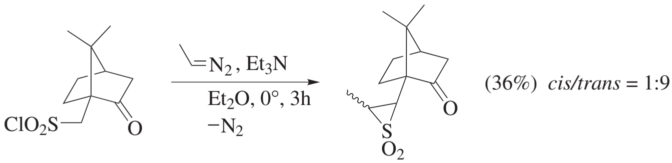
(Eq. 15)

The thermal extrusion of sulfur dioxide from a thiirane dioxide is known to be stereospecific,[34] and therefore the steps that lead to the thiirane dioxide determine the configuration of the alkene products. A number of studies disagree on the effect of solvents on the stereochemical course of the reaction of phenyl diazomethane with sulfur dioxide.[24,31,35,36] When conducted in the same solvent, the Staudinger-Pfenninger reaction and the corresponding sulfene–diazo compound reaction both lead to approximately the same 1:1 *cis/trans* ratio of thiirane 1,1-dioxide products in this relatively non-sterically hindered case (Scheme 6).[37]



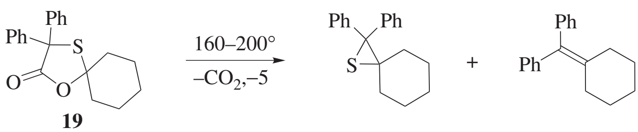
Scheme 6

From unsymmetrical substrates containing a bulky substituent, the *trans*-thiirane 1,1-dioxide isomer predominates (Eq. 16).[37]



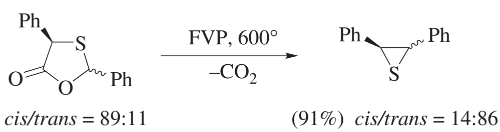
(Eq. 16)

A number of other twofold extrusion reactions afford alkenes or imines. Some mechanistic information is available for these processes, and it is based largely on the ability to isolate intermediates, in addition to some limited stereochemical observations. These reactions include the thermal extrusion of carbon dioxide and sulfur from oxathiolan-4-ones such as **19** (Eq. 17).[38] If the reaction is carried out without added tertiary phosphine, thiiranes can be isolated in some cases.[12,39] Aryl substitution on the oxathiolanone is needed for the initial extrusion of carbon dioxide to take place at moderate temperatures.[38]



(Eq. 17)

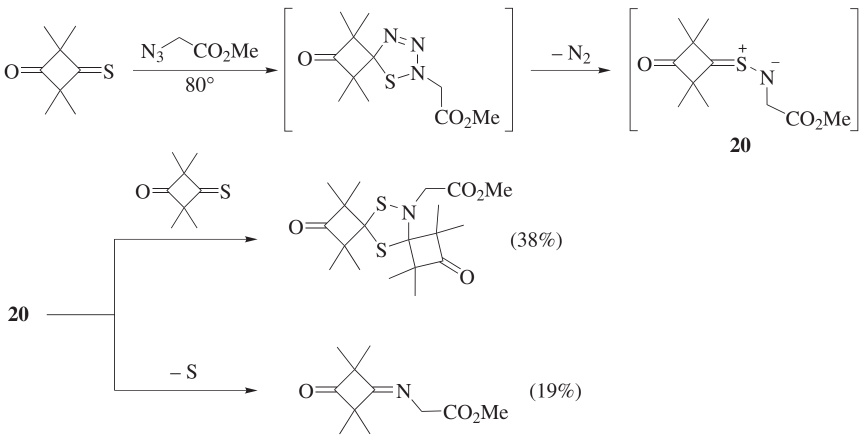
FVP of oxathiolanones at high temperatures (550–750°) leads to clean extrusion of carbon dioxide to give the corresponding thiirane (Eq. 18).[40] The stereochemical outcomes of these extrusions are independent of the nature of the substituents and are consistent with a thiocarbonyl ylide intermediate that undergoes conrotatory ring closure in the manner shown earlier in Scheme 1.



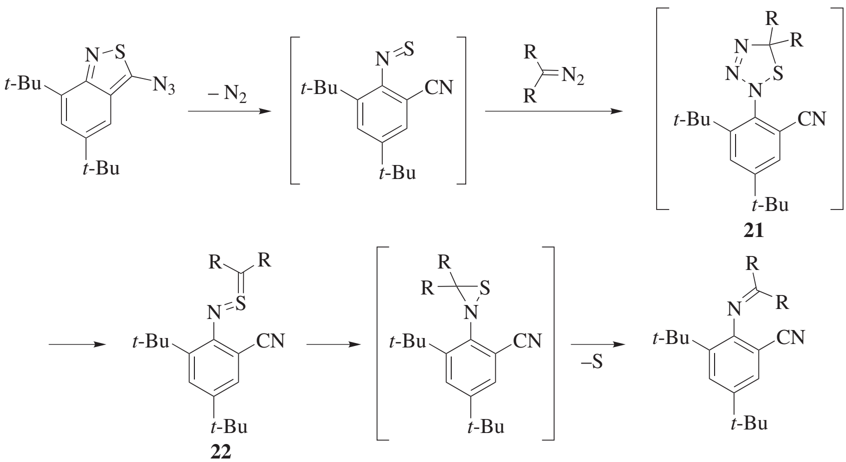
(Eq. 18)

The reactions of azides with thiones or selones afford imines via thermal extrusions of nitrogen and sulfur or selenium. With a thione as the coreactant, trapping experiments indicate the formation of a thiocarbonyl-*S*-imide intermediate **20** after an initial cycloaddition and nitrogen extrusion (Scheme 7).[41,42]

In situ generated thionitroso compounds react with moderately hindered diazo compounds such as diphenyldiazomethane or diazofluorene to afford the corresponding imines (Scheme 8).[43] The proposed mechanism involves an initial 1,3-dipolar cycloaddition to form thiatriazoline **21**, which extrudes nitrogen affording the thiocarbonyl imine **22**. Isolated thiocarbonyl imines are known to lose sulfur via an intermediate thiaziridine to give the corresponding imines.[44] With increasing substituent size, the thiocarbonyl imine and, in one case, the thiatriazoline can be isolated from the reaction.[43]



Scheme 7



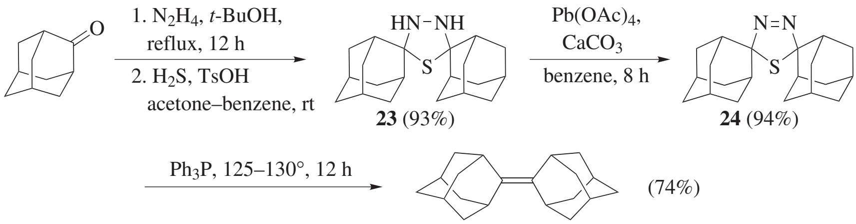
Scheme 8

SCOPE AND LIMITATIONS

In general, the immediate precursors for the twofold extrusion reactions are relatively complex cyclic systems, often generated in situ by cycloaddition reactions. Accordingly, in addition to the alkene- and imine-forming processes, this section also discusses methods for the preparation of the precursors to these systems, notably thiones and selones (thio- and selenoketones).

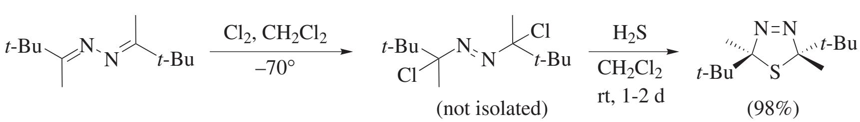
Alkene Formation: Scope

Alkenes from Thiadiazolines. The most widely used method for the preparation of extremely hindered alkenes involves the two-fold extrusion reaction of a 1,3,4-thiadiazoline. This reaction is often termed the Barton-Kellogg reaction, particularly when the intermediate 1,3,4-thiadiazolidines such as **23** and 1,3,4-thiadiazolines such as **24** are isolated (Scheme 9). The thiadiazolines thermally extrude nitrogen, affording the corresponding thiirane (see Scheme 2). Desulfurization of the thiirane to the alkene is carried out with a variety of reagents, including tertiary phosphines and phosphites, copper bronze, or organolithium reagents. Frequently, extrusion of nitrogen and sulfur are carried out in "one pot" without isolating the thiirane, as is done for the last step in Scheme 9.[9]



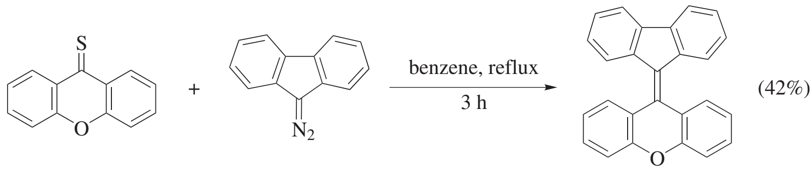
Scheme 9

For the preparation of symmetrical, moderately hindered alkenes the azine addition reaction is generally effective and uses easily accessible starting materials; for more hindered systems the cycloaddition route becomes the method of choice. As steric hindrance increases, the hydrogen sulfide addition step that affords the intermediate 1,3,4-thiadiazolidine becomes much more difficult. The employment of a medium-pressure hydrogenation apparatus converted for use with hydrogen sulfide can sometimes facilitate the addition.[12,45] However, although the thiadiazolidine can be isolated as an unstable solid in some very hindered cases, oxidation fails because of rapid loss of hydrogen sulfide from this intermediate. For some substitution patterns, an alternative route to thiadiazolines from azines involves the initial, low temperature addition of chlorine, followed by treatment with hydrogen sulfide (Eq. 19).[46,47]



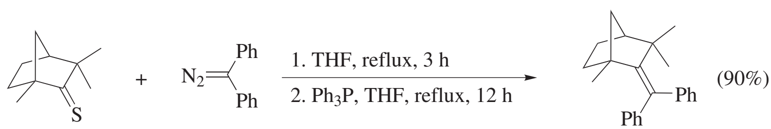
(Eq. 19)

The thiadiazolines required for two-fold extrusion processes are also conveniently generated by the cycloaddition of a thione and a diazo compound.[48–50] With substrates that contain multiple, aromatic substituents the direct, thermal extrusion of sulfur often occurs without the need for added desulfurizing reagents (Eq. 20).[51] In a few instances alkenes appear to be obtained directly from thiones and diazo compounds at room temperature, but it is likely that the alkene products are generated thermally in the process of their isolation by preparative gas chromatography or recrystallization.[51a]



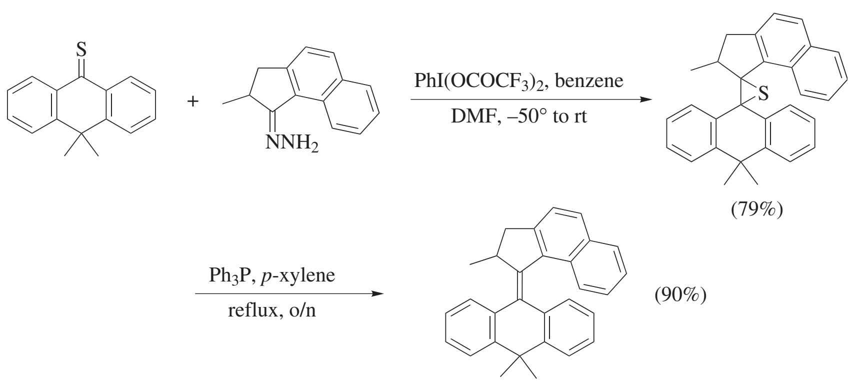
(Eq. 20)

Usually the intermediate thiirane is desulfurized by being heated with a tertiary phosphine that is added after the cycloaddition step is complete. As in the azine route described above, the thiirane is frequently desulfurized without isolation (Eq. 21).[50]



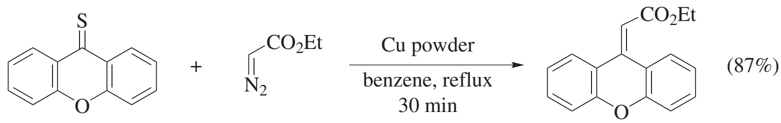
(Eq. 21)

Occasionally, unstable diazo compounds are generated in situ by the oxidation of the corresponding hydrazone. The diazo compound then reacts with the thione, and in the example shown (Scheme 10)[52] nitrogen extrusion on warming and work-up gives the thiirane. A subsequent desulfurization step affords the desired alkene.



Scheme 10

The reaction of highly deactivated thiones such as xanthione with ethyl diazoacetate to afford β,β-disubstituted acrylates is promoted by salts of copper or rhodium, and by metallic copper. The latter is also involved in the subsequent desulfurization step (Eq. 22).[53,54] As discussed in the "Mechanism and Stereochemistry" section, such reactions, which also allow the use of highly stabilized diazomalonates as shown earlier in Eq. 4,[10] most likely involve the initial formation of the metal carbenoid that reacts with the thione to form the thiirane. With α-diazo ketones, reactions conducted without metal salts can give either alkenes or 1,3-oxothiolanes, depending on the structure of the thione.[55]

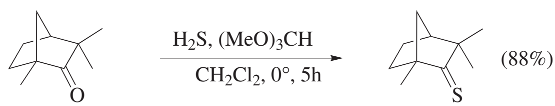


(Eq. 22)

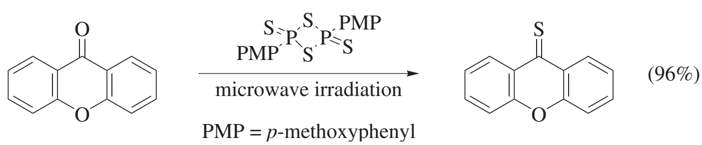
Although the azine route is limited by steric hindrance, the reverse is true for the cycloaddition approach because thione stability increases significantly with increasing steric hindrance. A similar increase in stability has been noted with hindered diazo compounds.[50] In addition to leading directly to hindered thiadiazolines, the cycloaddition approach is also the method of choice for unsymmetrical alkene targets.

Preparation of Thiones. Numerous methods are available for the preparation of sterically hindered thiones, and this topic has been well reviewed.[56,57] Although extremely hindered or conjugated thiones are stable, storable substances, less hindered thiones and thials (thioaldehydes) often cannot be isolated, and most preparations result in the isolation of dimers. Trapping is possible in principle, but diazo compounds generally do not survive the conditions necessary for thione generation.

For relatively stable thiones, a useful method of preparation involves treating a ketone with hydrogen sulfide in the presence of an acid catalyst.[50] Frequently, a water scavenger such as trimethyl orthoformate is added to obtain a favorable equilibrium in the reaction (Eq. 23).[50] Reaction of a conjugated ketone with Lawesson's reagent under microwave irradiation affords the thione in excellent yield (Eq. 24).[58]

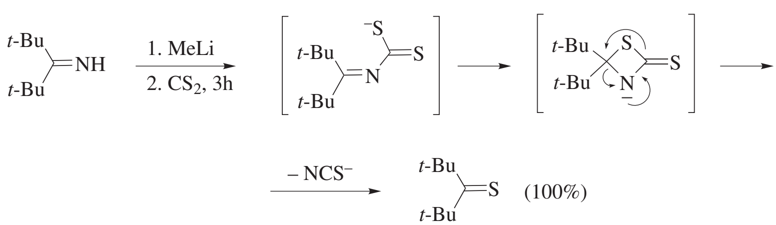


(Eq. 23)



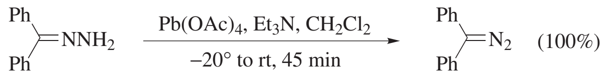
(Eq. 24)

Di-*tert*-butylthione is prepared by deprotonating di-*tert*-butylketimine with methyllithium, followed by the addition of carbon disulfide. The resulting dithiocarbamate salt loses lithium thiocyanate upon heating (Eq. 25).[50]

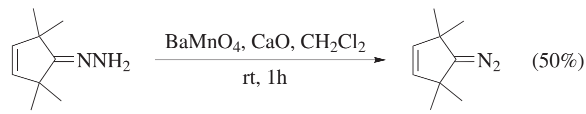


(Eq. 25)

Preparation of Diazo Compounds. Aryl-substituted diazo compounds are most frequently prepared by oxidizing the corresponding hydrazones, most conveniently with lead(IV) acetate (Eq. 26).[50] Hindered, aliphatic diazo compounds are best prepared by oxidizing the hydrazone with barium manganate (Eq. 27).[18]



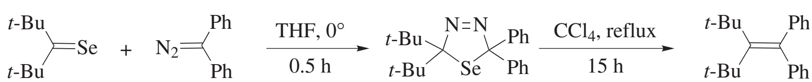
(Eq. 26)



(Eq. 27)

Sterically hindered aliphatic diazo compounds can also be prepared in situ by the standard method of pyrolysis of the salts of the corresponding *p*-toluenesulfonylhydrazones.[50] As previously described (Scheme 10),[52] the in situ, oxidative generation of sterically hindered diazo compounds in the presence of a thione has recently been introduced as a useful method for twofold extrusions.

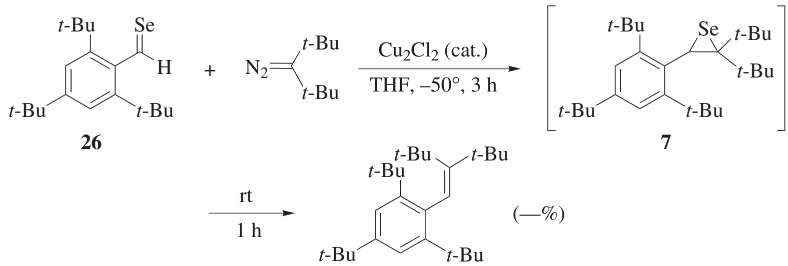
Alkenes from Selenadiazolines. 1,3,4-Selenadiazolines also undergo the twofold extrusion process.[59] For the preparation of these intermediates, the only successful route involves the cycloaddition of a selone to a diazo compound. In contrast to hydrogen sulfide, hydrogen selenide reduces azines rather than adding to them, precluding this approach to selenadiazolines. Reactions of selones with diazo compounds are typically more facile than the corresponding reactions of thiones[59,60] and the resulting 1,3,4-selenadiazolines such as **25** (Scheme 11) extrude nitrogen more readily than the corresponding thiadiazolines. Mild heating affords the corresponding seleniranes, which are thermally unstable and directly extrude elemental selenium, affording the alkene.



25 (73%) (67%)

Scheme 11

As mentioned in the Mechanism section, the extremely sterically hindered selenirane **7** is prepared in solution at low temperature by the reaction of 2,4,6-tri-*tert*-butylselenobenzaldehyde (**26**) with di-*tert*-butyldiazomethane. Upon warming the reaction mixture to room temperature selenium extrusion occurs, affording the corresponding alkene (Eq. 28).[19]

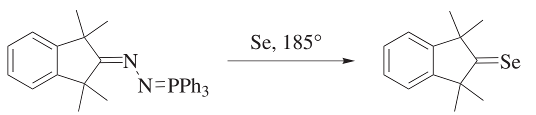


26 7 (—%)

(Eq. 28)

Preparation of Selones. A variety of methods are available for the preparation of selones.[61–63] A limited number of these methods have proved applicable to in situ trapping for twofold extrusion reactions. However, all reactions involving selones, even when they are generated in situ, are limited to those stabilized either by conjugation or by bulky substituents.

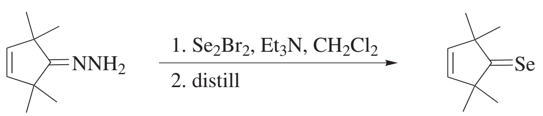
The reaction of triphenylphosphoranylidene hydrazones such as **27** (Eq. 29) with elemental selenium at elevated temperature is used for the preparation of a variety of isolable selones.[59,64] This reaction generally succeeds in those cases where the product selone is volatile or where the corresponding "dimeric" alkene forms slowly or not at all (compare to Eq. 36).



27 (85%)

(Eq. 29)

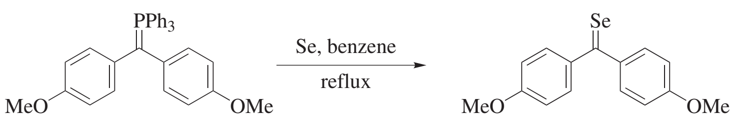
Reactions of hydrazones with diselenium dibromide in the presence of triethylamine, followed by pyrolysis, also afford volatile selones in useful yields (Eq. 30).[65]



(70%)

(Eq. 30)

Ylides such as **28** (Eq. 31) react with selenium at elevated temperatures. The especially stable bis-(4-methoxyphenyl)selone **29** is most conveniently prepared using this method.[66]



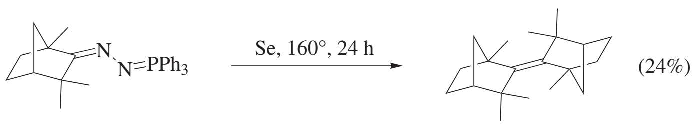
28 29 (58%)

(Eq. 31)

Reactions of triphenylphosphoranylidene hydrazones with thiones or selones at elevated temperatures also afford alkenes (Eq. 32).[50] In these reactions, the ylides act as stable, isolable sources of thermally unstable diazo compounds.

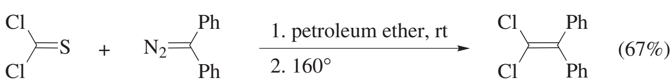
(Eq. 32)

Executing the reaction of a triphenylphosphoranylidene hydrazone with elemental selenium under conditions where the selone is not removed as it forms gives symmetrical alkenes as products. These reactions also proceed by thermal cleavage of the phosphoranylidene hydrazone to the corresponding diazo compound and triphenylphosphine. The in situ generated diazo compound reacts with elemental selenium to generate the corresponding selone (see Eq. 29),[67] which then reacts with the diazo compound via the selenadiazoline pathway (Eq. 33).[59] In general, long reaction times favor alkene formation rather than selone isolation.

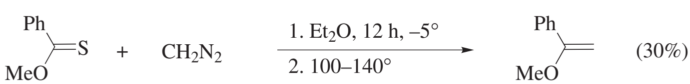


(Eq. 33)

Heteroatom-Substituted Alkenes from Thiocarbonyl Compounds. In addition to the sulfur and selenium analogues of ketones and aldehydes, other thio- and selenocarbonyl compounds undergo related twofold extrusion reactions, permitting the synthesis of a variety of heteroatom-substituted alkenes. These processes have most commonly been applied to thiocarbonyl compounds because they are more easily obtained than their selenium analogues. Examples of these transformations include: the use of thiophosgene to obtain 1,1-dichloroalkenes[68,69] (Eq. 34);[68] and reactions of *O*-thioesters[70−72] and *O*-selenoesters[73] to obtain enol ethers (Eq. 35).[71] Dithioesters react in the same manner to form thioenol ethers.[74,71]

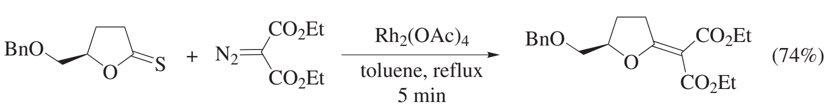


(Eq. 34)

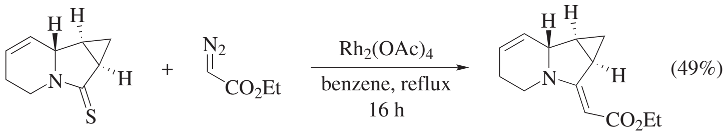


(Eq. 35)

Similar reactions of thionolactones[70,75] (Eq. 36),[75] thioamides,[76] and thiolactams[77,78] with conjugated diazo compounds are most conveniently carried out using metal catalysis. An example of an intermolecular thiolactam extrusion reaction is shown in Eq. 37.[77]

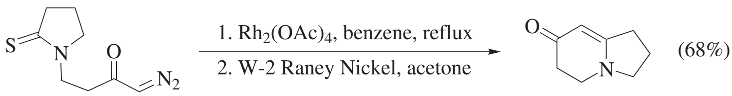


(Eq. 36)



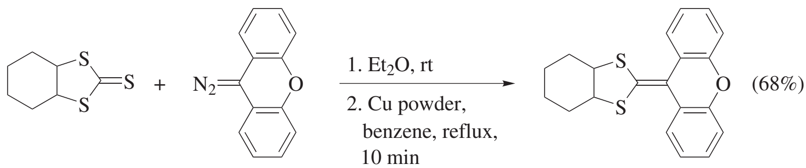
(Eq. 37)

The corresponding intramolecular reaction (Eq. 38)[78] is also known.

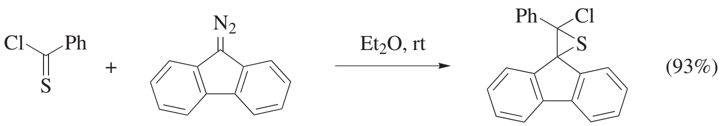


(Eq. 38)

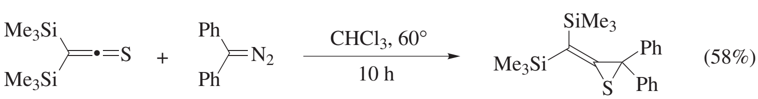
Trithiocarbonates react efficiently with diazo compounds to form ketene dithioacetals[79,80] (Eq. 39),[80] and monochloroalkenes or their 2-chlorothiirane precursors are obtained from thioacyl halides[68,69,79] (Eq. 40).[68] Stable, silyl-substituted thioketenes also participate in these reactions[81,82] (Eq. 41).[81]



(Eq. 39)

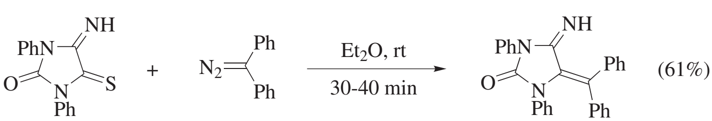


(Eq. 40)



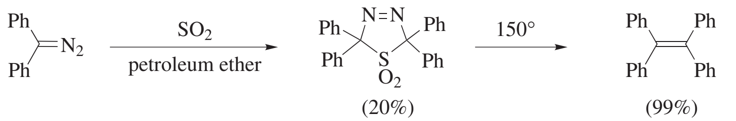
(Eq. 41)

Heterocycles containing a thiocarbonyl group undergo similar cycloaddition-twofold extrusion processes upon reaction with diazo compounds, further extending the scope of the reaction.[83−87] An example involving an imidazoline derivative is shown in Eq. 42.[83]



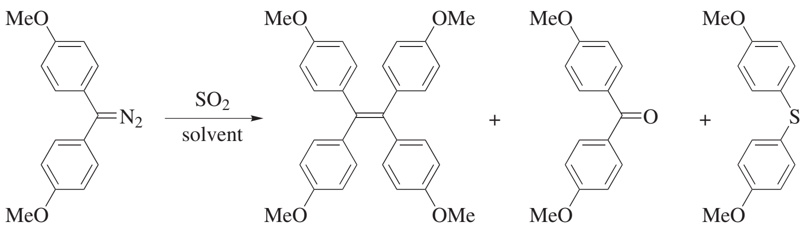
(Eq. 42)

Alkenes from Other Twofold Extrusions. The sulfur dioxide-promoted "dimerization" of diazo compounds, the Staudinger-Pfenniger reaction, is also formally a twofold extrusion process. Direct extrusion from a cycloadduct is seen for diazo systems with multiple, aromatic substituents (Scheme 12).[11]



Scheme 12

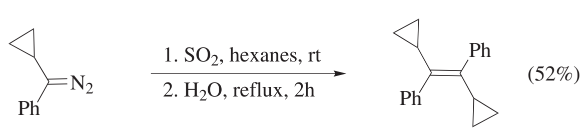
As discussed in the Mechanism section, thiadiazoline dioxide formation is not the major path toward alkene production, and isolated thiadiazoline dioxides with aliphatic substituents give mostly non-olefinic products on being heated at moderate temperatures. The solvent effect on the reaction of diazo compounds with SO_2 is very noticeable with the electron-rich 4,4′-dimethoxydiphenyldiazomethane; both ketone **31** and sulfide **32** are obtained in addition to the symmetrical alkene **30** (Eq. 43).[27] The formation of product **32** appears to involve initial *ipso* electrophilic attack of SO_2 on the aryl ring.



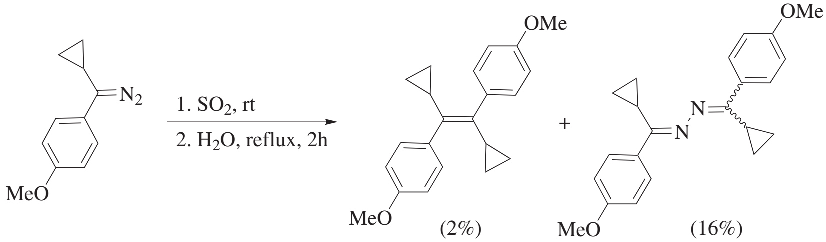
30 **31** **32** (Eq. 43)

	Yield (%)		
Solvent	**30**	**31**	**32**
THF	69	21	—
CCl_4	64	18	12
benzene	61	3	6
DMF	56	35	8
MeCN	11	67	—
MeOH	—	59	35

The course of the reaction is also affected by small variations in structure, although the reasons for this behavior are not clear. Although (*E*)-1,2-dicyclopropyl-1,2-diphenylethylene is prepared in 52% yield by reaction of cyclopropyl(phenyl)diazomethane with sulfur dioxide (Eq. 44), the corresponding reaction with cyclopropyl(4-methoxyphenyl)diazomethane under identical conditions leads primarily to the isolation of the corresponding azine, with the formation of only traces of the desired alkene (Eq. 45).[88]

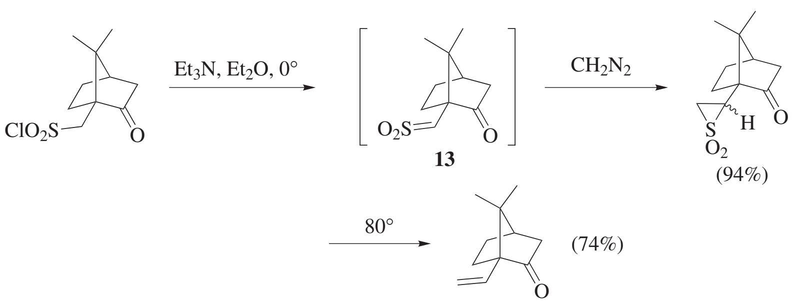


(Eq. 44)



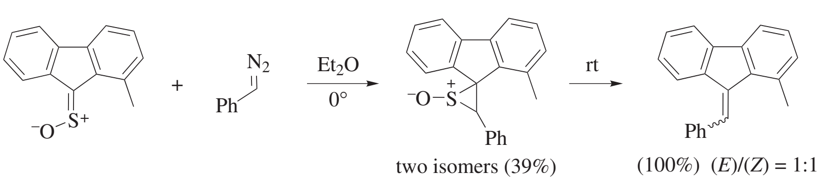
(Eq. 45)

A related and more generally applicable twofold extrusion reaction involves the in situ generation of sulfenes such as **13** (Scheme 13)[28] via the base-promoted dehydrochlorination of sulfonyl chlorides that bear an α-proton. When this reaction is carried out in the presence of diazo compounds, the thiirane 1,1-dioxide is obtained. Warming the thiirane dioxide leads to sulfur dioxide extrusion, providing a convenient route to a variety of moderately hindered alkenes. This method complements most other direct C=C bond forming routes to alkenes, in that it replaces a carbonyl or thiocarbonyl component with a sulfonyl chloride. This method also succeeds with low-molecular-weight, unhindered diazoalkanes that can be problematic (discussed later) in their reactions with thiones.



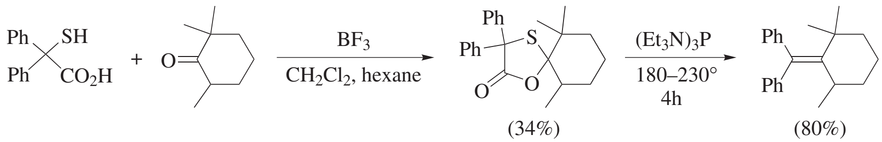
Scheme 13

In the related reactions of diazo compounds with sulfines, thiirane oxides can be isolated from reactions carried out below room temperature, and can be converted into alkenes by warming (Scheme 14).[21] This reaction, with one exception,[25] is restricted to aromatic sulfines and offers no advantages over the thione or sulfonyl chloride routes.



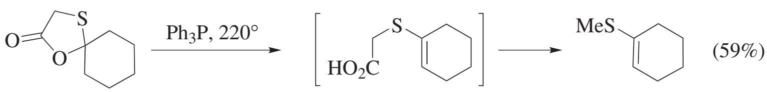
Scheme 14

A limited number of twofold extrusion reactions utilizing combinations of other extrudable groups not including dinitrogen also afford alkenes, but the availability of the required precursors and, in some cases, the reaction conditions needed for clean extrusions can limit the synthetic utility of these approaches. Reactions that involve carbon dioxide and sulfur as extrudable groups form alkenes from 1,3-oxathiolan-4-ones and can provide products with significant steric hindrance. This process has been used primarily for the preparation of 1,1-diphenyl-substituted alkenes from thiobenzilic acid (Scheme 15).[38]



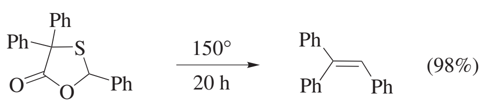
Scheme 15

Substituent patterns significantly affect the course of the extrusion; heating the 2,2-unsubstituted spiro-oxathialanone with triphenylphosphine gives 1-(methylthio)cyclohexene rather than methylenecyclohexane (Eq. 46).[38]



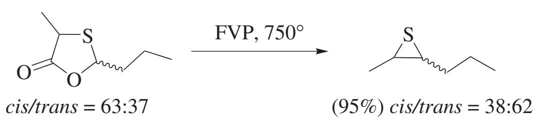
(Eq. 46)

Oxathiolanones with three aromatic substituents directly extrude both carbon dioxide and sulfur at elevated temperatures, affording the corresponding alkenes in very good yields (Eq. 47).[39]



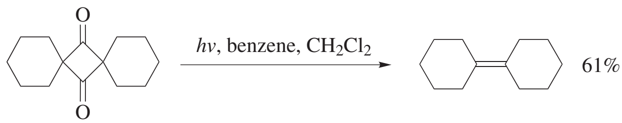
(Eq. 47)

As noted in the "Mechanism and Stereochemistry" section, the FVP of oxathiolanones affords the corresponding thiiranes in excellent yields, even when the starting heterocycle bears only aliphatic substituents (Eq. 48).[40,89]

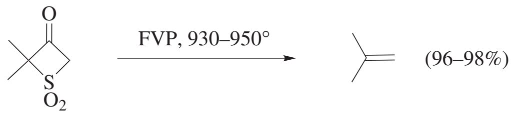


(Eq. 48)

Twofold extrusion routes to alkenes using other combinations of extrudable moieties are also known, although they are not extensively investigated in terms of their scope. Photochemically induced double extrusions of carbon monoxide take place from 1,3-cyclobutanediones (Eq. 49)[90,91] and FVP of thietan-3-one-1,1-dioxides leads to extrusion of both carbon monoxide and sulfur dioxide (Eq. 50).[92]



(Eq. 49)

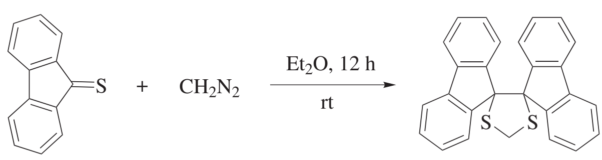


(Eq. 50)

Alkene Formation: Limitations

For the thia- and selenadiazoline routes, limitations imposed by the instability of unhindered or non-stabilized thiones and selones were discussed in the preceding section. Other limitations have also been identified largely for the formation of alkenes through thia- or selenadiazolines, and fall into two categories: (1) competing reaction pathways in the cycloaddition step; and (2) limitations imposed either on the cycloaddition or on the subsequent extrusion by exceptionally high levels of steric hindrance.

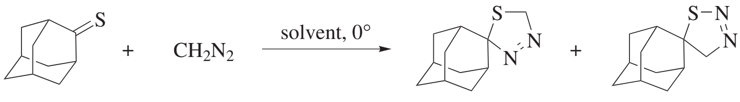
The cycloaddition route using unhindered, non-stabilized diazo compounds, notably diazomethane, is limited by the fact that the addition to a thione can take different courses depending upon the type of thione involved. Relatively unhindered thiocarbonyl compounds react with diazomethane to afford 1,3-dithiacyclopentane derivatives such as **34** in high yield (Eq. 51).[93] This transformation has been termed the "Schönberg Reaction".[94] Mechanistically, it involves the trapping of the intermediate thiocarbonyl ylide by the thione.[95]



34 (92%)

(Eq. 51)

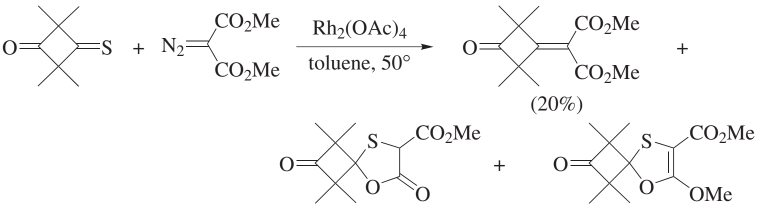
In additions of diazomethane to moderately hindered, aliphatic thiones, solvent-dependent regioisomeric selectivity is sometimes observed and can lead to 1,2,3-thiadiazolines such as **36** as the major products; in methanol isomer **35** predominates (Eq. 52).[96–98] A theoretical basis for these regiochemical preferences has been reported.[99] As expected, these side reactions become much less important with increasing steric hindrance. Furthermore, other routes easily make the 1,1-disubstituted alkenes that would result from desulfurizing the product of the normal addition mode.



35 36 (Eq. 52)

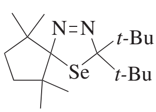
Solvent	35/36
pentane	91:9
Et_2O	80:20
MeOH	26:74

Another side-reaction is encountered when the initially formed, intermediate thiocarbonyl ylide undergoes intramolecular interception by an appropriately located carbonyl group. This process can occur in both the uncatalyzed[100] and rhodium-catalyzed reactions (Eq. 53).[101]



(20%) (10%) (45%) (Eq. 53)

As previously discussed in a mechanistic context (Scheme 3), a significant limitation to both the thia- and selenadiazoline-based twofold extrusion reactions is the tendency of these intermediates, in exceptionally hindered cases, to undergo retrocyclization-recombination processes affording, when possible, the less hindered symmetrical alkene as the major olefinic product. This side-reaction has been particularly noticeable in the attempted twofold extrusion preparations of tetra-*tert*-butylethylene and closely related molecules. Executing the extrusion step at high pressure does not change the course of the reaction.[18] Complete retrocyclizations are seen from the isolated selenadiazolines **37**–**42**, which contain either a di-*tert*-butyl moiety, as in **37**–**39**[18] and **40**,[102] or a tied-back equivalent in **41**[18] and **42**.[103] The cycloaddition step also fails with extremely hindered substrates. No experimental evidence is extant for the formation of tetra-*tert*-butylselenadiazoline (**43**).[104]



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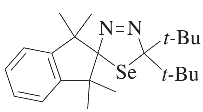

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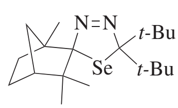

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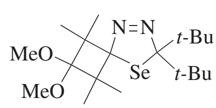

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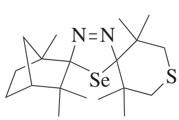

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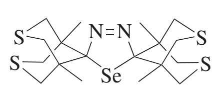

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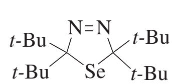
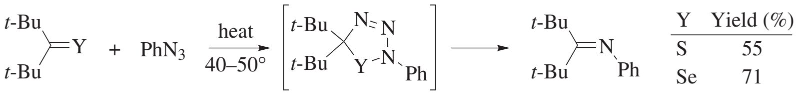


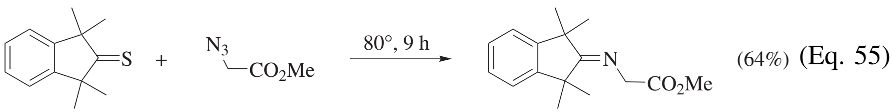
43

Imine Formation

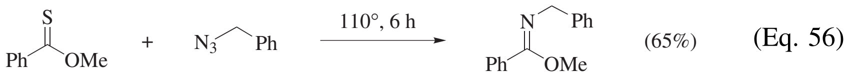
Twofold extrusion reactions of thiones or selones with aryl azides allow the preparation of extremely sterically hindered imines that cannot be prepared using standard methods. The reactions with selones are more facile and generally give higher yields (Eq. 54).[13] Azides bearing functional groups can be used in this transformation (e.g. Eq. 55).[41]



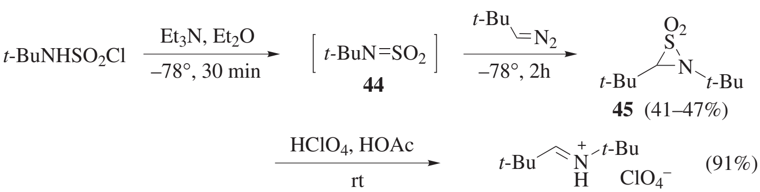
(Eq. 54)



O-Thioesters react with azides producing imidates (Eq. 56),[105] and dithioesters react similarly affording thioimidates.[105]



In a manner analogous to their reactions with sulfenes, diazo compounds react with in situ generated *N*-sulfines **44** to afford thiaziridine 1,1-dioxides **45**. Upon treatment with perchloric acid, these heterocycles are converted into iminium salts with expulsion of sulfur dioxide (Scheme 16).[106]

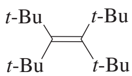


Scheme 16

APPLICATIONS TO SYNTHESIS

Twofold extrusion methods have been little used in natural product synthesis,[77,78] primarily due to the lack of naturally occurring, sterically hindered alkenes. These reactions have, however, proved to be extremely useful in the preparations of many molecules of theoretical interest that explore the effects of steric hindrance on alkene geometry and reactivity. Most approaches to the still elusive tetra-*tert*-butylethylene (**46**) involve a twofold extrusion reaction as the key step, and have involved "tied-back" intermediates such as **47** or **48**[60,107] where steric interactions are diminished by incorporation into ring structures. The steric limits for the "tied-back" reaction seem to be reached with **49**, bearing five- and six-membered rings, which is prepared via the corresponding selenadiazoline.[108]

Alkene **50** is similarly prepared.[109] As previously mentioned (see Scheme 3), the main limitation of the twofold extrusion reaction is the tendency of extremely sterically hindered thia- or selenadiazolines to retrocyclize, and attempts to prepare other "tied-back" intermediates such as compounds **51**–**53** for the potential synthesis of tetra-*tert*-butylethylene have been unsuccessful.[103,110,111] To date, the closest structure to **46** is its tetraformyl analogue **54**, prepared by oxidative cleavage of **48**. Neither **47** nor **54** could be converted into **46**, despite significant effort.[111,112]



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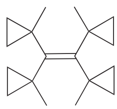

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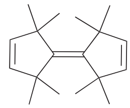

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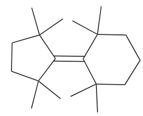

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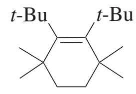
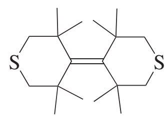
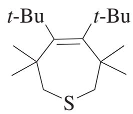


50



51



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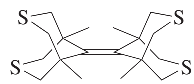

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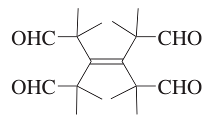
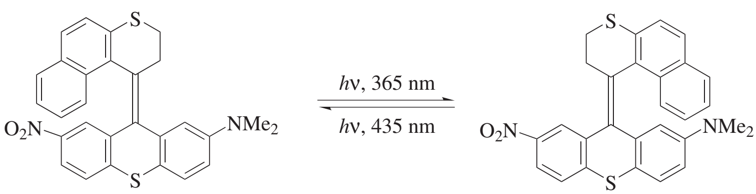


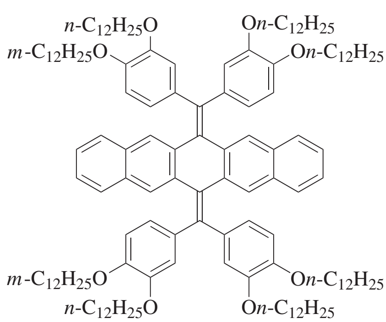
54

Another area of considerable interest in which twofold extrusion reactions have proven to be particularly effective is the preparation of molecular machines.[113] Such molecular switches and molecular motors often operate by the photochemical or thermal interconversion of the (Z)- and (E)-isomers of extremely hindered alkenes (Eq. 57).[114] See Eq. 20 for a related example.

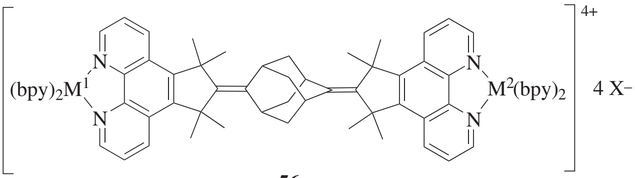


(Eq. 57)

Finally, twofold extrusion procedures afford sterically hindered alkenes that serve as key precursors for components of nanoscale devices,[115] including **55** for electronic devices[116] and **56** for photonic devices.[117]



55



56

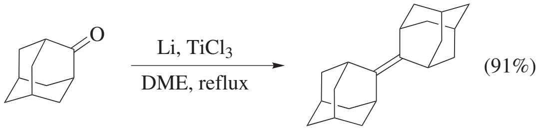
M^1, M^2 = Ru or Os, X = $CF_3SO_3^-$ or PF_6^-, bpy = 2,2'-bipyridyl

COMPARISON WITH OTHER METHODS

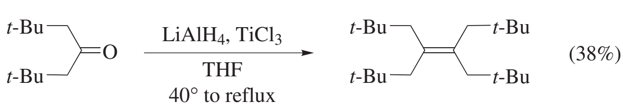
Synthesis of Alkenes

As shown in the preceding section, twofold extrusion reactions are particularly useful for the preparation of extremely sterically hindered alkenes and their precursor thiiranes. Very few standard synthetic methods provide useful routes to these substances. The Wittig reaction[118–120] might initially appear to be a potential alternative, but this reaction is very sensitive to steric hindrance and yields are frequently poor even for the preparation of moderately hindered, trisubstituted alkenes. The Horner-Wadsworth-Emmons reaction proves to be more useful for some preparations,[119,121] although that process is restricted to anions derived from phosphonates bearing additional, anion-stabilizing groups. Neither method is particularly useful for the preparation of tetrasubstituted alkenes. The Peterson olefination, the reaction of aldehydes or ketones with an α-silyl carbanion followed by acid- or base-promoted elimination of a silanol to afford the alkene, has also had very limited success in the preparation of sterically hindered systems.[122] Similar limitations imposed by bulky substituents are seen for titanium-based olefinations such as the Tebbe reaction.[123,124]

The titanium-mediated coupling of aldehydes or ketones (the McMurry coupling)[125] affords a good route to moderately hindered alkenes, provided that no other reducible functional groups are present. Examples of tetrasubstituted alkenes that are made in this way are biadamantylidene (Eq. 58)[126,127] and tetrakis(neopentyl)ethylene (Eq. 59).[128] With very hindered substrates, however, reduction of the carbonyl components predominates, leading to the corresponding alcohols.[129,130]

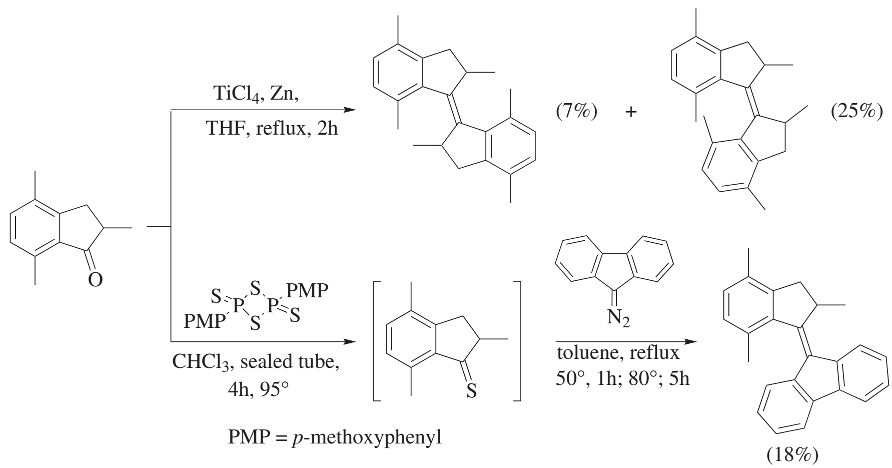


(Eq. 58)



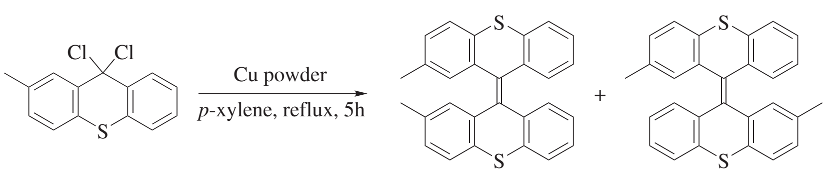
(Eq. 59)

This coupling reaction, with some notable exceptions,[127,131] is most frequently used for the preparation of symmetrical molecules. The utility of the McMurry coupling for the preparation of symmetrical, sterically hindered alkenes compared to the twofold extrusion method for the preparation of related, unsymmetrical alkenes is shown in the preparation of "molecular machines" (Scheme 17).[132] The modest yield in the twofold route probably reflects the poor stability of the intermediate thione.



Scheme 17

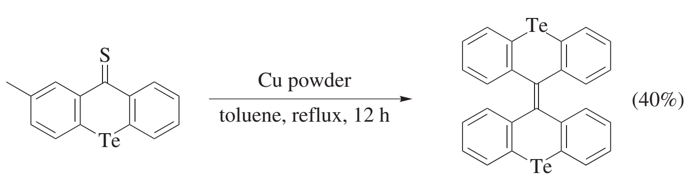
Two other methods are useful alternatives to twofold extrusion reactions for the preparation of some symmetrical, tetrasubstituted alkenes: direct, metal-promoted couplings of geminal dihalides as exemplified in the generation of products **57** and **58** (Eq. 60);[133] and similar couplings of thiones (Eq. 61).[134]



57 **58**

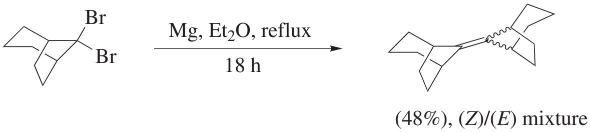
57 + **58** (68%), **57**/**58** = 3:2

(Eq. 60)



(Eq. 61)

The dihalide coupling method is useful for the synthesis of a number of moderately sterically hindered "tied-back" aliphatic alkenes, as exemplified in Eq. 62,[135] but this process fails with more hindered reactants.[104,111]

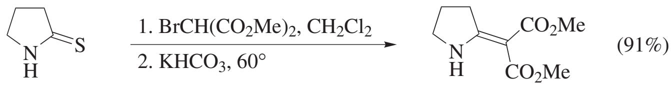


(Eq. 62)

As discussed in the Scope and Limitations section, less hindered alkenes are also accessible by extrusion methods, and those involving diazo esters and related substrates produce functionalized products. Whereas the rhodium-catalyzed process is effective for thiocarbonyl compounds that correspond to systems that bear highly deactivated carbonyl groups, including cyclic, aromatic systems, lactones and lactams, the Wittig, Horner, and Knoevenagel reactions[136] do not provide effective options for most of these substrates, except for some intramolecular Wittig reactions.[137] For example, the conversion of thioxanthone into an unsaturated ester via a copper-catalyzed, twofold extrusion reaction is efficient (see Eq. 22), but the corresponding reaction of xanthone with triethyl phosphonoacetate plus base affords the same product in only 3% yield.[138] Attempted condensation reactions of malonic acid or its esters with this ketone fail completely.[139] The two reactions are complementary, in that the phosphonate-based methods work well with ketones that are non-hindered and/or have only moderate levels of resonance stabilization, factors that would reduce the stability and utility of the corresponding thione or selone, whereas the latter reactants facilitate the synthesis of hindered and/or resonance-stabilized alkenes.

A similar situation occurs for other types of carbonyl compounds. As previously shown (Eq. 36), thionolactones readily react with diazo compounds in the presence of rhodium(II) acetate affording the corresponding unsaturated esters.[75] In contrast, these products are obtained in only poor yields by the condensation of the corresponding lactone acetals with active methylene compounds.[140–142] The titanium-based systems discussed earlier will convert esters and amides into enol ethers and enamines, respectively, but are limited to methylenation or simple alkylidenation processes.[123,124]

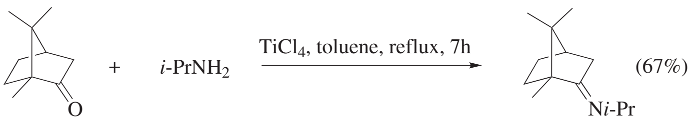
Eschenmoser coupling reactions, which also involve the conversion of a thioamide into a thiirane followed by the extrusion of sulfur, are generally applied to thiolactams. The highly nucleophilic sulfur facilitates the first (S_N2) step and the second step requires the presence of a carbanion-stabilizing group in the initially employed electrophile. An example is shown in Eq. 63.[143] The previously described Rh-catalyzed reactions of thiolactams with diazo compounds (Eq. 37) produce equivalent results, although the Eschenmoser coupling reaction has, to date, found more applications in the syntheses of complex molecules.[8]



(Eq. 63)

Synthesis of Imines

Numerous methods for preparing imines are available, generally involving loss of the elements of water in the reaction of an aldehyde or ketone with a primary amine. Non-hindered imines form readily from these components, usually with acid catalysts.[144] For the preparation of moderately sterically hindered imines, stoichiometric amounts of dehydrating agents such as tetrakis(ethoxy)silane[145] or titanium(IV) chloride (Eq. 64)[146] are usually necessary.



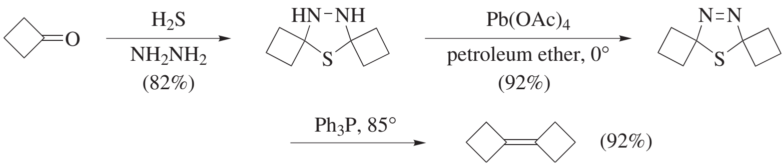
(Eq. 64)

In contrast to the twofold extrusion method, these procedures have not been utilized for the preparation of compounds where the imine carbon is flanked by two tertiary carbons.

EXPERIMENTAL CONDITIONS

Twofold extrusion reactions are generally undertaken in anhydrous, non-polar solvents or, less frequently, under neat conditions at moderately elevated temperatures. The reactions are routinely carried out under an atmosphere of dry argon or nitrogen. For the majority of reactions in which sulfur is extruded, a tertiary phosphine or copper bronze is added after the initial extrusion and the mixture is again heated to effect the second extrusion. For reactions in which the thiocarbonyl compound is deactivated through conjugation, the presence of a copper or rhodium salt may be required from the outset, especially when a similarly stabilized diazo compound is involved. A limited number of extrusion reactions are carried out using flash vacuum pyrolysis (FVP) conditions at highly elevated temperatures. *Many of the twofold extrusion transformations described in the literature involve the use of toxic and foul-smelling reagents (e.g. hydrogen sulfide, volatile thiones and selones, and sulfur dioxide). These reactions should be carried out in an efficient fume-hood. Similarly, manipulations of diazo compounds, which are potentially explosive, should be carried out in an efficient fume-hood behind adequate shielding.*

EXPERIMENTAL PROCEDURES

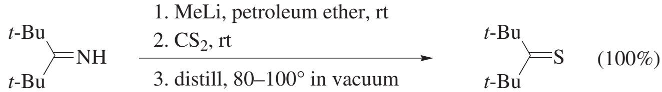


Cyclobutylidenecyclobutane [Formation of a Thiadiazolidine, Oxidation to the Thiadiazoline, and Conversion into the Alkene].[147] Hydrogen sulfide was bubbled through vigorously stirred cyclobutanone (21 g, 0.30 mol) for 20 min, and then aqueous hydrazine (20 mL, 7.5 M solution, 0.15 mol) was added dropwise over 20 min with continued passage of H_2S. After completion of the addition of hydrazine, H_2S was passed for a further 20 min, a solid product having formed. The crude reaction mixture was treated with CH_2Cl_2 (200 mL), the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried ($MgSO_4$) and the solvent was removed under reduced pressure to give 5-thia-10,11-diazadispiro[3.1.3.2]undecane (21.0 g, 82%). A sample was recrystallized from petroleum ether (bp 40–60°) to afford white crystals: mp 96–97°; IR (KBr) 3200, 2910, 1425, 1245, 1170, 1140, 1075, 860, 850, 820 cm^{-1}; ^1H NMR (CCl_4) δ 3.53 (br s, 2H), 2.64–1.61 (m, 12 H); HRMS (m/z): M^+ calcd for $C_8H_{14}N_2S$, 170.0878; found, 170.0868.

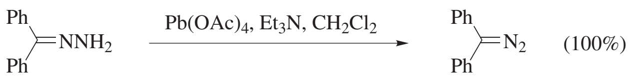
5-Thia-10,11-diazadispiro[3.1.3.2]undecane (21.0 g, 0.12 mol) was dissolved in dry petroleum ether (800 mL), and the solution was then added slowly over 40 min to a vigorously stirred suspension of powdered lead(IV) acetate (66 g, 0.15 mol) in anhydrous petroleum ether (100 mL) at 0°. After completion of the addition the reaction mixture was stirred for a further 40 min at 0°. The reaction mixture was filtered through a pad of filtering aid, and the solid was washed with petroleum ether (2×100 mL). The filtrates were combined and the solvent was removed under reduced pressure to give 5-thia-10,11-diazadispiro[3.1.3.2]undec-10-ene as colorless crystals (19.0 g, 92%). A sample was recrystallized from MeOH to afford colorless crystals: mp 72.5–73°; IR (KBr) 2950, 1565, 1425, 1250, 1090, 950, 880, 800 cm^{-1};^1H NMR (CCl_4) δ 2.96–2.24 (m, 10H), 2.14–1.85 (m, 2H); MS (m/z):168 (M^+). Anal. Calcd for $C_8H_{12}N_2S$: C, 57.11; H, 7.19; N, 16.65. Found: C, 56.67; H 7.21; N, 17.06.

A mixture of powdered 5-thia-10,11-diazadispiro-[3.1.3.2]undec-10-ene (4.2 g, 0.025 mol) and dry triphenylphosphine (12.5 g, 0.075 mol) was heated at 85° for 1 h under reduced pressure (100 mm). The volatile liquid product was condensed from the evolved gases and purified by distillation over $MgSO_4$ at 85° (100 mm) to give cyclobutylidenecyclobutane (2.5 g, 92%): IR (KBr) 2930, 1425, 1035, 915 cm^{-1}; ^1H NMR (CCl_4) δ 2.66–2.36 (m, 8H), 2.12–1.72 (m, 4H); MS

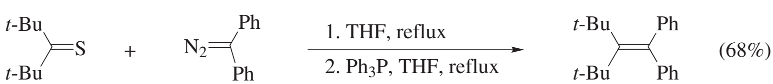
(m/z):108 (M^+). Anal. Calcd for C_8H_{12}: C, 88.83; H, 11.18. Found: C, 88.86; H, 11.07.



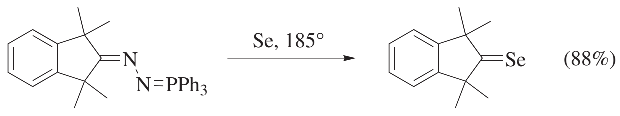
2,2,4,4-Tetramethyl-3-pentanethione (Di-*tert*-butylthione) [Preparation of a Thione from an Imine].[50] 3-Imino-2,2,4,4-tetramethylpentane[50] (5.64 g, 42.1 mmol) in anhydrous petroleum ether (100 mL) under dry nitrogen was treated at rt with methyllithium (1.4 M in Et_2O, 30.1 mL, 42.1 mmol). After methane evolution had ceased, dry carbon disulfide (3.2 mL) was added and the mixture was stirred for 3 h. The solvent was removed under reduced pressure at rt and the solid, brown residue was heated at 80–100° under reduced pressure while the crude thione distilled into a dry-ice/acetone trap. Redistillation afforded pure, deep violet 2,2,4,4-tetramethyl-3-pentanethione in near-quantitative yield: bp 61° (14 mm); IR (CCl_4) 1400, 1365, 1120 cm^{-1}; ^1H NMR (CCl_4) δ 1.50.



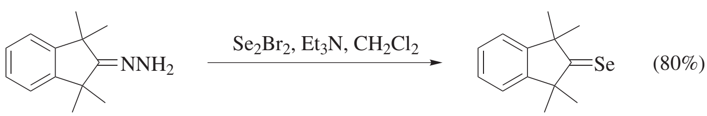
Diphenyldiazomethane [Preparation of an Aryl-Substituted Diazo Compound by Oxidation of a Hydrazone].[50] A solution of lead (IV) acetate (889 mg, 2.00 mmol) in CH_2Cl_2 (5 mL) was added dropwise over 45 min to a stirred solution of benzophenone hydrazone (295 mg, 1.50 mmol) in CH_2Cl_2 (5 mL) and triethylamine (5 mL) at −20°, resulting in the immediate appearance of a crimson color. The solution was allowed to warm to rt, the solid was removed by filtration through Celite, washing with CH_2Cl_2, and the filtrate was washed with water and dried over Na_2SO_4. Concentration and drying under reduced pressure at rt afforded diphenyldiazomethane as a crimson solid (292 mg, 100%): IR (neat) 2037 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.19 (m). These data are identical to those of material prepared by mercuric oxide oxidation of the hydrazone.[148]



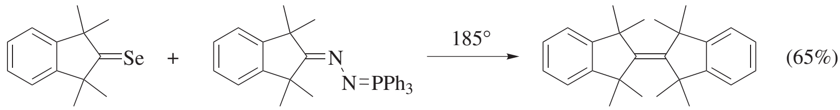
1,1-Diphenyl-2-(1,1-dimethylethyl)-3,3-dimethyl-1-butene [Preparation of an Alkene via an In Situ Generated Thiadiazoline].[50] Diphenyldiazomethane (582 mg, 3.00 mmol) and 2,2,4,4-tetramethyl-3-pentanethione (456 mg, 3.00 mmol) in anhydrous THF (5 mL) were heated at reflux under nitrogen for 3 h. Triphenylphosphine (787 mg, 3.00 mmol) was added, and the mixture was heated at reflux overnight. After cooling to rt, the mixture was carefully treated with excess iodomethane (0.5 mL) (*caution: exothermic*) and after 30 min the mixture was filtered through a short column of silica gel, washing with petroleum ether (10 mL). The solvent was removed under reduced pressure, affording a colorless solid. Recrystallization from EtOH/H_2O afforded 1,1-diphenyl-2-(1,1-dimethylethyl)-3,3-dimethyl-1-butene as colorless crystals (596 mg, 68%): mp 140–141°; IR (CCl_4) 1600, 1490, 1440, 1400 cm^{-1}; ^1H NMR (CCl_4) δ 7.05 (m, 10H), 1.15 (s, 18H). Anal. Calcd for $C_{22}H_{28}$: C, 90.4; H, 9.6. Found: C, 90.3; H 9.7.



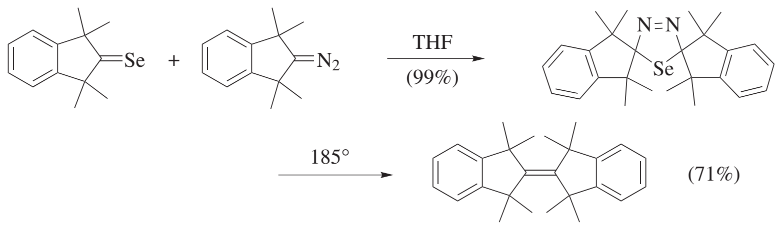
1,3-Dihydro-1,1,3,3-tetramethyl-2*H*-indene-2-selone [Preparation of a Selone by the Reaction of a Phosphoranylidenehydrazone with Selenium].[18] A mixture of 1,1,3,3-tetramethylindan-2-one triphenylphosphoranylidenehydrazone[64] (20.0 g, 46.0 mmol) and selenium powder (12 g; 0.15 mol) was heated to 185° at 1 mm while volatiles were distilled into a dry-ice acetone trap. After thawing the contents of the trap, the resulting blue liquid was purified by bulb to bulb distillation at 70° (0.5–5 mm) to afford deep blue crystals of 1,3-dihydro-1,1,3,3-tetramethyl-2*H*-indene-2-selone (9.5 g, 88%): mp 40–43°; IR (neat) 1590, 1485, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32 (s, 4H), 1.51 (s, 12H). These data are identical to a previously reported analysis.[149]



1,3-Dihydro-1,1,3,3-tetramethyl-2*H*-indene-2-selone [Preparation of a Selone from a Hydrazone and Selenium(I) Bromide].[65] 1,1,3,3-Tetramethylindan-2-one hydrazone[64](1.01 g, 5.00 mmol) in CH_2Cl_2 (15 mL) and selenium(I) bromide (1.59 g, 5.03 mmol) in CH_2Cl_2 (15 mL) were simultaneously added dropwise over 15 min to an ice-cooled solution of freshly distilled triethylamine (1.53 mL, 11.0 mmol) in CH_2Cl_2 (20 mL). The mixture was warmed to rt and stirred for 30 min. The resulting suspension was filtered under vacuum, washed with water, filtered through a layer of potassium carbonate (4.0 g) and dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was pyrolyzed under vacuum (0.5–5 mm) with a heat gun, condensing the product, which distilled at 50–70° (0.5–5 mm) into a dry-ice/acetone trap. Upon thawing to rt, 1,3-dihydro-1,1,3,3-tetramethyl-2*H*-indene-2-selone (1.01 g, 80%) was obtained as a deep blue, low-melting solid, spectroscopically identical to the sample prepared from the phosphoranylidenehydrazone.

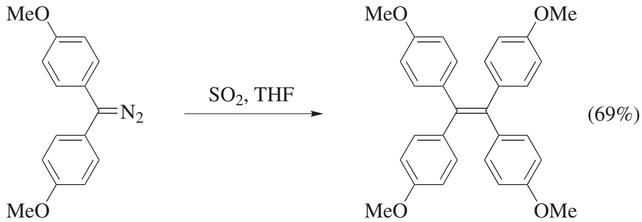


2-(1,3-Dihydro-1,1,3,3-tetramethyl-2*H*-inden-2-ylidene)-2,3-dihydro-1,1,3,3-tetramethyl)-1*H*-indene [Formation of an Alkene by In Situ Generation and Thermolysis of a Selenadiazoline].[18] 1,3-Dihydro-1,1,3,3-tetramethyl-2*H*-indene-2-selone[18] (4.50 g) and 1,3-dihydro-1,1,3,3-tetramethyl-2*H*-indene-2-selone triphenylphosphoranylidenehydrazone[18] (8.25 g) were heated with stirring to 185° under argon. After 5 d, CH_2Cl_2 (10 mL) was added to the cooled reaction mixture. Filtration afforded colorless crystals, which upon recrystallization from $CHCl_3$/MeOH gave the pure title product (4.0 g. 65%): mp 255°; IR (KBr) 1600, 1490, 1450, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.15 (bs, 8H), 1.77 (s, 24H); MS (m/z): 344 (M^+). Anal. Calcd for $C_{26}H_{32}$: C, 90.64; H, 9.36. Found: C, 90.60; H, 9.45.

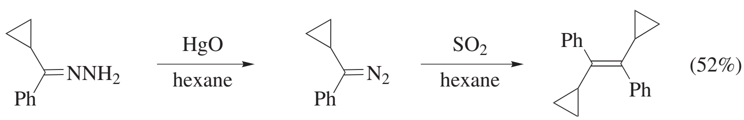


2-(1,3-Dihydro-1,1,3,3-tetramethyl-2*H*-inden-2-ylidene)-2,3-dihydro-1,1,3,3-tetramethyl)-1*H*-indene [Formation of an Alkene by Thermolysis of an Isolated Selenadiazoline].[18] To a stirred solution of 1,3-dihydro-1,1,3,3-tetramethyl-2*H*-indene-2-selone (146 mg, 0.62 mmol) in THF (2 mL) was added dropwise a solution of 2-diazo-1,1,3,3-tetramethylindane (116 mg, 0.62 mmol) in THF (2 mL). Solvent removal afforded the crude selenadiazoline as a colorless solid (261 mg, 99%). Recrystallization from THF afforded light-yellow crystals: mp 170°; IR (KBr) 1590, 1580, 1485, 1450, 1380, 1365, 1310 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.15 (s, 8H), 1.48 (s, 12H), 1.16 (s, 12H); ^{13}C NMR ($CDCl_3$) δ 148.4, 131.3, 127.4, 122.6, 52.8, 34.3, 14.4. Anal. Calcd for $C_{26}H_{32}N_2Se$: C, 69.16; H, 7.14; N, 6.20. Found: C, 69.70; H, 7.15; N, 6.20.

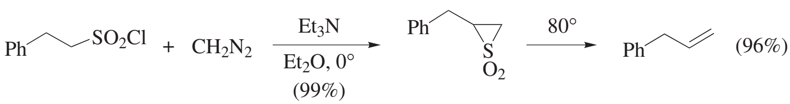
The crude selenadiazoline (261 mg) was heated at 185° for 24 h under a nitrogen atmosphere, cooled, and the residue was dissolved in hot $CHCl_3$ and filtered. The filtrate was evaporated under vacuum and the residue was recrystallized from $CHCl_3$/MeOH to afford the pure title compound (147 mg, 71%), mp 255°, analytically identical to the material obtained using the in situ generated selenadiazoline procedure.



Tetrakis(4-Methoxyphenyl)ethylene [Formation of an Alkene from a Diazo Compound Using the Staudinger-Pfenninger Reaction].[27] Sulfur dioxide was bubbled through a solution of bis(4-methoxyphenyl)diazomethane (1.27 g, 5.0 mmol) in THF (100 mL). The solution decolorized with concurrent evolution of nitrogen. Removal of solvent under reduced pressure followed by column chromatography on silica gel afforded tetrakis(4-methoxyphenyl)ethylene (0.78 g, 69%). Recrystallization from benzene/Et_2O gave a solid: mp 187–188° (lit. 184–185°);[150] ^1H NMR ($CDCl_3$) δ 6.98 (d, $J = 8$ Hz, 2H), 6.67 (d, $J = 8$ Hz, 2H), 3.73 (s, 12H). 4,4′-Dimethoxybenzophenone (0.25 g, 21%) was isolated from later chromatographic fractions.

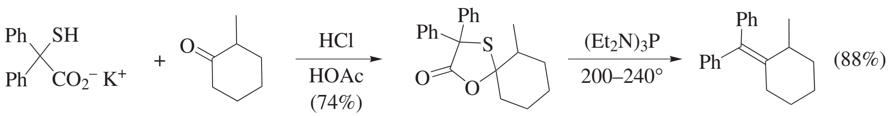


(*E*)-1,2-Dicyclopropyl-1,2-diphenylethylene [Formation of an Alkene from a Hydrazone Using the Staudinger-Pfenninger Reaction].[88] Cyclopropyl phenyl ketone hydrazone (16.0 g, 0.11 mol) and freshly prepared yellow mercuric oxide (43.2 g, 0.2 mol) in *n*-hexane (500 mL) were shaken for 20 h. The mixture was filtered to give a cherry-red solution through which anhydrous sulfur dioxide was passed until the color was discharged. Upon removal of the hexane in vacuum, a solid was obtained which was boiled with water for 2 h, cooled, and extracted with Et_2O. The extract was dried over K_2CO_3 and concentrated, affording fine needles of the crude alkene. These were recrystallized from EtOH using decolorizing charcoal, affording pure (*E*)-1,2-dicyclopropyl-1,2-diphenylethylene in two crops (6.7 g, 52%): mp 140°. Anal. Calcd for $C_{20}H_{20}$: C, 92.26; H, 7.74. Found: C, 92.23; H, 7.94.



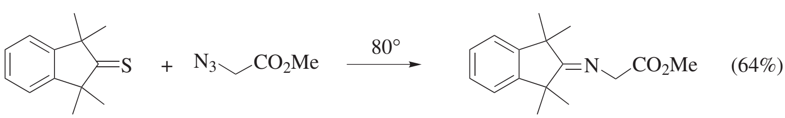
1-Phenyl-2-propene [Formation of a Thiirane Dioxide and Conversion into an Alkene Using an In Situ Generated Sulfene].[37] 2-Phenylethanesulfonyl chloride (10.3 g, 50 mmol) in Et_2O (60 mL) was added dropwise to a cooled (0°) solution of diazomethane (80 mmol) and triethylamine (6.2 g, 60 mmol) in Et_2O (150 mL) over 2 h. The mixture was filtered and the triethylamine hydrochloride was washed with ether. The combined filtrate and washings were concentrated under vacuum at rt, affording the crude thiirane dioxide (9.0 g, 99%), mp 40−42°. Crystallization from methanol by cooling to −20° afforded colorless crystals of 2-(phenylmethyl)thiirane-1,1-dioxide: mp 49−51°; IR (KBr) 3050, 1300, 1155 cm^{-1}.

Crude 2-(phenylmethyl)thiirane-1,1-dioxide (3.0 g) was heated at 80° for 10 min during which time sulfur dioxide was liberated. The yellow residue was distilled, affording 1-phenyl-2-propene (1.9 g, 96% overall yield based on the starting sulfonyl chloride), bp 43−44° (10 mm).

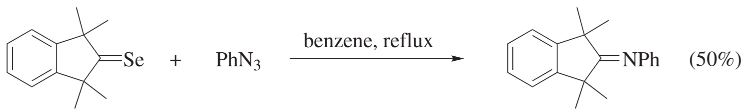


1-Diphenylmethylene-2-methylcyclohexane [Formation of an Alkene by the Preparation and Twofold Extrusion Reaction of an Oxathiolanone].[12] Hydrogen chloride gas was passed into a solution of potassium 2-mercapto-2,2-diphenylacetate (6.00 g, 21 mmol) and 2-methylcyclohexanone (2.47 g, 22 mmol) in glacial acetic acid (12 mL) for 5 h at 65−75°. Ice and water were added, and the mixture was extracted with ether. Drying with sodium sulfate and concentrating under vacuum afforded an oil that was triturated with light petroleum to afford crude 6-methyl-3,3-diphenyl-1,4-oxathiaspiro[5.4]decan-2-one as a mixture of isomers as solid conglomerates (5.25 g, 74%): mp 66.5−68.5°; IR ($CHCl_3$) 1750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.5 (m, 10H), 1.7 (m, 9H), 1.1 (m, 3H). Anal. Calcd for $C_{21}H_{22}O_2S$: C, 74.50: H, 6.55; S, 9.4. Found: 74.4; H, 6.5; S, 9.4.

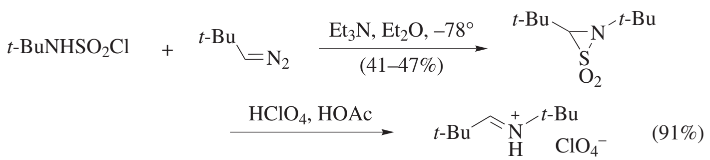
The crude 6-methyl-3,3-diphenyl-1,4-oxathiaspiro[5.4]decan-2-one (0.60 g, 0.89 mmol) and hexaethylphosphorous triamide (0.48 g, 1.85 mmol) were heated at 210−230° under nitrogen for 4 h. Chromatography over silica gel (light petroleum/benzene 1:1) afforded 1-diphenylmethylene-2-methylcyclohexane as an oil (230 mg, 88%). Crystallization from light petroleum afforded colorless rods: mp 73.5−74°; IR (hexachlorobutadiene) 1600, 1490, 1445 cm^{-1}; ^{1}H NMR (CCl_4) δ 7.1 (s, 10H), 1.4 − 3.0, m, 9 H 1.2, s, 3H. Anal. Calcd for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.4; H, 8.3.



Methyl *N*-(1,1,3,3-Tetramethylindan-2-ylidene)aminoacetate [Formation of an Imine by the Reaction of a Thione with an Azide].[41] A solution of 1,3-dihydro-1,1,3,3-tetramethyl-2*H*-indene-2-thione[151] (612 mg 3.0 mmol) in freshly distilled methyl azidoacetate (2 mL) was stirred at 80° until nitrogen evolution ceased, about 9 h. Excess azide was removed under vacuum and the crude product was purified by distillation at 120–125° (0.1 mm), affording methyl *N*-(1,1,3,3-tetramethylindan-2-ylidene)aminoacetate (498 mg, 64%): IR (neat) 1760, 1690, 1490, 1460, 1440, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.22 (bs, 4H), 4.62 (s, 2H), 3.75 (s, 3H), 1.48 (s, 6H), 1.38 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 190.2, 171.0, 148.2, 147.5, 127.5, 122.8, 122.5, 122.3, 52.8, 52.0, 48.8; 47.1, 29.6, 27.7, MS (*m/z*): 290 (M^+). Anal. Calcd for $C_{16}H_{21}NO_2$: C, 70.10; H, 8.16; N, 5.40. Found: C, 74.88; H, 8.15; N, 5.44.



***N*-(1,1,3,3-Tetramethyl-2-indanylidene)aniline [Formation of an Imine by the Reaction of a Selone with an Azide].[152]** 1,3-Dihydro-1,1,3,3-tetramethyl-2*H*-inden-2-selone (553 mg, 2.2 mmol) and azidobenzene (393 mg, 3.3 mmol) were heated to reflux in benzene (5.0 mL) for 14 h under positive nitrogen pressure. The mixture was filtered through a pad of Celite to remove selenium and the filtrate was evaporated under reduced pressure. The residue was crystallized from hexanes to give *N*-(1,1,3,3-tetramethyl-2-indanylidene)aniline (290 mg, 50%) as colorless crystals, mp 120–122°: IR (neat) 1683, 1599 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.30–7.26 (m, 5H), 7.08 (t, 2H), 6.79 (d, 2H), 1.51 (s, 6H), 1.30 (s, 6H). Anal. Calcd for $C_{19}H_{21}N$: C, 86.64; H, 8.04; N, 5.32. Found: C, 86.46; H, 8.21; N, 5.39.



***N*-(1,1-Dimethylethyl)-2,2-dimethylpropaniminium Perchlorate [Preparation of an Iminium Salt by the Cycloaddition of an In Situ Generated *N*-Sulfonylamine to a Diazo Compound Followed by Extrusion of Sulfur Dioxide].[106]** *tert*-Butylsulfamoyl chloride[106] (1.72 g, 10.0 mmol) in Et_2O (20 mL) was added dropwise over 0.5 h at −78° to a stirred solution of *tert*-butyldiazomethane (0.98 g, 10 mmol) and triethylamine (1.11 g, 11 mmol) in Et_2O (70 mL). The mixture was stirred at −78° for 2 h and then filtered at −78° to remove triethylammonium chloride. The filtrate was evaporated under vacuum at −50 to −30° and the residue was taken up in pentane (50 mL), filtered at −20°, and cooled to −78° to give colorless needles of *trans*-2,3-bis(1,1-dimethylethyl)thiaziridine-1,1-dioxide (0.84–0.97 g, 41–47%): mp 40–43° (decomp). Anal. Calcd for $C_9H_{19}NO_2S$: S. 15.62. Found: S. 15.72, 15.65.

Titration of *trans*-2,3-bis(1,1-dimethylethyl)thiaziridin-1,1-dioxide with 0.1 M perchloric acid (1.0 equiv) in acetic acid afforded *N*-(1,1-dimethylethyl)-2,2-dimethylpropaniminium perchlorate in 91% yield as colorless plates: mp > 300°; IR (Nujol) 3210, 1690 cm^{-1}; ^{1}H NMR (CF_3CO_2H) δ 8.37 (d, J = 18 Hz, 1H), 1.62 (s, 9H), 1.40 (s, 9H). Anal. Calcd for $C_9H_{20}ClNO_2S$: Cl, 14.67; N, 5.80. Found: Cl 14.70, N 5.80.

TABULAR SURVEY

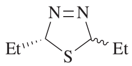
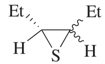
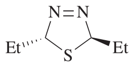
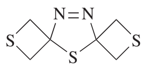
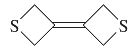
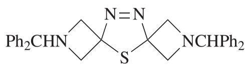
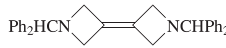
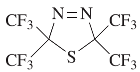
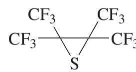
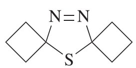
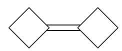
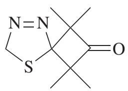
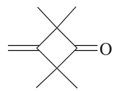
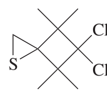
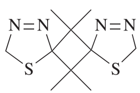
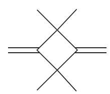
Tables 1 through 11 contain all examples found in the literature through the end of 2007. The 2008–2009 entries are in Supplemental Table 12. For thiadiazoline and selenadiazoline extrusions, the tables are divided into "isolated" and "in situ generated" intermediates. Entries within each table are arranged by increasing carbon count of the substrate. The counts do not include the carbon atoms in standard protecting groups for oxygen and nitrogen and do not include the methyl carbons on $-OMe$ and $-NMe_2$ groups. Where intermediates are generated in situ, the designated substrate is the thione or selone, and for Staudinger-type reactions it is the diazo compound or its precursor. The carbon count used for these entries is that of the in situ generated thione, selone, or diazo compound as dictated by the table contents.

Within a given carbon count, similar substrates are grouped together whenever possible. For completeness, thiiranes obtained by the extrusion of nitrogen from thiadiazolines are also included in Tables 1 and 2 in examples where the sulfur extrusion is not reported.

The following abbreviations (those not included in the *Journal of Organic Chemistry* list of standard abbreviations and acronyms) are used in the tables:

diglyme	bis(2-methoxyethyl) ether
DMI	1,3-dimethyl-2-imidazolidinone
eq	equivalents
FVP	flash vacuum pyrolysis
ia	inverse addition
o/n	overnight
PMP	4-methoxyphenyl
Ra-Ni	Raney nickel

TABLE 1. ALKENES AND THIIRANES VIA EXTRUSIONS FROM ISOLATED THIADIAZOLINES

	Thiadiazoline	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6		THF, reflux, 2 h	 **I** (73)[a], *cis/trans* = 4:1	45
		THF, >10°	**I** (36)[a,b], *cis/trans* = —	14
		Melt, 40–55°	**I**[a] (100), *cis/trans* = 93:7	15
		1. Petroleum ether/toluene, 80°, 5 h 2. Ph_3P, benzene/toluene, reflux, 6 h	 (82)	153
		1. Toluene, reflux, 12 h 2. Ph_3P, benzene, sealed tube, 140°, 18 h	 (66)	154
		Neat, reflux, 4 h	 (95)[a]	155
C_8		Ph_3P, melt, 85°, 1 h	 (92)	147, 156
C_9		1. Pentane, reflux, 1 h 2. Ph_3P, benzene, reflux, 38 h	 (67)	157
		THF, 45° [c]	 (58)[a]	158
C_{10}		$CHCl_3$, reflux, 4 h	 (64)	96, 159

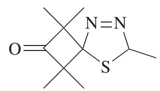
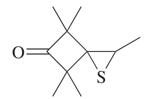
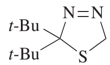
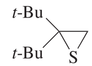
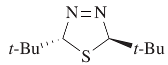
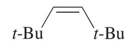
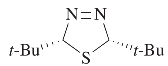
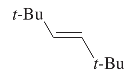
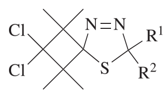
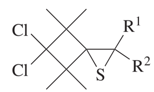
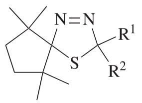
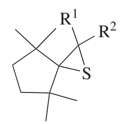
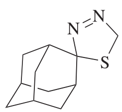
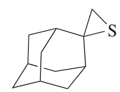
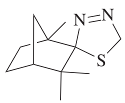
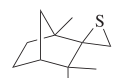
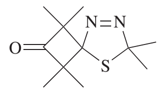
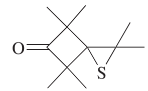
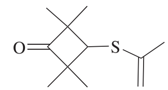
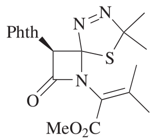
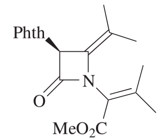
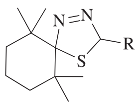
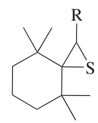
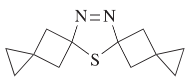
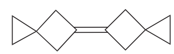
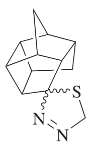
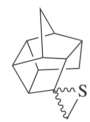
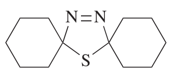
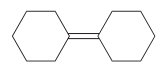
	Toluene, 50°, 4 h	 (81)[a]	160
	Neat, 50°	 (73)[a]	160
	1. Melt, 85–100° 2. PhLi, Et_2O	 (100)	15
	1. Melt, 85–100° 2. PhLi, Et_2O	 (—)	15
$C_{10–11}$			
	Solvent	 R^1 R^2 Solvent Temp (°)[c] H Me THF 45 (56)[a] Me Me xylene 70 (57)[a]	158
$C_{10–12}$			
	Solvent	 R^1 R^2 Solvent Temp (°) Time (h) H H benzene 40 15 (60) Me H benzene reflux 2 (100) Me Me octane 130 1 (85)	161 160 160
C_{11}			
	Xylene, 80°, 8 min	 (94)[a]	94, 162
	Toluene, 52°[c]	 **I** +  **II** **I** + **II** (63)[a], **I**:**II** = 6:4[a]	163

TABLE 1. ALKENES AND THIIRANES VIA EXTRUSIONS FROM ISOLATED THIADIAZOLINES (*Continued*)

Thiadiazoline	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
	Toluene, 51°, 10 h	 I (38) +  (38)	160
	MeCN, 70°	**I** (94)	160
	1. Benzene, 70°, 30 min 2. Ph_3P, benzene, reflux, 24 h	 (94)	164
C_{11-12}			
	Solvent	 R / Solvent / Temp (°) / Time (h) H / xylene / 100 / 2 / (99)[a] Me / octane / 130 / 1 / (89)[a]	160
C_{12}			
	Ph_3P, melt, 150°, 2 h	 (86)	165
	Benzene, 50°, 0.5 h	 (78)[a]	166
	Ph_3P, melt, 100°, 2 h	 I (75)	38, 12
	$(Et_2N)_3P$, neat, 100°, 2 h	**I** (77)	14

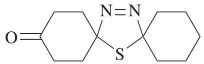
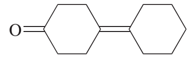
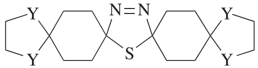
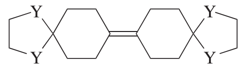
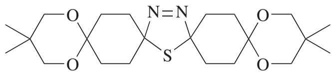
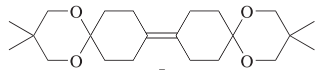
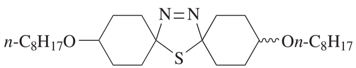
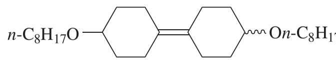
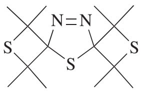
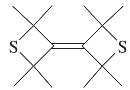
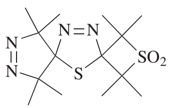
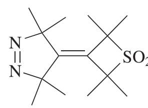
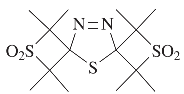
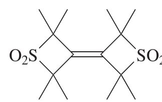
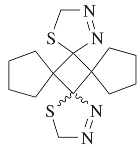
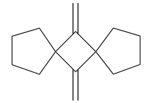
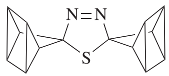
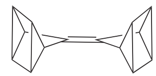
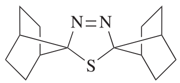
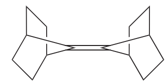
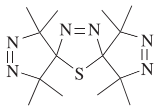
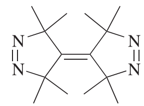
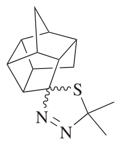
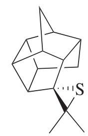
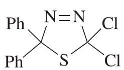
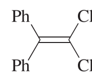
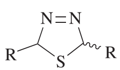
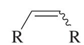
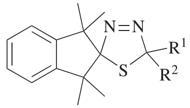
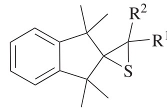
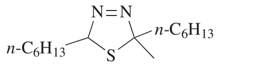
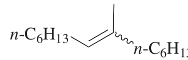
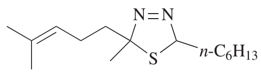
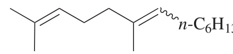
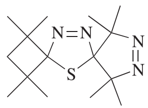
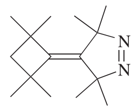
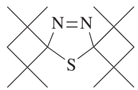
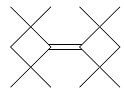
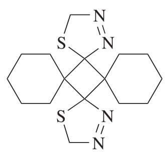
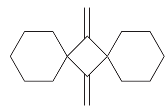
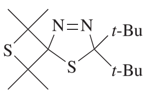
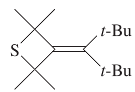
	Reactant	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}		1. Toluene, reflux, 3 h 2. $(EtO)_3P$, toluene, reflux, o/n	 (42)	115
		Ph_3P, melt	 Y / Temp (°) / Time (h) O / 120 / 2 / (100) O / 130 / 1 / (76) S / 140 / 1 / (55)	167 168 168
		$(EtO)_3P$, toluene, reflux, o/n	 **I** (92)	115
		Ph_3P, melt, 120–140°, 12 h	**I** (89)	169
		1. Toluene, reflux, 3 h 2. $(EtO)_3P$, reflux, o/n	 (83), *trans*/*cis* = 3:2	115
C_{14}		1. Melt, 160°, 40 min 2. $(MeO)_3P$, neat, 60°, 1 h	 **I** (100)	170
		$(Et_2N)_3P$, neat, 140°, 1 h	**I** (7)	108
		1. Melt, 150°, 1 h 2. $(MeO)_3P$, neat, 80°, 1 h	 (100)	170
		1. Melt, 160°, 40 min 2. $(MeO)_3P$, neat, 60°, 1 h	 (100)	170

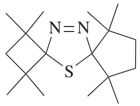
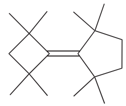
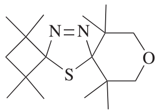
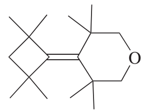
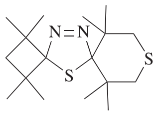
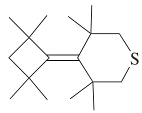
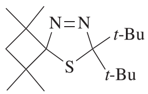
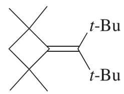
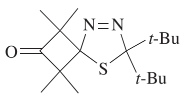
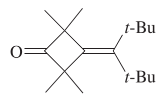
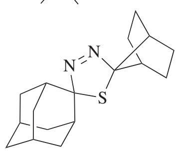
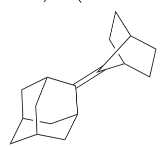
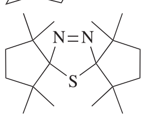
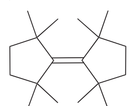
TABLE 1. ALKENES AND THIIRANES VIA EXTRUSIONS FROM ISOLATED THIADIAZOLINES (*Continued*)

	Thiadiazoline	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}		1. CCl_4–hexane, reflux[c] 2. $(n\text{-Bu})_3P$, neat, 100°, 36 h	 (73)	96, 159
		$(EtO)_3P$, neat, 80°	 (—)	171
		$(n\text{-Bu})_3P$, neat, 150°[c]	 (—)	172
		1. Melt, 120°, 1 h 2. $(MeO)_3P$, neat, 0.5 h	 (100)	173, 174
		Benzene, 50°, 0.5 h	 (20)[a]	166
		Melt, 160° "short heating"	 (100)	68
		1. THF, reflux, 2 h 2. Ph_3P, THF, reflux, o/n	 R | | (Z)/(E) $c\text{-}C_6H_{11}$ (44) 6:1 cyclohex-3-en-1-yl (42) 6:1 $n\text{-}C_6H_{13}$ (53) 4:1	45

C_{14-16}				
	Solvent			
C_{15}				
	$(Et_2N)_3P$, benzene, reflux		(13)	175
	$(Et_2N)_3P$, benzene, reflux		(10)	175
	1. Melt, 140°, 1 h 2. $(MeO)_3P$, neat, reflux, 0.5 h		(62)	108
C_{16}				
	1. Melt, 140°, 30 min 2. (n-Bu_3)P, neat, 140°, 0.5 h		(50)	108
	1. $CHCl_3$, reflux, 1 h 2. (n-Bu)$_3$P, neat, 100°, 18 h		(70)	96, 159
	1. Melt, 150°, 1 h 2. $(Et_2N)_3P$, neat, 140°, 2 h		(76)	108

R^1	R^2	Solvent	Temp (°)	Time (h)		
H	H	C_6D_6	50	17	(100)[a,d]	161
H	Me	$CDCl_3$	80	1	(94)[a,d]	160
Me	Me	toluene	120	5	(100)[a,d,e]	160

TABLE 1. ALKENES AND THIIRANES VIA EXTRUSIONS FROM ISOLATED THIADIAZOLINES (*Continued*)

	Thiadiazoline	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17}		1. Melt, 140°, 30 min 2. $(n\text{-Bu})_3P$, neat, 150°, 1 h	 (54)	108
		1. Melt, 175°, 30 min 2. $(n\text{-Bu})_3P$, neat, 140°, 3 h	 (31)	108
		1. Melt, 190°, 2 h 2. $(n\text{-Bu})_3P$, neat, 140°, 1 h	 (6)	108
		1. Melt, 150°, 2 h 2. $(n\text{-Bu})_3P$, neat, 140°, 0.5 h	 (56)	108
		Ph_3P, neat, 140°, 8 h	 (23)	176
		$(n\text{-Bu})_3P$, neat, 165° [c]	 (—)	172
C_{18}		1. Melt, 140°, 1 h 2. $(n\text{-Bu})_3P$, neat, 140°, 1.5 h	 **I** (63)	177
		$(n\text{-Bu})_3P$, neat, 150° [c]	**I** (45)	172

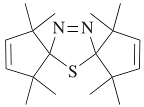
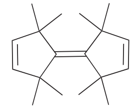
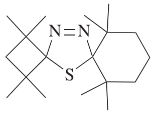
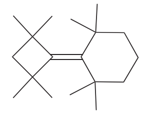
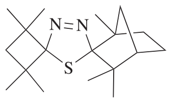
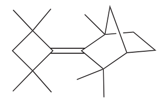
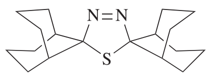
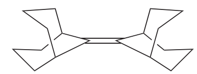
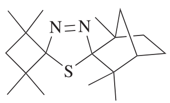
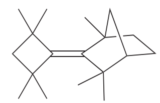
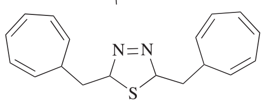
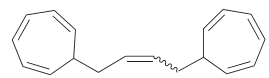
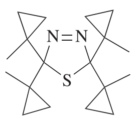
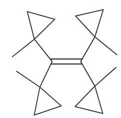
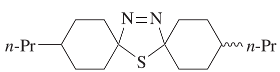
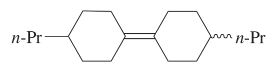
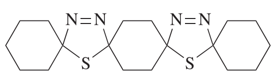
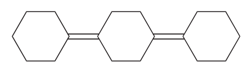
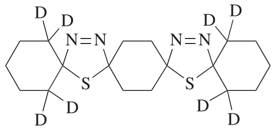
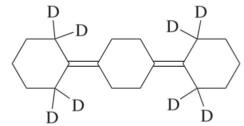
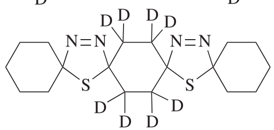
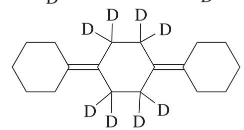
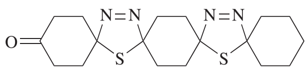
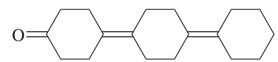
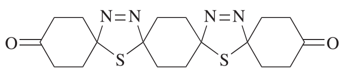
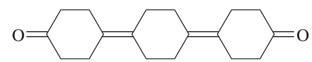
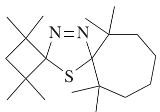
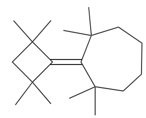
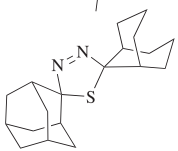
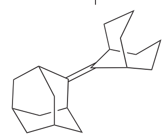
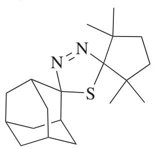
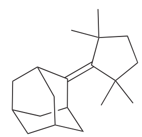
	1. 140°, 1 h 2. $(n\text{-Bu})_3P$, 140°, 1.5 h		(38)	60
	1. Melt, 150°, 2.5 h 2. $(n\text{-Bu})_3P$, neat, 150°, 1 h		(46)	108
	1. Melt, 140°, 1 h 2. $(n\text{-Bu})_3P$, neat, 140°, 1.5 h		(53)	108
	$(n\text{-Bu})_3P$, neat, 150° [b]		(—)	172
	1. Melt, 140°, 1 h 2. $(n\text{-Bu})_3P$, neat, 140°, 1.5 h		(53)	108
	$(MeO)_3P$, toluene, reflux, 1 h		(70), (*Z*)/(*E*) = 70:30	178
	1. "Heat" 2. $(n\text{-Bu})_3P$, "heat"		(73)	179
	Ph_3P, melt, 120–140°, 2–12 h		(47)	169
	1. Toluene, reflux, 2.5 h 2. $(EtO)_3P$, toluene, reflux, o/n		(41)	115

TABLE 1. ALKENES AND THIIRANES VIA EXTRUSIONS FROM ISOLATED THIADIAZOLINES (*Continued*)

	Thiadiazoline	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18}		1. Toluene, reflux, 2 h 2. $(EtO)_3P$, toluene, reflux, o/n	 (65)	115
		1. Toluene, reflux, 2 h 2. $(EtO)_3P$, toluene, reflux, o/n	 (15)	115
		1. Toluene, reflux, 3 h 2. $(EtO)_3P$, toluene, reflux, o/n	 (7)	115
		1. Toluene, reflux, 3 h 2. $(EtO)_3P$, toluene, reflux, o/n	 (73)	180
C_{19}		1. Melt, 140°, 45 min 2. $(n\text{-Bu})_3P$, neat, 140°, 1 h	 (42)	108
		$(n\text{-Bu})_3P$, neat, 165° [b]	 (—)	172
C_{20}		$(n\text{-Bu})_3P$, neat, 165° [b]	 (—)	172

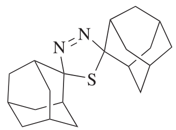
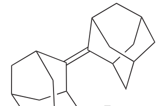
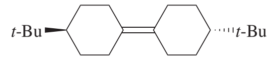
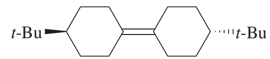
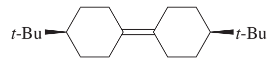
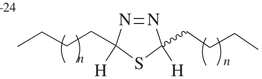
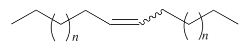
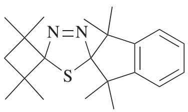
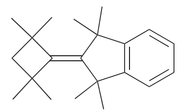
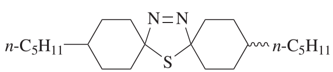
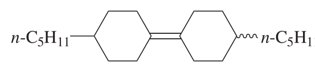
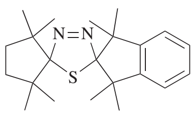
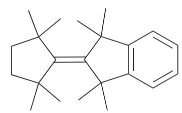
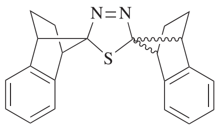
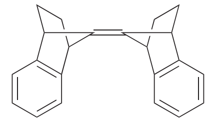
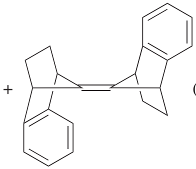
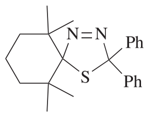
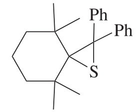
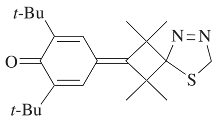
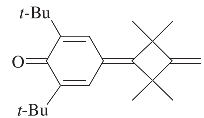
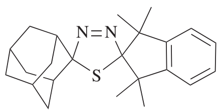
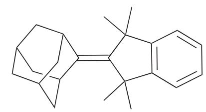
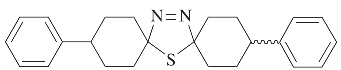
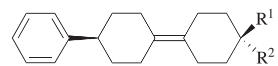
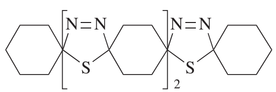
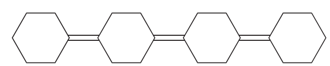
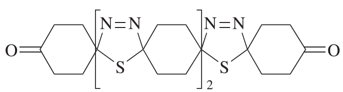
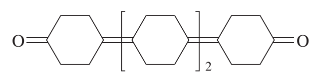
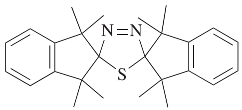
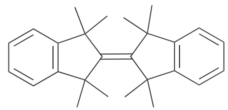
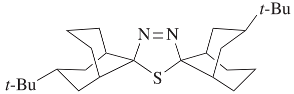
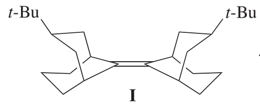
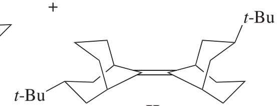
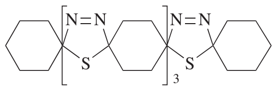
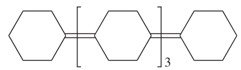
C_{20}		Ph_3P, melt, 125–130°, 12 h	 **I**	(74)	9
		$(n\text{-}Bu)_3P$, neat, 150° [b]	**I** (—)		172
		1. Methylcyclohexane, reflux, 5 h 2. $(n\text{-}Bu)_3P$, xylene, reflux, 5 h		(69)	181a, 181b
		1. Methylcyclohexane, reflux, 5 h 2. $(n\text{-}Bu)_3P$, xylene, reflux, 5 h		(69)	181a, 181b
		1. Methylcyclohexane, reflux, 6 h 2. $(n\text{-}Bu)_3P$, xylene, reflux, 4 h		(82)	181a, 181b
$C_{20–24}$		1. THF, reflux, 2 h 2. Ph_3P, THF, reflux, o/n		*n* (Z)/(*E*) 6 (90) 4:1 8 (35) 4:1	45
C_{21}		1. Melt, 140°, 0.5 h 2. $(n\text{-}Bu)_3P$, neat, 140°, 2 h		(36)	108
C_{22}		Ph_3P, melt, 120–140°, 2–12 h		(78)	169
		1. Melt, 140°, 30 min 2. $(n\text{-}Bu)_3P$, neat, 140°, 2 h		(20)	108

TABLE 1. ALKENES AND THIIRANES VIA EXTRUSIONS FROM ISOLATED THIADIAZOLINES (*Continued*)

Thiadiazoline	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{22} 	1. Heat 2. Ph_3P, melt, 120°, 20 h	 (41)[e] +  (44)[e]	182
C_{23} 	Benzene, 50°, 24 h	 (42)	183
	Ph_3P, benzene, reflux, 24 h	 (72)	184
	$(n\text{-}Bu_3)P$, neat, 150° [c]	 (—)	172
C_{24} 	Ph_3P, melt, 120–140°, 2–12 h	 R^1 R^2 Ph H (89) H Ph (4)	169
	1. Toluene, reflux, 5 h 2. $(EtO)_3P$, toluene, reflux, o/n	 (79)	115
	1. Toluene, reflux, 2 h 2. $(EtO)_3P$, toluene, reflux	 (30)	185

C_{26}		$(n\text{-}Bu_3)P$, neat, 150° [c]	 (—)	172
		$(n\text{-}Bu)_3P$, neat, 165° [c]	 **I** +  **II** **I** + **II** (82)	172
C_{30}		1. Toluene, reflux, 2 h 2. $(EtO)_3P$, toluene, reflux, o/n	 (67)	180

[a] No attempts to desulfurize this product were reported.

[b] The formation of small amounts of the corresponding alkenes was reported, but these products were not characterized.

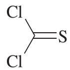
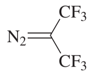
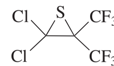
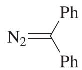
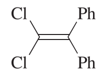
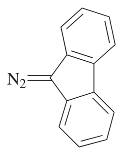
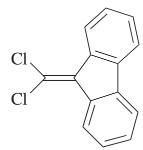
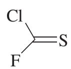
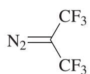
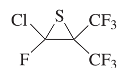
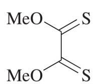
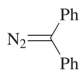
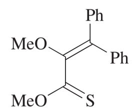
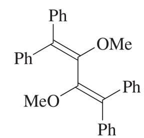
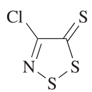
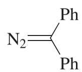
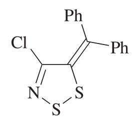
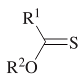
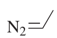
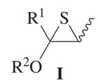
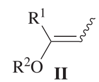
[c] The reaction was allowed to proceed until nitrogen evolution had ceased.

[d] The yield was determined by NMR spectroscopy.

[e] The reaction was carried out in a seated tube.

[f] The products were obtained after isolation and desulfurization of the individual episulfide stereoisomers.

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES

	S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1			Neat, rt, 24 h	 (49)[a]	69
			1. Petroleum ether, rt[b] 2. 160°, "short time"	 (67)	68
			1. Petroleum ether, rt[b] 2. "Heat until melted"	 (—)[c]	68
			Neat, 60°, autoclave, 18 h	 (60)[a]	69
C_2			1. Petroleum ether, 20°, 72 h 2. Cu-bronze, CCl_4, reflux, 45 min	 (51) +  (17)	186
			CH_2Cl_2, rt, 1 h	 (83)	87
C_{2-7}			1. Et_2O, –5°, 12 h 2. Neat	 **I** +  **II**	187

R^1	R^2	Temp (°)[b]	**I**[d]	**I** *cis/trans*	**II**[d]	**II** (*E*)/(*Z*)
Me	Me	100	(100)	(—)	—	—
Et	Et	100	—	(—)	(100)	55:45
Ph	Me	120	(50)	3:2	(50)	3:2

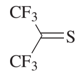
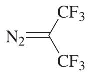
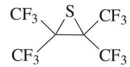
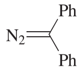
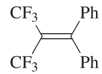
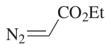
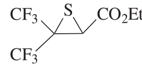
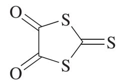
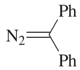
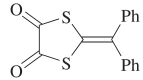
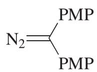
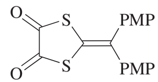
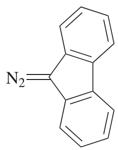
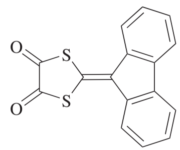
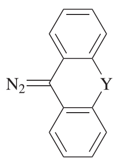
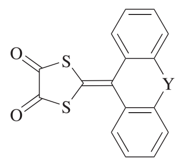
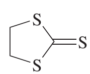
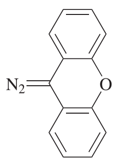
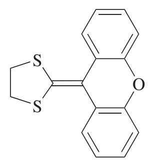
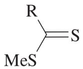
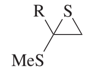
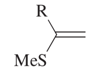
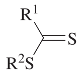
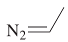
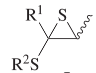
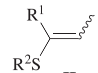
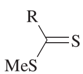
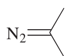
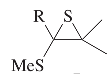
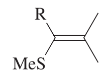
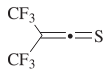
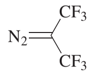
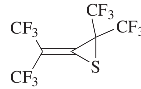
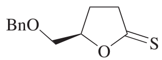
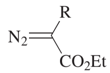
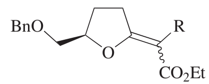
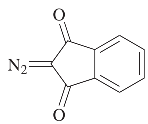
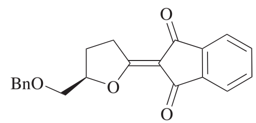
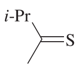
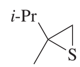
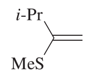
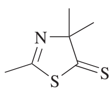
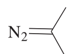
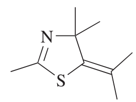
C_3 		1. Neat, –30° [e] 2. Reflux, 4 h		(87)[a]	155
		1. Pentane, –78° [b] 2. Neat, 250°, 15 min		(69)	188
		Pentane, –78° [b]		(19)[a]	188
		1. Et_2O, rt, 20 min 2. Cu powder, benzene, reflux, 10 min		(86)	80
		1. Et_2O, rt, 20 min 2. Cu powder, benzene, reflux, 10 min		(81)	80
		1. Et_2O, rt, 20 min 2. Cu powder, benzene, reflux, 10 min		(86)	80
		1. Et_2O, rt, 20 min 2. Cu powder, benzene, reflux, 10 min		Y: O (—); S (87)	80
		1. Et_2O, rt, 6 h 2. EtOH, reflux		(64)	80

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{3-6}  R = Me, Et, *i*-Pr, *t*-Bu	CH_2N_2	1. Ether, –5°, 12 h 2. 60–100° [d]	 (40–60)[a] +  (~20)	71
C_{3-10} 		1. Ether, –5°, 12 h 2. Temp [d]	 **I** +  **II**	187
C_{3-8} 		1. Ether, –5°, 12 h 2. 100-140° [a,d]	 **I** +  **II**	187

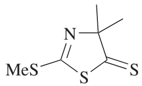
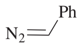
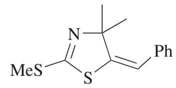
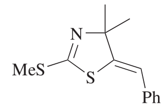
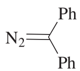
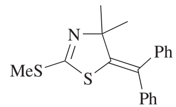
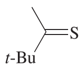
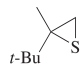
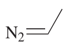
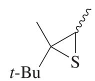
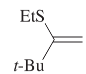
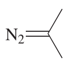
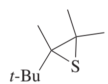
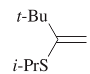
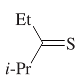
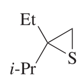
R^1	R^2	Temp (°)	**I**[a,e]	*cis*/*trans* **I**	**II**[e]	(*Z*)/(*E*)
Me	Me	90	(80)	1:1	(20)	1:1
Et	Me	120	(70)	4:3	(30)	1:2
i-Pr	Me	90	(90)	4:5	(10)	3:2
t-Bu	Me	100	(63)	20:1	(37)	5:32
MeS	Me	120	(0)	—	(100)	—
Et	Bn	130	(0)	—	(100)	1:1

R	**I**	**II**
Me	(—)	(—)
t-Bu	(—)	(—)
Ph	(0)	(—)

C_4				
		1. Neat, –78° to rt 2. Neat, reflux, 24 h	 (—)	155
C_5				
		$Rh_2(OAc)_4$, toluene, reflux		75
		$Rh_2(OAc)_4$, toluene, reflux, 15 min	 (74)	75
	CH_2N_2	Et_2O, 0°, 12 h	 (70)[a] +  (25)	71, 189
C_6				
		1. Pentane, 2–3°; rt, 24 h 2. $(MeO)_3P$, $CHCl_3$, reflux, 2 h	 (63)	84

R	Time (min)		(E)/(Z)
CO_2Et	5	(74)	—
$P(O)(OEt)_2$	40	(96)	1:1

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6				
		1. Toluene, rt, 3–4 h 2. Ph_3P, THF, reflux, 16–18 h	 (21) +  (30)	85
		1. THF, rt, 18–20 h 2. Ph_3P, THF, reflux, 16–18 h	 (57)	86
	CH_2N_2	Et_2O, 0°, 12 h	 (60)[a]	71, 189
		1. Ether, –5°, 12 h 2. 100–140° [d]	 (75)[a] +  (25)	187
		1. Ether, –5°, 12 h 2. 100–140° [d]	 (75)[a] +  (25)	187
	CH_2N_2	Et_2O, 0°, 12 h	 (85)[a]	71, 189

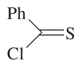
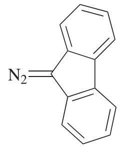
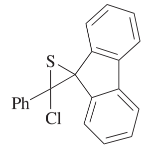
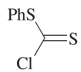
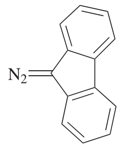
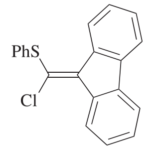
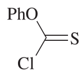
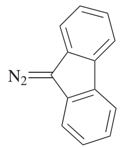
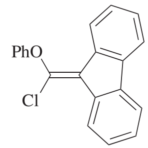
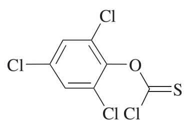
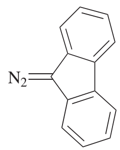
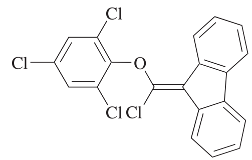
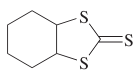
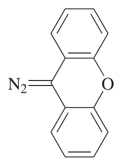
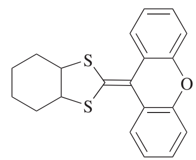
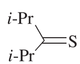
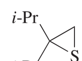
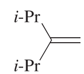
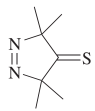
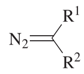
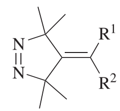
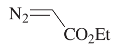
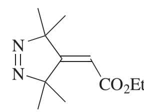
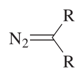
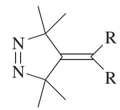
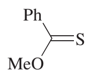
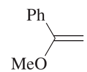
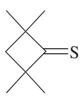
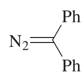
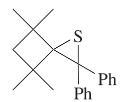
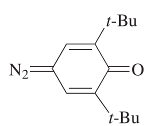
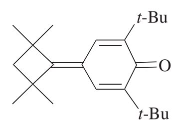
C_7					
		Et_2O, rt[b]		(93)[a]	68
		1. Et_2O, rt, 2 d 2. Cu bronze, benzene, reflux, 1 h		(43)	79
		Benzene, rt, 4 d		(35)	79
		Et_2O, rt, 3 h		(47)	79
		1. Et_2O, rt, 20 min 2. Cu powder, benzene, reflux, 10 min		(68)	80
	CH_2N_2	Et_2O, 0°, 12 h	 **I** (70)[a] + 	(25)	71, 189
	CH_2N_2	1. Et_2O, 0° 2. MeCN, 70°, 30 min	**I** (70)[a]		83

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7				
		1. Et_2O, –10°, 18 h 2. $(MeO)_3P$, $CHCl_3$, reflux	 R^1 / R^2 / Time H / H / 3 d (70) H / Me / 3 d (86) Me / Me / 18 h (98) H / *t*-Bu / 4 d (58) H / Ph / 6 d (98) Ph / Ph / 18 h (94) *i*-Pr / CO_2Et / 2 d (70)	174, 190 174, 190 174, 190 174, 190 174, 190 174, 190 191
		1. Et_2O, –10°, 18 h 2. $(MeO)_3P$, neat, 100°, 1 h	 (74)	174, 190
		Et_2O, –10°, 18 h	 R CO_2Et (58) CN (13)	174, 190
	CH_2N_2	1. Ether, –5°, 12 h 2. 100–140° [d]	 (30)	71
C_8				
		DMF, 40°, 1 h	 (93)[a]	49
		CCl_4, rt, 30 d	 (13)	184

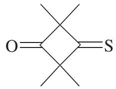
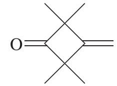
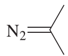
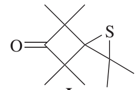
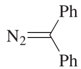
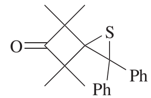
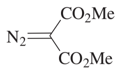
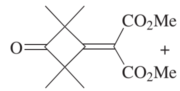
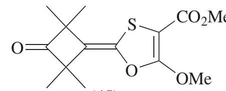
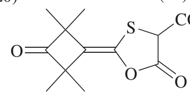
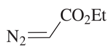
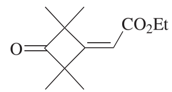
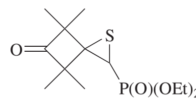
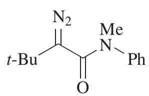
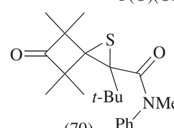
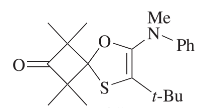
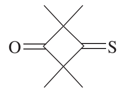
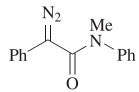
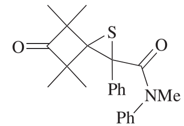
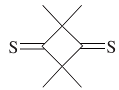
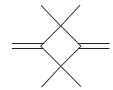
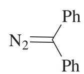
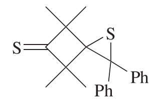
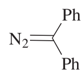
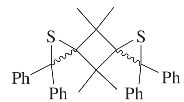
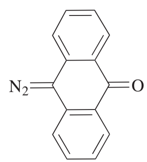
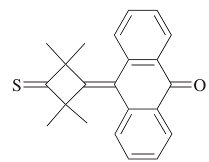
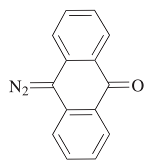
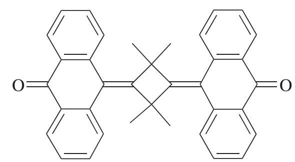
	CH_2N_2	1. Et_2O, 0° [e] 2. Pentane, reflux[b] 3. Ph_3P, benzene, reflux, 38 h	 (67)	157, 192
		1. Pentane, 0° 2. MeCN, 70° [b]	 **I** (79)[a]	193
		DMF, 40°, 1 h	**I** (82)[a]	84
		DMF, 40°, 1 h	 (82)[a]	49
		$Rh_2(OAc)_4$, toluene, 50°, 48 h	 (20) +  (45) +  (10)	101
		1. $LiClO_4$, THF, rt[b] 2. $(Me_2N)_3P$, neat, rt, 2 h	 (54)	194
		THF, reflux, 1 h	 (59)[a]	195
		1. $LiClO_4$, THF, rt, 30 min 2. 60°, 5 h	 (70) +  (21)	100

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

	S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8			$LiClO_4$, THF, rt, 5 h	 (55)	100
		CH_2N_2	1. Et_2O, 0° [e] 2. $CHCl_3$, reflux, 4 h 3. $(n\text{-Bu})_3P$, 80°, 60 h	 (64)	96, 159
			DMF, 40°, 1 h	 (95)[a]	49
			Et_2O, rt, 1 h	 (100)[a]	96
			1. CCl_4 , rt, 10 d 2. Ph_3P, benzene, reflux, 25 d	 (71)	184
		 2 eq	1. CCl_4 , rt, 10 d 2. Ph_3P, benzene, reflux, 25 d	 (47)	184

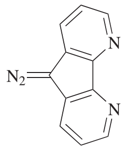
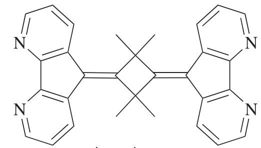
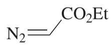
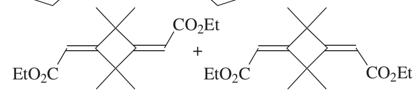
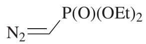
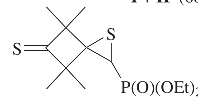
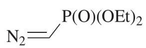
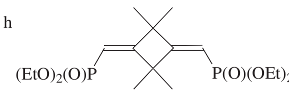
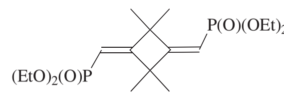
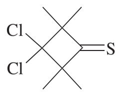
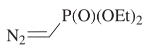
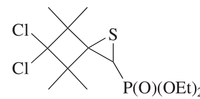
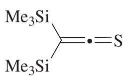
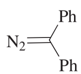
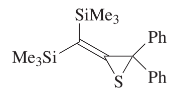
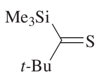
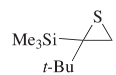
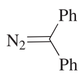
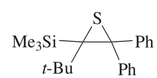
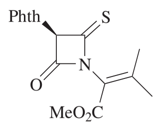
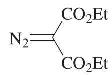
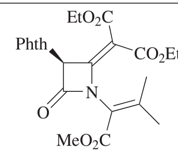
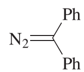
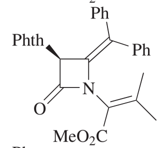
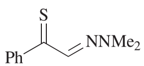
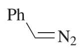
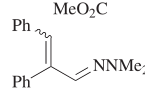
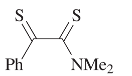
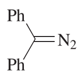
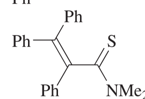
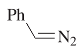
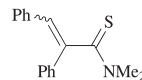
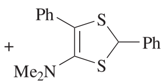
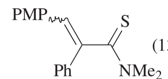
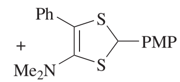
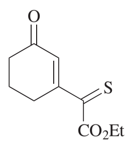
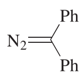
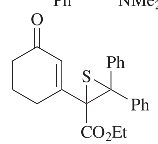
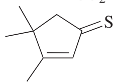
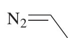
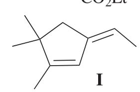
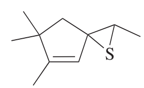
		Ph_3P, $CHCl_3$, reflux, 40 h	 (65)	196
		1. $LiClO_4$, THF, rt, 24 h 2. $(Me_2N)_3P$, THF, rt, 2 h	 **I** **II** **I** + **II** (60), **I**:**II** = 1:1	194
		THF, reflux, 1 h	 (62)[a]	195
		1. Toluene, reflux, 2–3 h 2. $(Et_2N)_3P$, THF, reflux, 2–4 h	 (13)[f] +  (51)[f]	195
		THF, reflux, 1 h	 (61)[a]	195
		$CHCl_3$, 60°, 10 h	 (58)[a]	81, 82
	CH_2N_2	1. Et_2O, –20°, 2 h 2. Benzene, reflux, 2 h	 (62)[a]	197
		Benzene, reflux, 2 h	 (77)[a]	197

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
		$Rh_2(OAc)_4$, benzene, 65°, 1 h	 (58)	164
		1. $Rh_2(OAc)_4$, benzene, 70°, 1.5 h 2. Ph_3P, benzene, reflux, 8 h	 (55)	164
		Hexane, EtOAc, toluene, rt, 1 h	 (17)	198
		Benzene, rt, 1 h	 (30)	198
		Toluene, CH_2Cl_2, rt[b]	 (25) +  (25)	76
		Benzene/toluene (1:1), rt[b]	 (13) +  (20)	76
		1. DBU,CH_2CI_2, −78° 30 min 2. diazo compound	 (30)[a]	199
		Et_2O, 20°, 15 min	 **I** (20)[d] +  (45)[d]	200

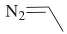
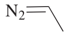
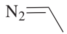
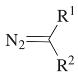
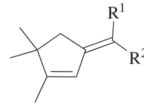
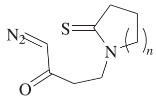
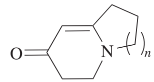
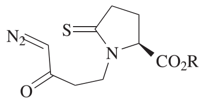
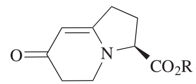
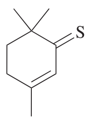
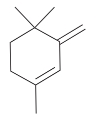
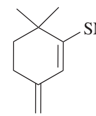
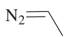
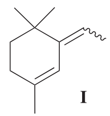
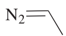
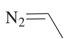
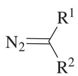
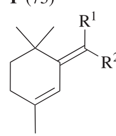
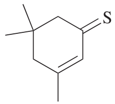
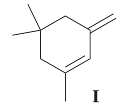
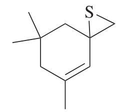
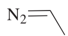
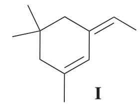
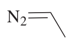
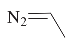
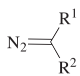
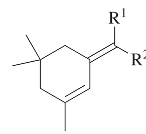
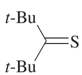
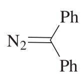
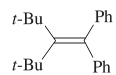
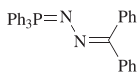
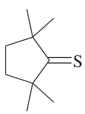
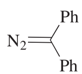
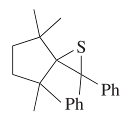
		Et_2O, ia, 20°, 15 min	**I** (70)[d]	200
		Et_2O, –60°, 15 min	**I** (75)[d]	200
		Et_2O, ia, – 60°, 15 min	**I** (65)[d]	200
		Et_2O, 20°, 15 min	 R^1 / R^2: Me / Me (85)[d]; Me / Ph (55)[d]; Ph / Ph (40)[d]	200
C_{8-10} 	Intramolecular	1. $Rh_2(OAc)_4$, benzene, reflux 2. W-2 Ra-Ni, acetone	 n: 1 (68); 2 (70); 3 (73)	78
C_9 	Intramolecular	1. $Rh_2(OAc)_4$, benzene, reflux 2. W-2 Ra-Ni, acetone	 R: Me (65); *t*-Bu (68)	78
	CH_2N_2	Et_2O, –60°, 15 min	 (10)[d] +  (70)[d]	200
		Et_2O, –60°, 15 min	 **I** (90)[d]	200
		Et_2O, 20°, 15 min	**I** (80)[e]	200
		Et_2O, ia, 20°, 15 min	**I** (75)[e]	200
		Et_2O, 20°, 15 min	 R^1 / R^2: Me / Me (90)[d]; H / CO_2Et (35)[d]	200

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
	CH_2N_2	Et_2O, –60°, 15 min	 **I** (20)[d] +  (20)[d]	200
	CH_2N_2	Excess *N*-substrate, Et_2O, –60°, 15 min	**I** (20)[d]	200
		Excess *S*-substrate, Et_2O, ia, –60°, 15 min	 **I** (85)[d]	200
		Excess *S*-substrate, Et_2O, 20°, 1 min	**I** (95)[d]	200
		Excess *N*-substrate, Et_2O, 20°, 15 min	**I** (75)[d]	200
		Et_2O, 15 min	 R^1 / R^2 / Temp (°) Me / Me / 20 / (70)[d] Me / Me / –60 / (90)[d] H / CO_2Et / 20 / (20)[d] H / Ph / –60 / (45)[d]	200
		1. THF, reflux, 3 h 2. Ph_3P, THF, reflux, 16 h	 **I** (68)	50
		Et_3N, reflux, 70 h	**I** (63)	50
		DMF, 40°, 1 h	 (83)[a]	49

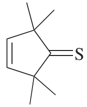
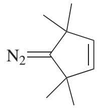
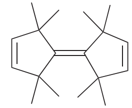
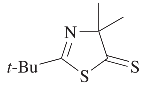
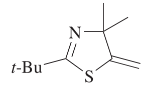
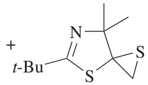
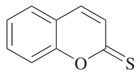
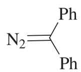
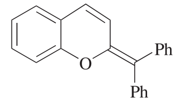
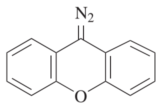
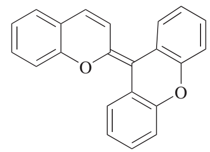
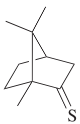
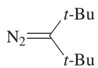
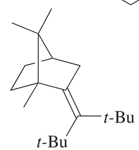
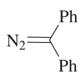
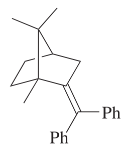
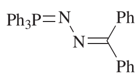
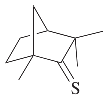
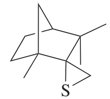
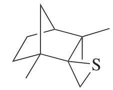
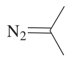
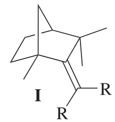
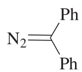
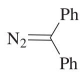
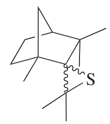
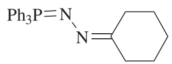
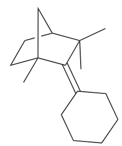
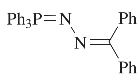
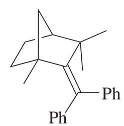
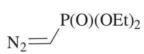
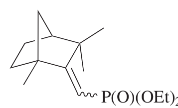
		1. Melt, 140° 2. n-Bu_3P, 140°	 (38)	60
	CH_2N_2	Et_2O, –78°, rt, 1 h	 (40) +  (—)	201
		Et_2O, rt, 1 h	 (—)	70
		Et_2O, rt, 1h	 (38)	70
C_{10} 		1. THF, reflux, 15 h 2. n-Bu_3P, neat, 120°, 15 h	 (64)	50
		1. THF, reflux, 3 h 2. Ph_3P, THF, reflux, 16 h	 **I** (90)	50
		DMA, 165°, 25 min	**I** (67)	50

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10} 	CH_2N_2	1. Et_2O, –5°, 12 h 2. 100–140°	 **I** (33)[a,d] +  **II** (18)[a,d]	71
	CH_2N_2	1. Et_2O, –10° 2. Toluene, 46°, 3 h	**I** (38)[a,d] + **II** (25)[a,d]	202
		1. Et_2O, –5°, 12 h 2. 100–140° [d]	 **I** (—) R = Me	187
		1. THF, reflux, 3 h 2. Ph_3P, THF, reflux, 16 h	**I** (90) R = Ph	50
		DMF, 40°, 1 h	 (90)[a] 2:1 isomer mixture	49
		DMA, 165°, 25 min	 (47)	50
		DMA, 165°, 25 min	 (44)	50
		1. Toluene, reflux, 2–3 h 2. $(Et_2N)_3P$, THF, reflux, 2–4 h	 (70) 4:1 isomer mixture	195

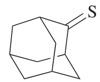
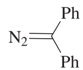
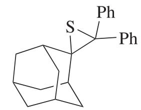
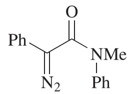
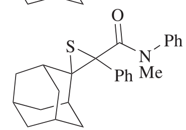
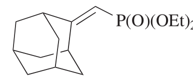
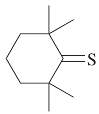
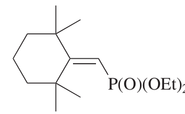
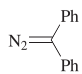
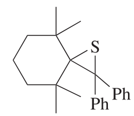
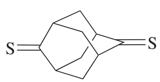
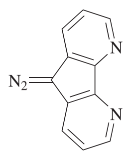
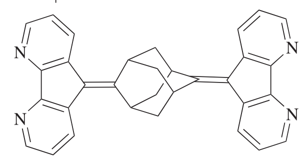
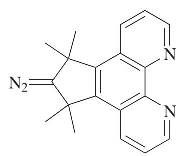
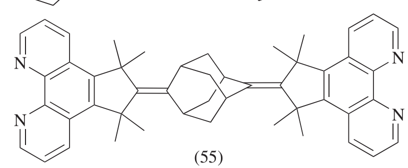
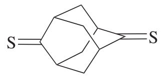
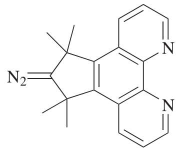
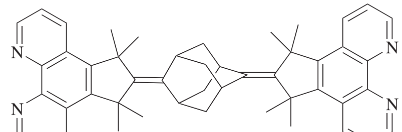
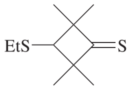
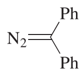
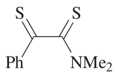
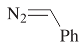
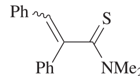
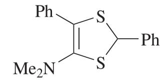
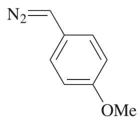
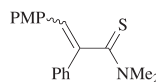
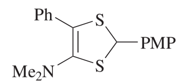
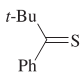
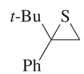
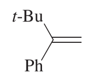
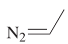
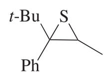
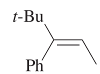
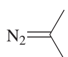
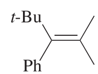
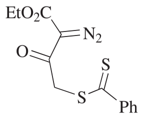
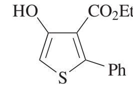
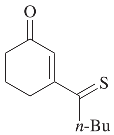
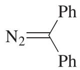
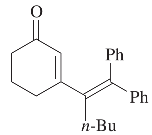
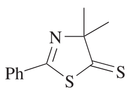
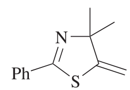
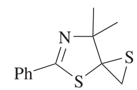
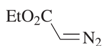
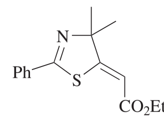
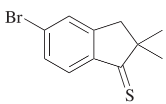
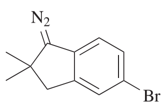
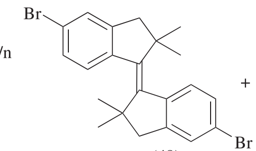
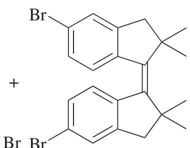
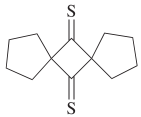
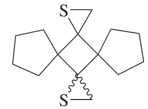
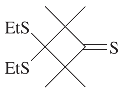
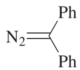
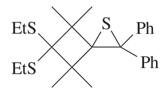
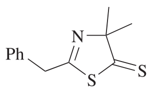
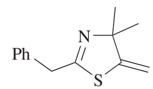
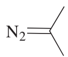
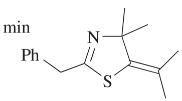
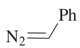
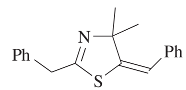
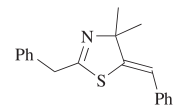
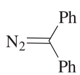
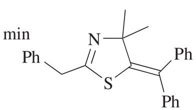
		DMF, 40°, 1	 (82)[a]	49
		$LiClO_4$, THF, 60°, 5 h	 (13)	100
		1.Toluene, reflux, 30 min 2. $(Et_2N)_3P$, THF, reflux, 2–4 h	 (56)	195
		1.Toluene, reflux, 30 min 2. $(Et_2N)_3P$, THF, reflux, 2–4 h	 (53)	195
		DMF, 40°, 1 h	 (83)[a]	49
		Ph_3P, $CHCl_3$, reflux, 40 h	 (45)	203
		1. THF/py, rt, 4 h 2. $(n\text{-}Bu)_3P$, py, 140°, 48 h	 (55)	117, 203

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
		1. Et_2O, THF, rt, 48 h 2. $(n\text{-}Bu_3)P$, py, 140°, 48 h	 (20)	196
		DMF, 40°, 1 h	 (93)[a]	49
		Toluene/CH_2Cl_2, rt[b]	 (25) +  (25)	76
		Benzene/toluene (1:1), rt[b]	 (13) +  (20)	76
C_{11}				
	CH_2N_2	1. Ether, –5°, 12 h 2. 100–140° [d]	 (~40)[a] +  (—)	71
		1. Ether, –5°, 12 h 2. 100–140° [d]	 (~40)[a] +  (—)	187
		1. Ether, –5°, 12 h 2. 100–140° [d]	 (—)	187

C_{11}

	Intramolecular	$Rh_2(OAc)_4$, benzene, reflux, 2 h	 (80)	74
		Benzene, THF, –78° to rt[b]	 (25)	199
	CH_2N_2	Et_2O, –78° to rt, 1 h	 (10) +  (23)	201
		Et_2O, rt, 72 h	 (6)	204
		1. CH_2Cl_2, –25° to rt, o/n 2. Cu powder, toluene, reflux, o/n	 (48) +  (10)	205

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}				
	CH_2N_2	1. Et_2O, 0° [e] 2. Hexane, CCl_4, reflux[b]	 (100)[a]	96
		DMF, 40°, 1 h	 (74)[a]	49
	CH_2N_2	Et_2O, –78° to rt, 1 h[b]	 (31)	201
		1. Pentane, 2–3°; rt, 2-3 min 2. $(MeO)_3P$, $CHCl_3$, reflux, 2 h	 (87)	84
		1. Toluene, rt, 3–4 h 2. Ph_3P, THF, reflux, 16–18 h	 (34) +  (61)	85
		1. Pentane, 2–3°; rt, 2-3 min 2. Ph_3P, THF, reflux, 18 h	 (55)	86

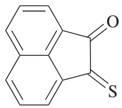
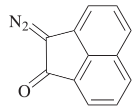
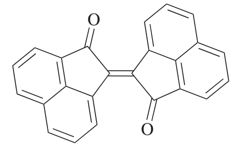
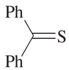
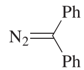
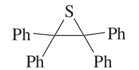
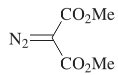
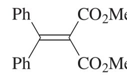
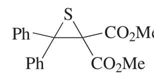
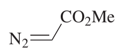
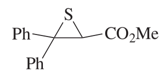
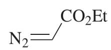
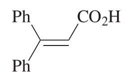
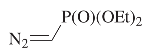
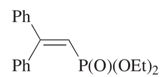
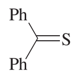
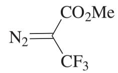
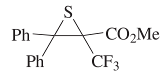
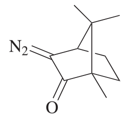
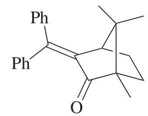
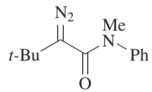
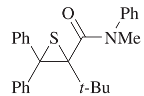
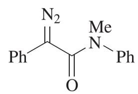
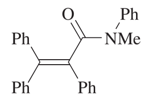
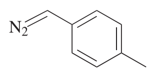
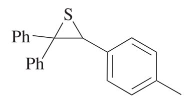
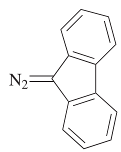
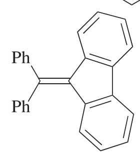
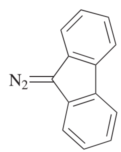
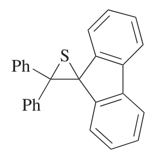
		1. Cu-bronze, toluene, reflux, 20 h 2. Ph_3P, toluene, reflux, 24 h	 (33)	206
C_{13}				
		Petroeum ether, rt[b]	 (—)	207
		$Rh_2(OAc)_4$, toluene, 50° [b]	 (18) +  (46)	10
		$CHCl_3$, 50°, 4 h	 (99)[a]	208
		1. CuS, Cu powder, petroleum ether, 100°, 25 min 2. NaOH, H_2O, reflux, 2 h	 (75)	53
		Toluene, reflux	 (—)	209

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

	S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}			$Rh_2(OAc)_4$, toluene, 50°, 6 h	 (57)[a]	210
			1. THF, 0° to rt, 1 h 2. Ph_3P, THF, reflux, 16 h	 (98)	211
			THF, rt, 15 min.	 (64)[a]	100
			1. THF, rt, 0.5 h 2. $(Me_2N)_3P$, THF, 60°, 2 h	 (45)	100
			Pentane/Et_2O, 0°	 (80)[a]	21
			1. Et_2O, rt, 12 h 2. Cu powder, xylene, reflux, 1 h	 (73)	212, 68
			Benzene, rt[b]	 (—)[a]	68

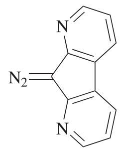
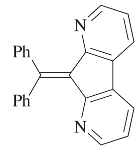
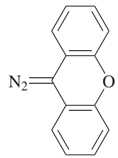
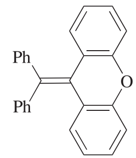
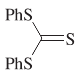
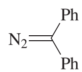
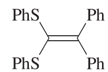
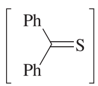
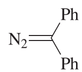
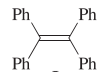
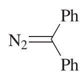
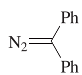
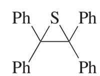
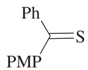
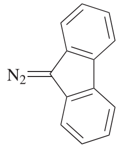
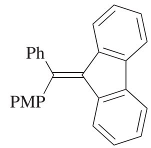
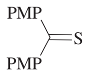
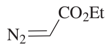
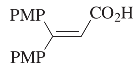
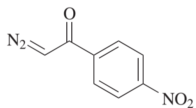
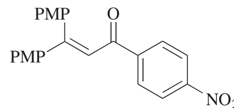
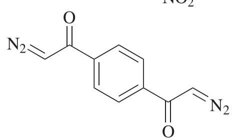
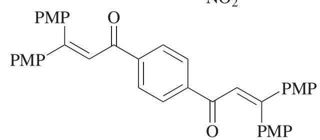
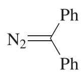
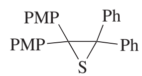
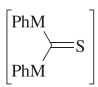
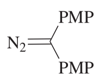
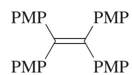
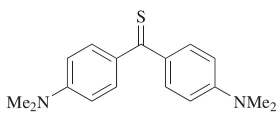
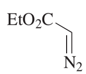
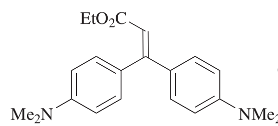
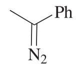
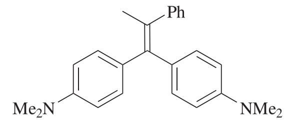
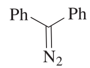
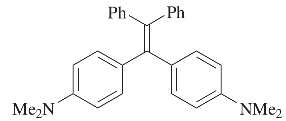
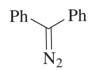
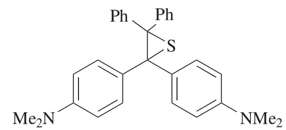
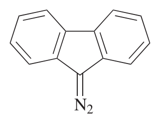
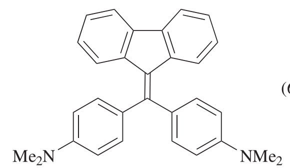
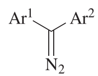
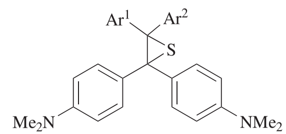
		1. Benzene, reflux, 5 h 2. Cu bronze, benzene, reflux, 2 h		(94)	213
		1. Benzene, rt, 1 h 2. Cu powder, benzene, reflux, 10 min		(74)	80
		1. Ether, rt, 2 d 2. Cu bronze, benzene, reflux		(75)	79
 [g]		1. S_8, toluene, reflux, 45 min 2. Cu bronze, xylene, reflux, 30 min	 **I**	(83)	214
		1. Toluene, reflux, 45 min 2. Ra-Ni, EtOH, reflux, 5 min	**I** (93)		214
		1. Ether, rt, 12 h 2. MeOH, reflux	**I** (—) + 	(—)	215

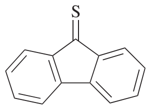
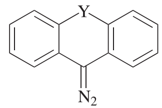
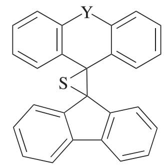
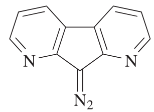
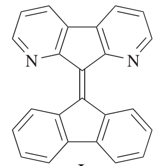
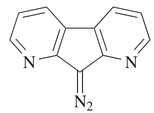
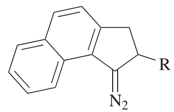
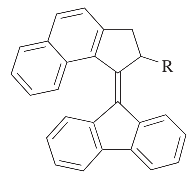
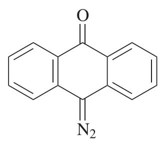
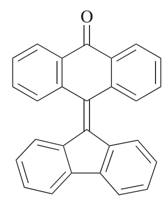
TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}				
		1. Benzene, rt[b] 2. Cu powder, petroleum ether, 100°, 3 h	 (87)	216
		1. Cu powder, petroleum ether, 100°, 25 min 2. NaOH, H_2O, reflux, 2.5 h	 (84)	53
		Cu powder, diglyme, 120°, 20 min	 (87)	53
		Cu powder, $(EtOCH_2CH_2)_2O$, 140°, 10 min	 (82)	53
		Benzene, rt[b]	 (—)[a]	68
 [g]		1. S_8, benzene, reflux, 40 min 2. Metal, solvent, reflux	 Metal / Solvent / Time (min) Cu bronze / xylene / 30 / (93) Ra-Ni / EtOH / 10 / (—)	214
		Cu powder, xylene, reflux, 3 h	 (96)	217

	1. Benzene, rt, 16 h 2. Cu bronze, *p*-xylene, reflux, 5 h		(—)	218
	Benzene, rt, 16 h; reflux, 12 h		(61)	218
	Benzene, rt, 48 h		(61)[a]	68
	1. Benzene, rt, 16 h 2. Cu bronze, *p*-xylene, reflux, 5 h		(60)	218
	Benzene, rt, 16 h; "heat"			218

Ar^1	Ar^2	
2-ClC_6H_4	Ph	(85)[a]
4-ClC_6H_4	4-ClC_6H_4	(86)[a]
4-MeC_6H_4	4-MeC_6H_4	(90)[a]
$2,5\text{-Me}_2C_6H_3$	Ph	(96)[a]
4-PhC_6H_4	Ph	(82)[a]

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

	S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}			Et_2O, rt[b]	 Y: O (100)[a]; S (—)[a]	215
			1. Benzene, rt[b] 2. Cu bronze, benzene, reflux, 2 h	 **I** (95)	213
			Benzene, reflux, 1 h; 70°, 72 h	**I** (—)	219
			Ph_3P, xylene, reflux	 R / Time (h): Me / 3 (39); Ph / o/n (36)	52, 220
			Benzene, reflux, 7 h	 (33)	221

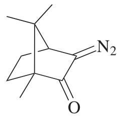
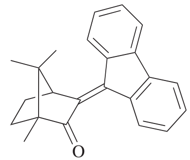
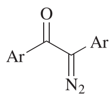
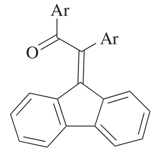
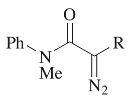
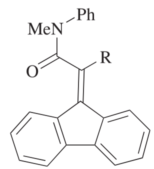
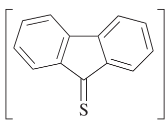
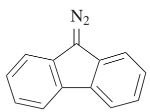
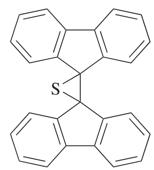
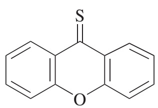
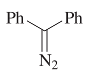
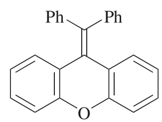
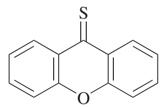
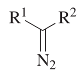
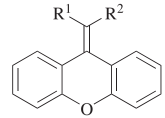
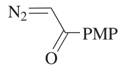
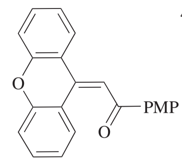
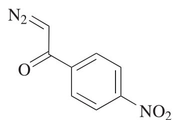
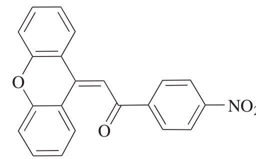
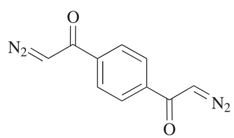
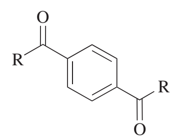
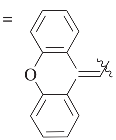
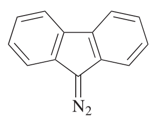
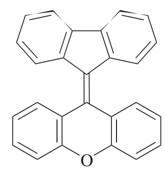
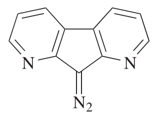
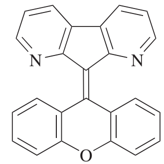
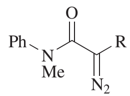
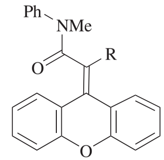
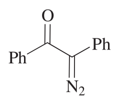
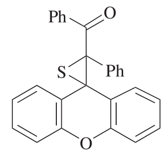
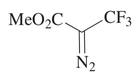
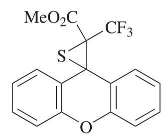
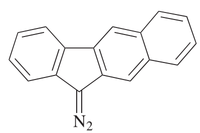
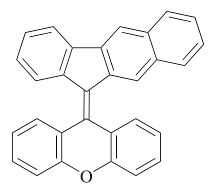
Thioketone	Diazo compound	Conditions	Product(s) and Yield(s) (%)		Refs.
		1. THF, rt, 20 min 2. Ph_3P, THF, reflux, 16 h		(95)	211
		Benzene, reflux, 30 min		Ar Ph (35) 4-ClC_6H_4 (86) 4-$MeOC_6H_4$ (82) 4-MeC_6H_4 (20)	222
		1. THF, rt, 5 min 2. $(Me_2N)_3P$, THF, 60°		R / Time (h) *t*-Bu 0.5 (35) Ph 22 (83)	100
 [g]		S_8, Et_2O, rt, 48 h		(75)[a]	215
		1. Et_2O, rt[b] 2. Cu powder, toluene, reflux, 3 h		(—)	223

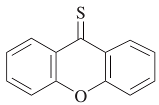
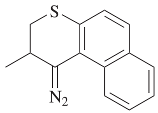
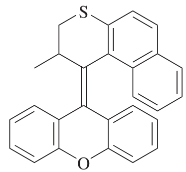
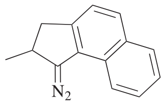
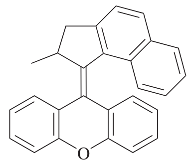
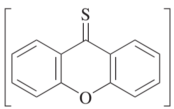
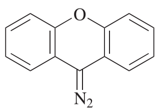
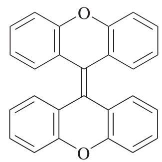
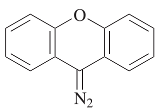
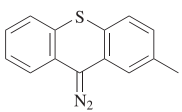
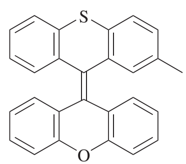
TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}				
		1. Benzene, rt, 16 h 2. Cu bronze, xylene, reflux, 5 h	 R¹ / R² / yield: Me / Ph / (—) 2-ClC_6H_4 / Ph / (82) 4-$O_2NC_6H_4$ / Ph / (91) 4-ClC_6H_4 / 4-ClC_6H_4 / (71) 4-MeC_6H_4 / Ph / (94) 4-MeC_6H_4 / 4-MeC_6H_4 / (70) 4-PhC_6H_4 / Ph / (71)	224
		Cu powder, petroleum ether, 100°, 20 min	 (90)	53
		Cu powder, diglyme, 120°, 20 min	 (86)	53
		Cu powder, $(EtOCH_2CH_2)_2O$, 140°, 10 min	 R =  (85)	53
		Benzene, reflux, 3 h	 (42)	51

	Benzene, reflux, 125 h		(—)	219
	$LiClO_4$, THF, 60°		R / Time (h): *t*-Bu, 7 (66); Ph, 40 (81)	100
	$Rh_2(OAc)_4$, toluene, rt, 15 min		(27)[a]	100
	$Rh_2(OAc)_4$, toluene, 50°, 3 h		(68)[a]	210
	Benzene, reflux, 45 h		(—)	225

R	Time (h)	
t-Bu	7	(66)
Ph	40	(81)

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}				
		Ph_3P, *p*-xylene, reflux, o/n	 (55)	226
		Ph_3P, *p*-xylene, reflux, o/n	 (55)	52
 [g]		1. S_8, benzene, 30–35°, 3 h 2. Cu bronze, benzene, reflux, 1 h	 **I** (93)	214
		1. S_8, benzene, 30–35°, 3 h 2. Ra-Ni, EtOH, reflux, 10 min	**I** (93)	214
		1. CH_2Cl_2, 0° to rt 2. Cu powder, xylene, reflux	 (70)	227

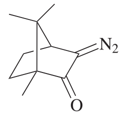
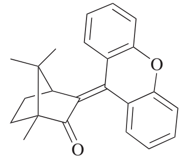
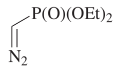
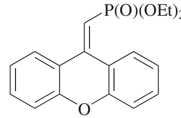
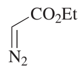
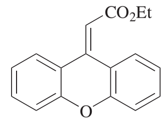
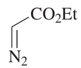
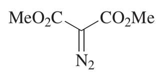
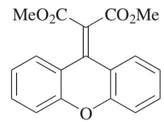
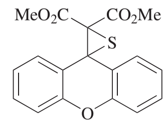
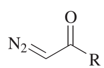
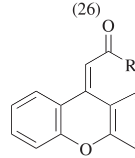
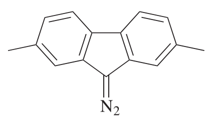
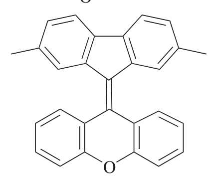
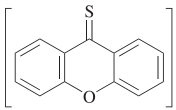
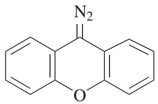
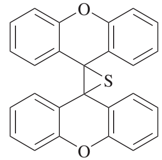
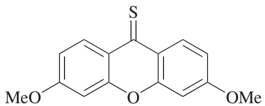
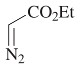
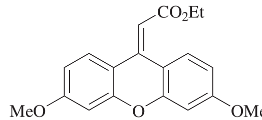
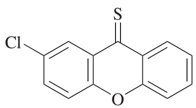
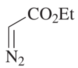
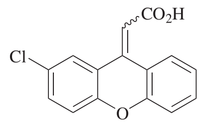
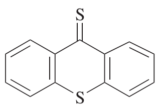
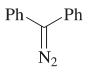
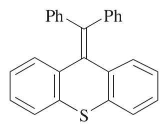
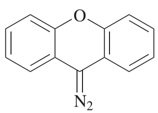
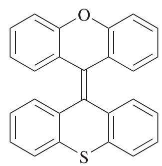
	1. THF, 45°, 5 h[e] 2. Ph_3P, THF, reflux, 16 h	 (92)	211
	Toluene, reflux, o/n	 (61)	209
	Cu powder, benzene, reflux, 25 min	 **I** (87)	53
	THF, $LiClO_4$, 60°, 9 h	**I** (51)	194
	$Rh_2(OAc)_4$, toluene, 50°, 40 h	 (26) +  (22)	10
	THF, 60° [e]	 R: *t*-Bu (94); Ph (96)	55
	1. Benzene, reflux, 4 h 2. Ph_3P, benzene, reflux, 3 h	 (21)	228

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}				
 [g]		S_8, Et_2O, rt, 30 min	 (67)[a]	215
		Cu powder, petroleum ether , 100°, 3 h	 (92)	217
		1. Cu powder, petroleum ether, 100°, 15 min 2. NaOH, EtOH, reflux, 2 h	 (83)	217
		1. Benzene, rt, 18 h 2. Zn/AcoH	 (—)	51
		1. Et_2O, rt[b] 2. Cu powder, xylene, reflux, 1 h	 (—)	215

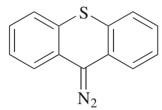
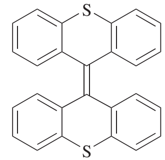
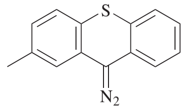
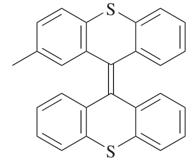
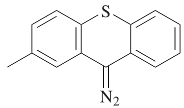
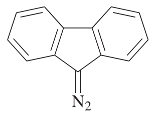
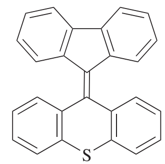
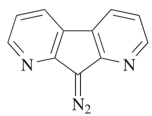
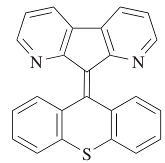
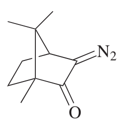
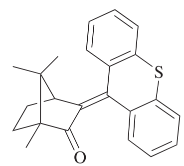
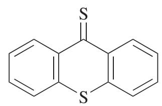
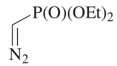
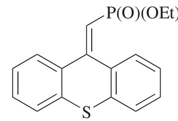
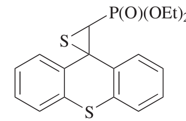
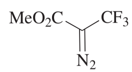
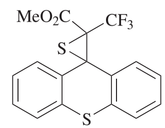
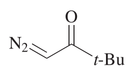
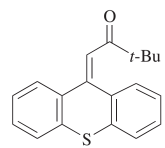
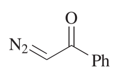
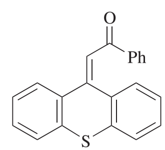
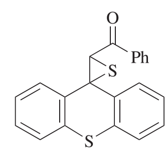
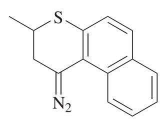
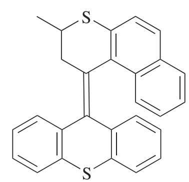
	1. Benzene, reflux, 2 h 2. Cu bronze, melt, 240–250°, 30 min		(25)	51
	Cu powder, *p*-xylene, reflux, 2 h	 **I**	(80)	133
	Cu powder, xylene, reflux	**I** (80)		227
	Benzene, reflux, 2 h		(43)	51
	Benzene, reflux, 80 h		(77)	219
	1. THF, 45°, 6 h[b] 2. Ph_3P, THF, reflux, 16 h		(92)	211

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 		Toluene, reflux, 24 h	 (29) +  (50)	209
		$Rh_2(OAc)_4$, toluene, 50°, 3 h	 (60)[a]	210
		THF, 60° [e]	 (94)	55
		THF, 60° [e]	 (54) +  (29)	55
		1. CH_2Cl_2, –30 to 0° [e] 2. Ph_3P, xylene, reflux, o/n	 (28)	229

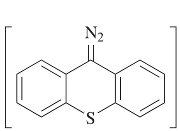
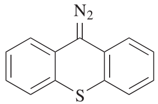
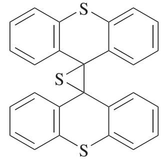
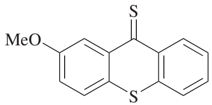
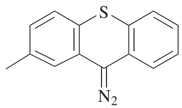
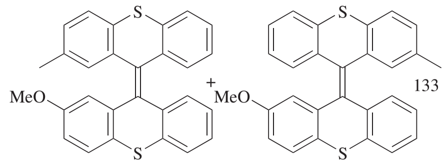
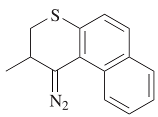
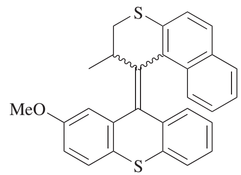
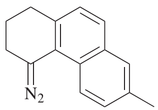
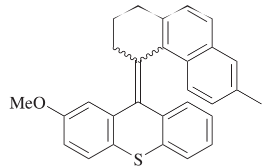
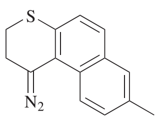
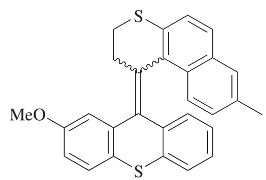
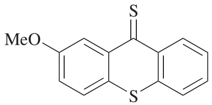
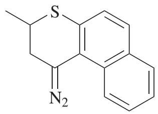
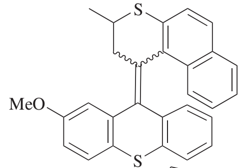
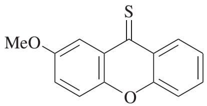
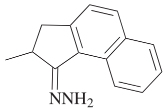
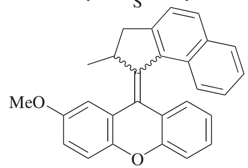
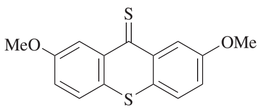
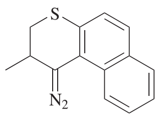
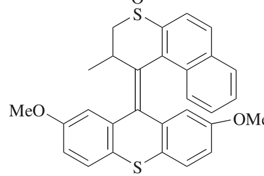
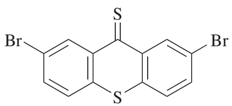
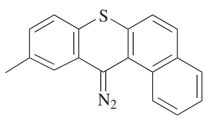
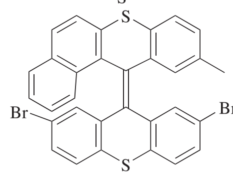
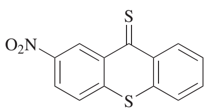
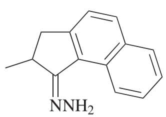
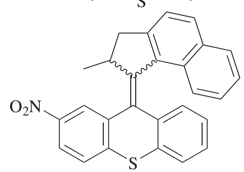
 [g]		S_8, Et_2O, rt, 12 h	 (62)[a]	215
		Cu powder, *p*-xylene, reflux, 2 h	 **I** + **II** (58), **I**:**II** = 1:1	133
		Cu bronze, *p*-xylene, reflux, o/n	 (54), (*Z*)/(*E*) = 1:1	226
		1. CH_2Cl_2, –30° to rt 2. Cu bronze, xylene, reflux	 (60), (*Z*)/(*E*) = 1:1	230
		1. Et_2O, 0° [e] 2. Cu bronze, *p*-xylene, reflux, 2 h	 (50), (*Z*)/(*E*) = 1:1	231

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}				
		1. CH_2Cl_2, –30 to 0° [e] 2. Ph_3P, xylene, reflux, o/n	 (29), (*Z*)/(*E*) = 7:8	229
		1. $PhI(OCOCF_3)_2$, DMF, –50°, 5 sec 2. Ph_3P, *p*-xylene, reflux, o/n	 (73)	52
		Cu bronze, *p*-xylene, reflux, o/n	 (91)	226
		1. CH_2Cl_2, 0°, 2 h 2. $(MeO)_3P$, toluene, 140°	 (66)	232
		1. $PhI(OCOCF_3)_2$, DMF, –50° 2. Ph_3P, *p*-xylene, reflux, o/n	 (55), (*Z*)/(*E*) = 1:1	52

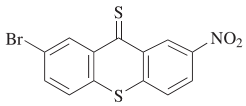
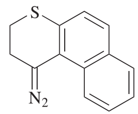
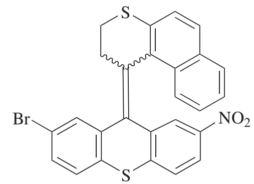
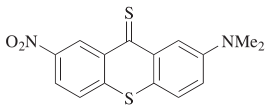
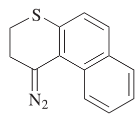
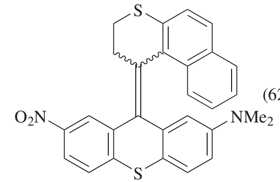
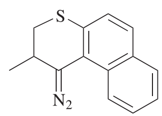
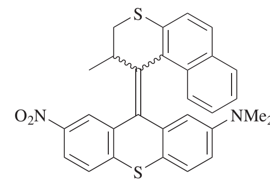
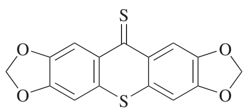
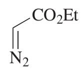
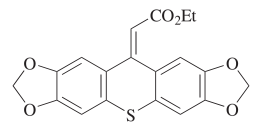
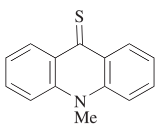
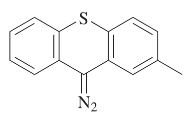
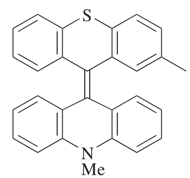
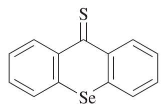
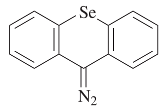
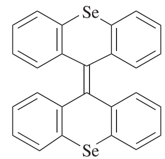
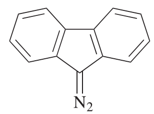
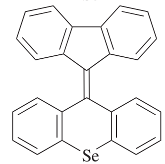
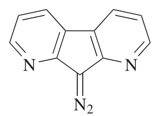
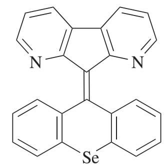
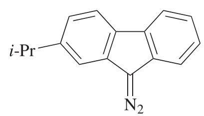
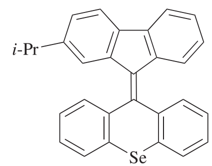
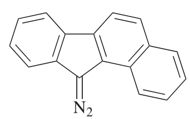
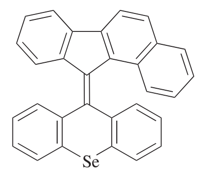
		1. CH_2Cl_2, –10 to 0°, 3 h 2. Ph_3P, toluene, reflux, 3 d		(58), (*Z*)/(*E*) = 1:1	233
		Cu bronze, *p*-xylene, reflux, 2 h		(62), (*Z*)/(*E*) = 3:2	114
		Cu bronze, *p*-xylene, reflux, o/n		(85)	234
		Cu powder, $(EtOCH_2CH_2)_2O$, 150°, 15 min		(89)	217
		1. CH_2Cl_2, –10° to rt 2. Cu, xylene, reflux		(88)	227

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13} 		1. Benzene, reflux, 2 h 2. Ph_3P, benzene, reflux, 30 h	 (41)	134
		1. Benzene, reflux, 4 h 2. Ph_3P, benzene, reflux, 12 h	 (42)	235
		Benzene, reflux, 52 h	 (72)	219
		1. Benzene, reflux, 8 h 2. Ph_3P, benzene, reflux, 7 h	 (22)	219
		1. Benzene, reflux, 7 h 2. Ph_3P, benzene, reflux, 3 h	 (49)	235

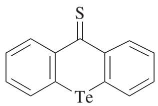
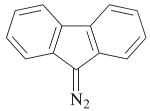
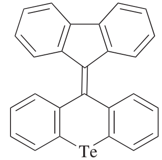
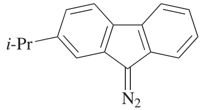
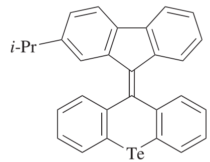
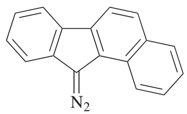
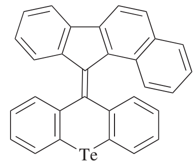
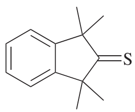
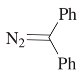
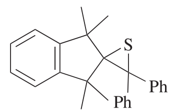
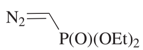
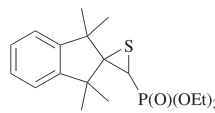
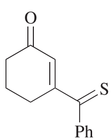
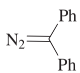
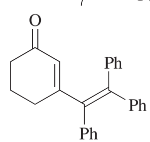
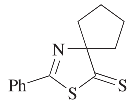
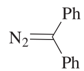
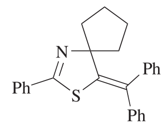
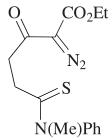
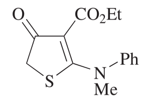
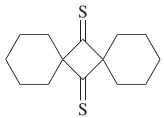
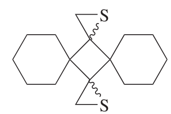
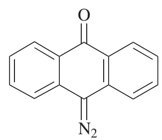
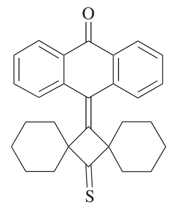
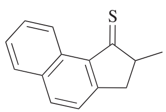
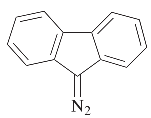
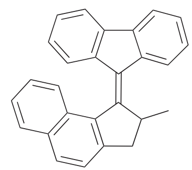
		1. Benzene, reflux, 6 h 2. Ph_3P, benzene, reflux, 4 h		(49)	219
		1. Benzene, reflux, 8 h 2. Ph_3P, benzene, reflux, 7 h		(34)	219
		1. Benzene, reflux, 3 h 2. Ph_3P, benzene, reflux, 25 h		(38)	235
		DMF, 40°, 1 h		(92)[a]	49
		THF, reflux, 5 h		(65)[a]	195
		Benzene, rt		(42)	199

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}				
		1. THF, rt, 18–20 h 2. Ph_3P, THF, reflux, 16–18 h	 (52)	86
	Intramolecular	$Rh_2(OAc)_4$, benzene, 60°	 (90)	74
C_{14}				
	CH_2N_2	1. Et_2O, 0° 2. $CHCl_3$, reflux, 1 h	 (100)[a]	96
		1. CCl_4, rt, 90 d 2. Ph_3P, benzene, reflux, 7 d	 (79)	184
		1. Toluene, reflux, 6 h 2. Ph_3P, toluene, reflux, 18 h	 (65)	220

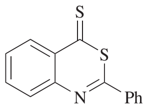
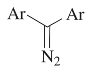
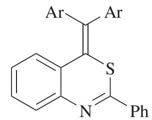
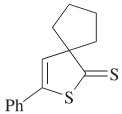
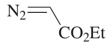
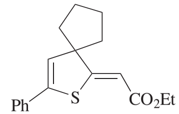
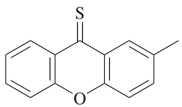
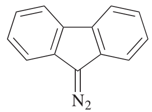
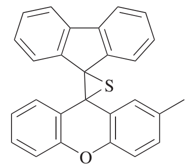
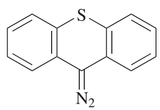
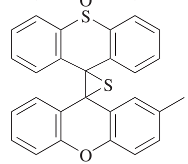
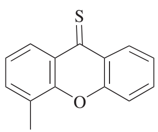
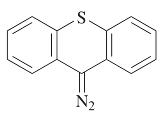
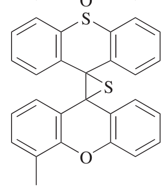
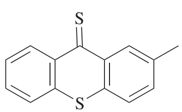
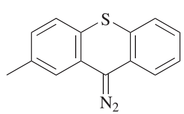
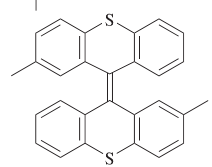
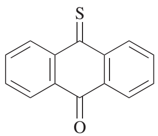
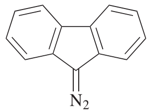
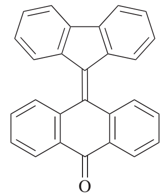
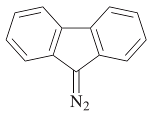
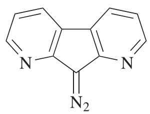
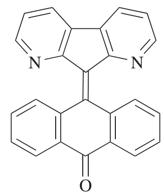
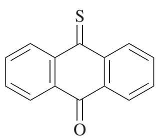
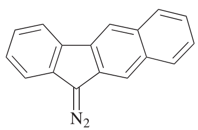
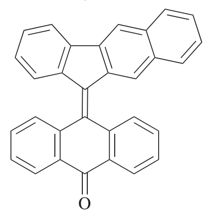
		1. Et_2O, rt, o/n 2. Cu bronze, xylene, reflux, 3 h		Ar / Ph (84) / PMP (48)	236
		Et_2O, rt, 72 h		(3)	204
		Benzene, reflux, 2 h		(41)[a]	51
		Benzene, reflux, 2 h		(27)[a]	51
		Benzene, reflux, 2 h		(21)[a]	51
		Cu, xylene, reflux		(68)	227

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}				
		$CHCl_3$, reflux, o/n	 **I** (46)	221
		1. CH_2Cl_2, rt, 48 h 2. Ph_3P, CH_2Cl_2, reflux, o/n	**I** (9)	221
		1. CH_2Cl_2, rt, 18 h 2. Ph_3P, CH_2Cl_2, reflux, 3 h	 (23)	221
		$CHCl_3$, reflux, o/n	 (13)	221

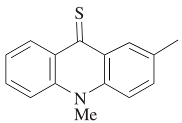
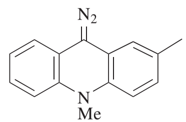
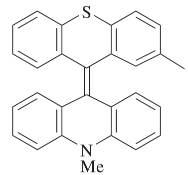
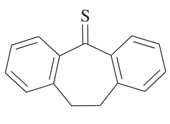
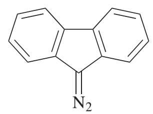
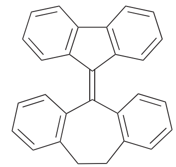
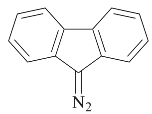
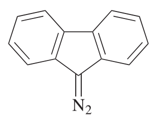
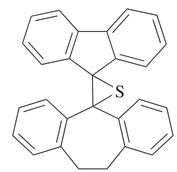
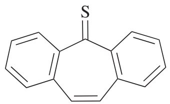
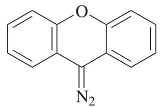
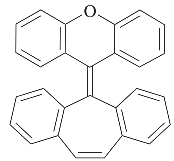
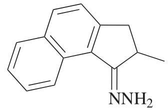
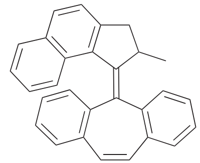
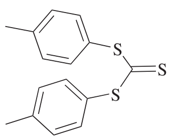
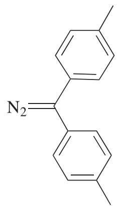
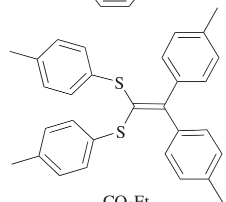
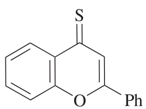
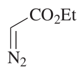
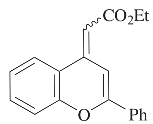
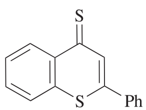
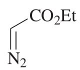
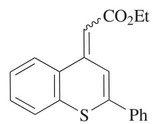
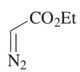
C_{15}			1. CH_2Cl_2, –10° to rt 2. Cu, xylene reflux	 (88)	227
			1. Benzene, reflux, 3 h 2. Cu bronze, toluene, reflux, 6 h	 **I** (38)	237
			1. Benzene, rt, "several days" 2. Cu powder, petroleum ether, 100°, 3 h	**I** (89)	216
			Benzene, rt, "several days"	 (90)[a]	216

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}				
		1. Benzene, rt, 30 min 2. Cu powder, petroleum Et_2O, 100°, 3 h	 (82)	216
		1. $PhI(OCOCF_3)_2$, DMF, –50°, 5 sec 2. Ph_3P, *p*-xylene, reflux, o/n	 (36)	52
		1. Et_2O, rt, 24 h 2. Cu bronze, benzene, reflux, 6 h	 (93)	79
		Cu powder, diglyme, 120°, 20 min	 (92), isomer mixture	217
		Cu powder, petroleum ether, 100°, 30 min	 **I** (96), isomer mixture	217
		Petroleum ether, 100°, 10 h	**I** (94)	53

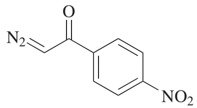
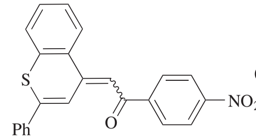
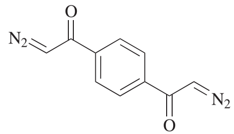
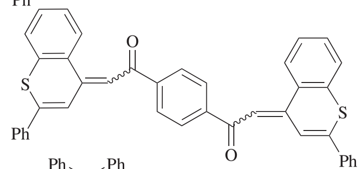
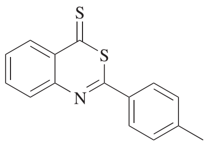
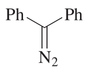
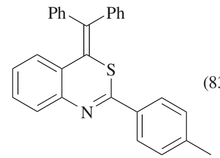
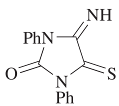
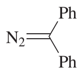
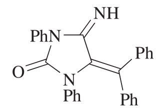
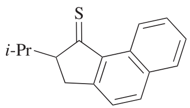
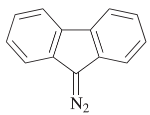
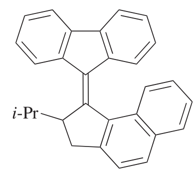
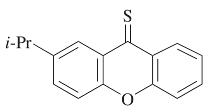
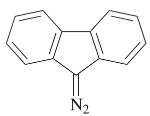
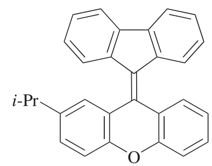
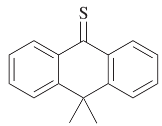
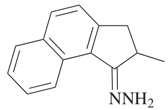
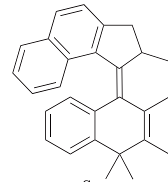
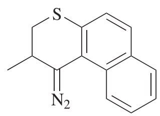
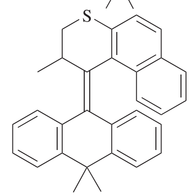
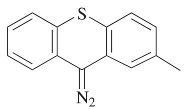
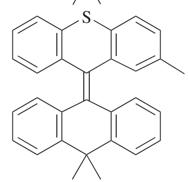
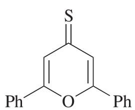
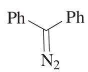
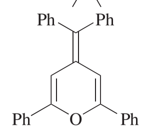
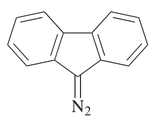
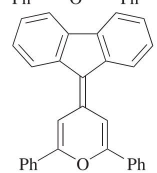
		Cu powder, diglyme, 120°, 20 min	 (87), (*Z*)/(*E*) = —	53
		Cu powder, $(EtOCH_2CH_2)_2O$, 140°, 10 min	 (88)	53
		1. Et_2O, rt, overnight 2. Cu bronze, xylene, reflux, 3 h	 (83)	236
		Et_2O, rt, 45 min	 (61)	83
C_{16}				
		1. Toluene, reflux, 6 h 2. Ph_3P, toluene, reflux, o/n	 (62)	220
		1. Benzene, reflux, 2 h 2. Ph_3P, benzene, reflux, 85 h	 (22)	225

TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

	S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{16}			1. $PhI(OCOCF_3)_2$, DMF, –50°, 5 sec 2. Ph_3P, *p*-xylene, reflux, o/n		(71)	52
			1. CH_2Cl_2, o/n 2. Cu bronze, *p*-xylene, reflux, o/n		(83)	226
			1. CH_2Cl_2, –10° to rt 2. Cu, xylene, reflux		(76)	227
C_{17}			Benzene, rt, o/n; reflux, 3 h		(33)	238
			Benzene, rt, o/n; reflux, 3 h		(26)	238

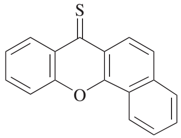
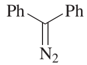
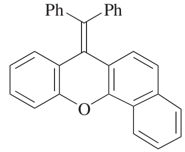
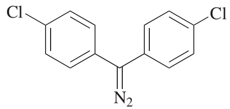
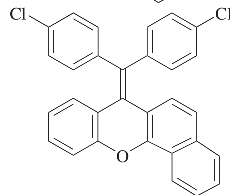
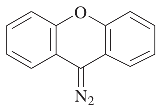
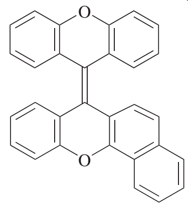
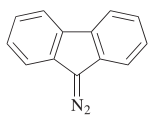
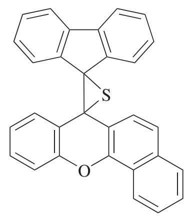
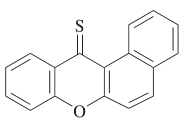
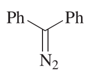
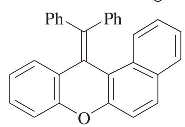
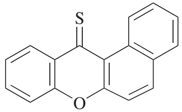
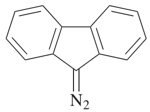
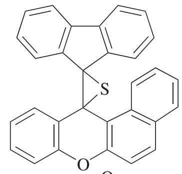
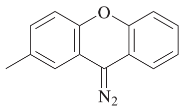
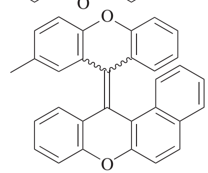
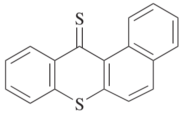
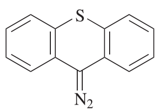
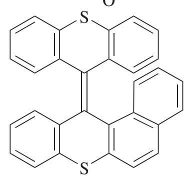
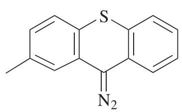
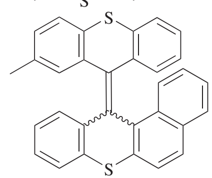
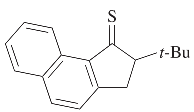
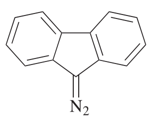
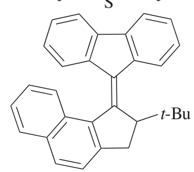
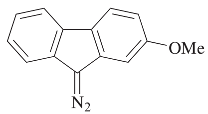
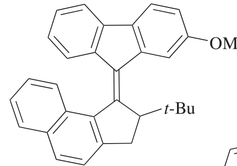
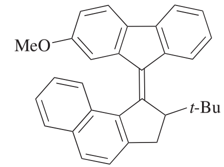
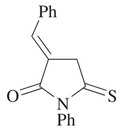
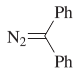
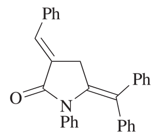
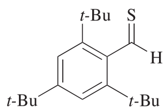
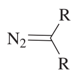
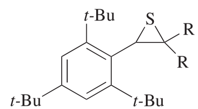
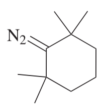
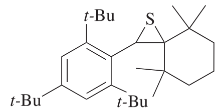
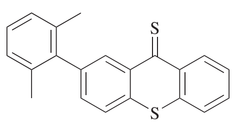
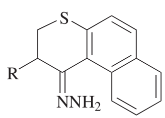
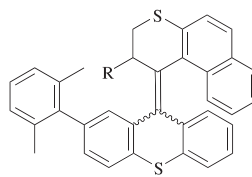
		1. Et_2O, rt[b] 2. Cu powder, xylene, reflux, 0.5 h		(—)	239
		1. Et_2O, rt[b] 2. Cu powder, xylene, reflux, 0.5 h		(—)	239
		1. Et_2O, rt[b] 2. Cu powder, xylene, reflux, 0.5 h		(—)	239
		Et_2O, reflux[b]		(—)[a]	239
		Et_2O, rt, 0.5 h		(80)	70

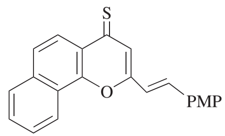
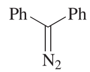
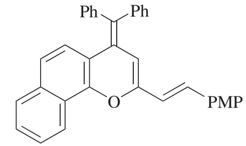
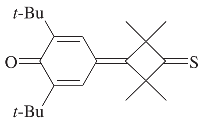
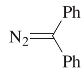
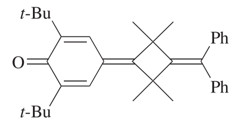
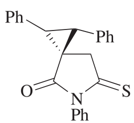
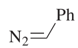
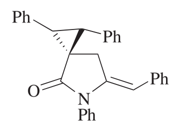
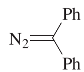
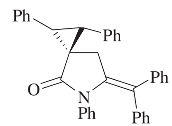
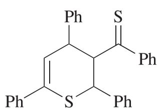
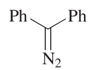
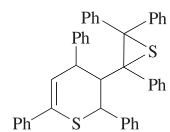
TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17} 		Et_2O, rt, 30 min	 (85)[a]	70
		1. Et_2O, rt, 0.5 h 2. Cu bronze, xylene, reflux, 1 h	 (90), (*Z*)/(*E*) = 1:1	70
		1. Et_2O 2. LAH, THF	 (—)	240
		1. Et_2O 2. LAH, THF	 (73), (*E*)/(*Z*) = 1:1	240
		1. Toluene, reflux, 6 h 2. Ph_3P, toluene, reflux, o/n	 (65)	220

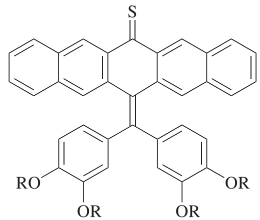
		1. Toluene, reflux, 6 h 2. Ph_3P, toluene, reflux, o/n	 (21) +  (42)	220
		Toluene, reflux, o/n	 (93)	241
C_{19}				
		Cu_2Cl_2 (cat.), THF, rt	 R: *t*-Bu (47); Ph (36)	242
		Cu_2Cl_2 (cat.), THF, rt	 (78)[a]	242
C_{21}				
		1. Ag_2O, $MgSO_4$, KOH, MeOH, CH_2Cl_2, 0°, 30 min 2. Add *S*-substrate, rt, 4 h 3. Ph_3P, toluene, reflux, 18 h		243, 244

R	(*Z*)+(*E*)	(*Z*)/(*E*)
H	(45)	1:1
Me	(82)	3.5:1

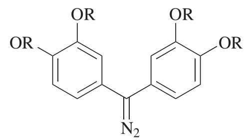
TABLE 2. ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

	S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)		Refs.
C_{21}			Benzene, reflux, 12 h		(80)	218
C_{22}			1. Et_2O, rt, 24 h 2. Ph_3P, benzene, reflux, 24 h		(84)	184
C_{24}			Toluene, reflux, 7 h		(53)	241
			Toluene, reflux, 4 h		(82)	241
C_{30}			Benzene, 50°		(51)[a]	199

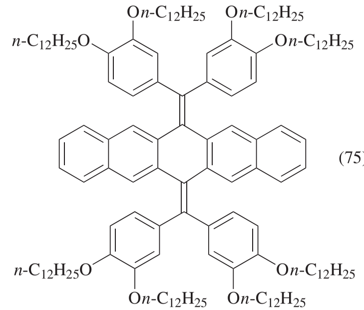
C_{35}



R = n-$C_{12}H_{25}$



1. CH_2Cl_2, rt, 1 h
2. Ph_3P, p-xylene, reflux, 12 h



(75) 116

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[a] No attempts to desulfurize this product were reported.

[b] The reaction was allowed to proceed until nitrogen evolution ceased.

[c] The intermediate episulfide was formed quantitatively.

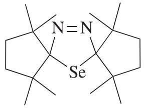
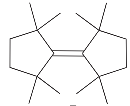
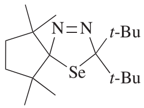
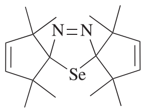
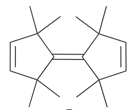
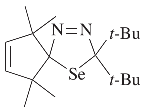
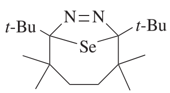
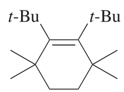
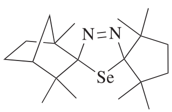
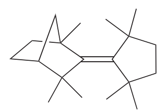
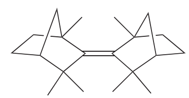
[d] The yields were determined using gas chromatography.

[e] The reaction was allowed to proceed until the thione color disappeared.

[f] The isomers were separated at the episulfide stage and separately desulfurized.

[g] Both the thione and the thiadiazoline were generated in situ.

TABLE 3. ALKENES VIA TWOFOLD EXTRUSIONS FROM ISOLATED SELENADIAZOLINES

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18}			
	Melt, 170°, 16 h	 **I** (70)	18
	Melt, 190°, 2 h	**I** (70)	18
	Melt, 190°, 24 h	**I** (—)[a]	18
	Melt, 185°, 8 h	 **I** (40)	107
	CH_2Cl_2, THF, 80°, 15 kbar, 36 h	**I** (7)[a]	18
	Melt, 100°, 2.5 h	 (43)	109
C_{19}			
	Melt, 190°, 12 h	 (29) +  (23)[a]	18

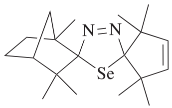
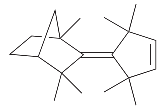
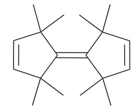
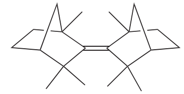
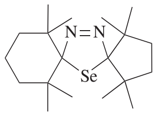
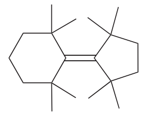
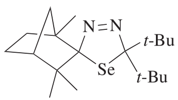
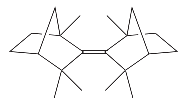
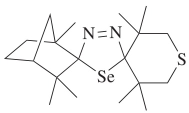
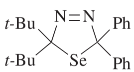
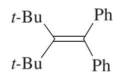
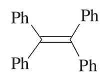
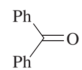
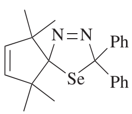
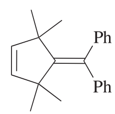
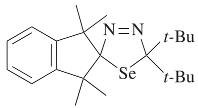
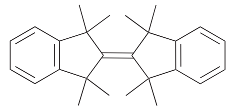
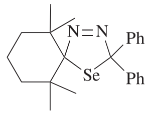
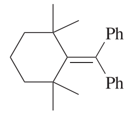
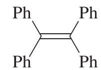
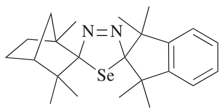
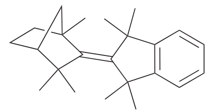
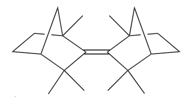
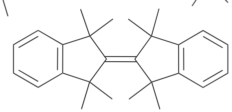
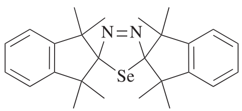
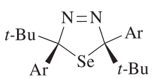
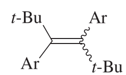
	1. Melt, 135°, 2 d 2. Melt, 170°, 4 h	 (42) +  (21)[a] +  (21)[a]	18
	Melt, 190° [b]	 (13)	108
	Melt, 190°, 24 h	 (—)[a] **I**	18
	Melt, 190°, 24 h	**I** (—)[a]	18
C_{22}			
	CCl_4, reflux, 15 h	 (67) **I**	112
	Benzene, reflux, 13 h	**I** (16) +  (12)[a] +  (55)	245
	CCl_4, reflux, 18 h	 (68)	112

TABLE 3. ALKENES VIA TWOFOLD EXTRUSIONS FROM ISOLATED SELENADIAZOLINES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{22} 	Melt, 190°, 24 h	 (—)[a]	112
C_{23} 	CCl_4, reflux, 18 h	 (80) +  (17)[a]	112
	Melt, 190°, 24 h	 (25) +  (10)[a] +  **I** (15)[a]	18
C_{26} 	Melt, 190°, 24 h	**I** (71)	18
	Melt, 190°, 5 min	**I** (50)	18
	Melt, 210°, 15 min	**I** (19)	108, 60
C_{34}  Ar = $PhOC_6H_4$	Melt, 180°, 10 min	 (85) (*Z*)/(*E*) = 1:3	246, 247

[a] This product was formed from the intial selenadiazoline via retrocyclization-recombination.

[b] The reaction was continued until nitrogen evolution ceased.

TABLE 4. ALKENES VIA TWOFOLD EXTRUSIONS FROM IN SITU GENERATED SELENADIAZOLINES

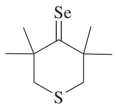
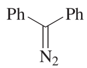
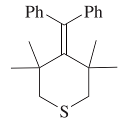
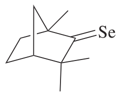
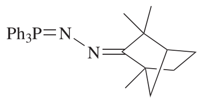
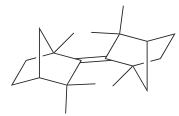
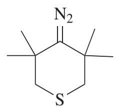
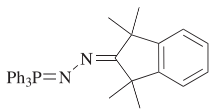
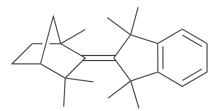
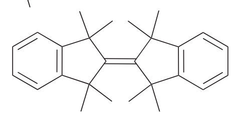
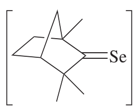
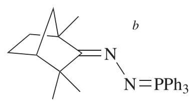
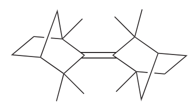
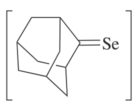
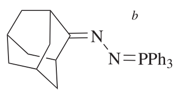
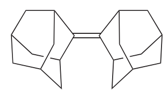
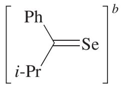
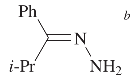
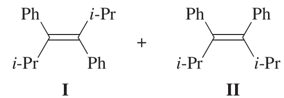
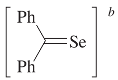
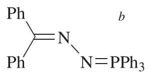
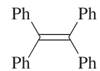
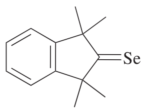
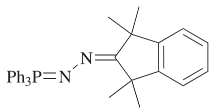
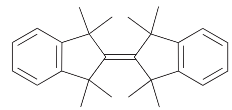
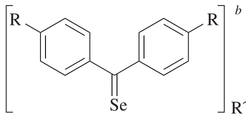
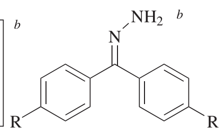
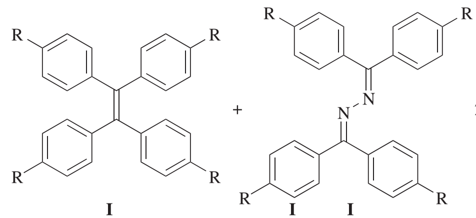
	Se-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			THF, rt, 16 h; reflux, 19 h	 (72)	110
C_{10}			Melt, 160°, 24 h	 **I** (72)	59
			Melt, 155°, 24 h	**I** (28)[a]	110
			Melt, 195°, 42 h	 (20) + **I** (8)[a] +  (12)[a]	64, 18
	 [b]	 [b]	Se, 160°, 24 h	 (24)	59
	 [b]	 [b]	Se, 160°, 24 h	 (24)	59

TABLE 4. ALKENES VIA TWOFOLD EXTRUSIONS FROM IN SITU GENERATED SELENADIAZOLINES (*Continued*)

Se-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}				
 [b]	 [b]	Se_2Br_2, Et_3N, benzene, reflux, 2 h	 **I** + **II** (42), **I**:**II** = 3:2	246
C_{13}				
 [b]	 [b]	Se, 160°, 24 h	 (84)	59
		Melt, 185°, 96 h	 (65)	64
C_{13-15}				
 [b]	 [b]	Se_2Br_2, Et_3N		245

R	Solvent	Temp (°)	Time (h)	**I**	**II**
H	CH_2Cl_2	rt	3	(72)	(2)
H	benzene	80	2	(85)	(0)
Cl	benzene	80	2	(83)	(0)
MeO	benzene	80	3	(66)	(0)
Me	CH_2Cl_2	rt	3	(44)	(34)
Me	benzene	80	2	(82)	(0)

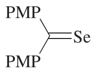
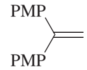
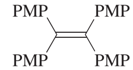
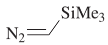
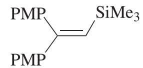
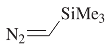
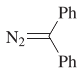
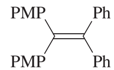
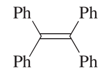
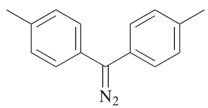
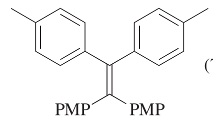
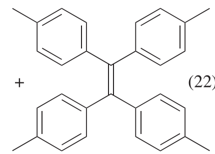
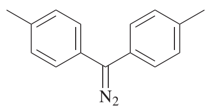
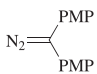
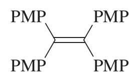
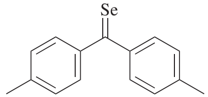
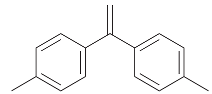
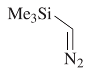
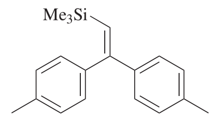
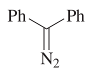
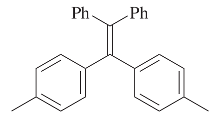
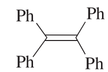
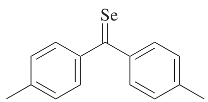
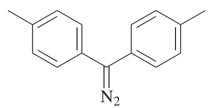
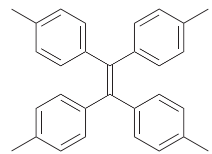
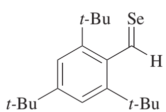
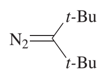
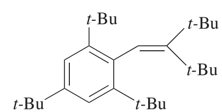
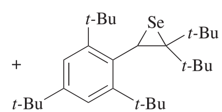
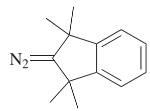
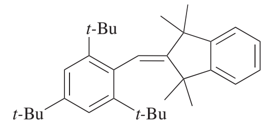
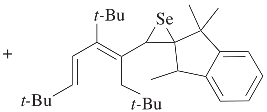
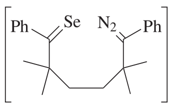
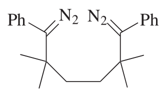
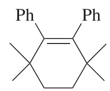
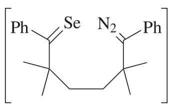
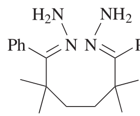
C_{13} 	CH_2N_2	Et_2O, benzene, rt, 30 min	 (50) +  **II** (5)[a]	245
		Et_2O, benzene, rt, 30 min	 **I** (62) + **II** (25)[a]	245
		THF, rt, 1 h	**I** (62) + **II** (26)[a]	248
		THF, –78° to rt, 1 h	 (34) +  (33)[a]	248
		THF, –78° to rt, 1 h	 **I** (76) +  **II** (22)[a]	248
		THF, rt, 1 h	**I** (54) + **II** (10)[a]	248
		THF, –78° to rt, 1 h	 (84)	248

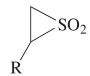
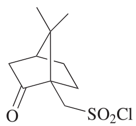
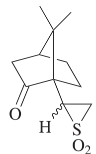
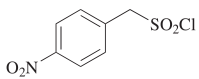
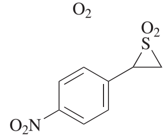
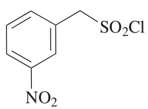
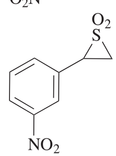
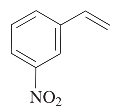
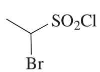
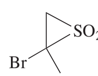
TABLE 4. ALKENES VIA TWOFOLD EXTRUSIONS FROM IN SITU GENERATED SELENADIAZOLINES (*Continued*)

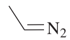
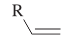
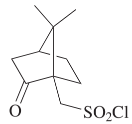
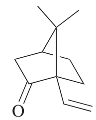
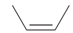
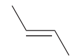
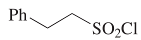
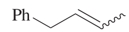
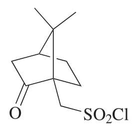
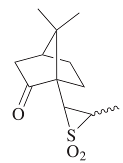
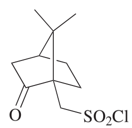
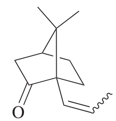
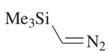
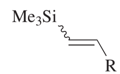
	Se-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}		CH_2N_2	Et_2O, benzene, rt, 30 min	 (48) + **II** (11)[a]	245
			THF, rt, 1 h	 (9) + **II** (31)[a]	248
			THF, rt, 1 h	 (26) +  (29)[a] + **II** (31)[a]	248
C_{15}			THF, rt, 1 h	 (75)	248
C_{19}			Cu_2Cl_2 (cat.), THF, –50°, 3h	 (—) +  (—)[c,d]	19

			Cu$_2$Cl$_2$ (cat.), THF, –50°, 3h	 (—)	19
				+  (—)[c,d]	
C_{22}	 [e]	 [e]	Se, DBU, 130°, 10 min	 **I** (64)	249
	 [b]	 [b]	Se$_2$Cl$_2$, (n-Bu)$_3$N, benzene, reflux, 6 h	**I** (12)	109, 250

[a] This product was formed from the initially formed selenadiazoline via retrocyclization-recombination.
[b] Both the selone and the diazo compound were generated in situ in this reaction.
[c] The compound is stable at –40° and was characterized by ^{1}H NMR.
[d] The alkene was produced by warming the corresponding selenirane to room temperature over 2 h.
[e] The selone and selenadiazoline were generated in situ in this reaction.

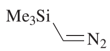
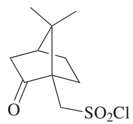
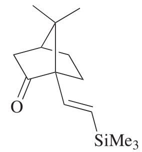
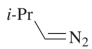
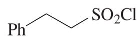
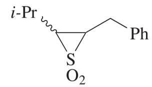
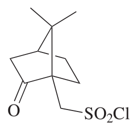
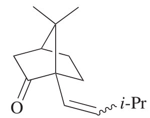
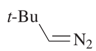
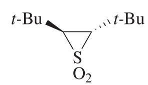
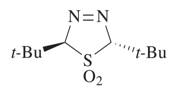
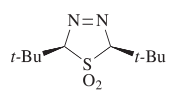
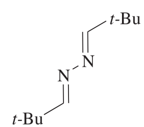
TABLE 5. ALKENES AND THIIRANE DIOXIDES VIA EXTRUSIONS OF NITROGEN AND/OR SULFUR DIOXIDE

	N-Substrate	*S*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1	CH_2N_2	SO_2	Et_2O, –10°, 2 h	$H_2C{=}CH_2$ (3)	251
		SO_2[a]	Et_2O, –10°, 2 h	 (53)	251
			Et_3N, Et_2O, 15–60 min[b]	 R / Temp (°)	
				H / 0 / (64)	28, 37
				Cl / –10 / (83)	37
				Et / 10 / (95)	28, 37
				CH_2=$CHCH_2$ / 0 / (68)	28, 37
				Ph / 0 / (35)	35
				Ph / –20 / (90)	252
				Ph / –30 / (70)	28, 37
				Bn / 0 / (99)	37
			Et_3N, Et_2O, 15–60 min[b]	 (94)	28, 37
			Et_2O, 0° [b,c]	 (—)	253
			Et_2O, 0° [b,c]	 (—) +  (—)	253
			1. Et_3N, Et_2O, 0° 2. Neat, 80°	 (64)	254

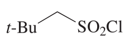
C_2 		1. Et_3N, Et_2O, 0° 2. Melt, 80°	 R: Ph (67); Bn (97)	28
		1. Et_3N, Et_2O, 0° 2. Melt, 80°	 (74)	28
	SO_2	1. Et_2O, –10 to –45° 2. Melt, >59°	 (98)[d] +  (—)[e]	34
		1.Et_3N, Et_2O, 0° 2. Melt, 80°	 (91)	28
		Et_3N, Et_2O, 0°	 (36)	28
		1. Et_3N, Et_2O, 0° 2. Melt, 80°	 (64)	28
C_4 	RCH_2SO_2Cl	Et_3N, THF, 0°, 1–2 h		255

R		(E)/(Z)
Ph	(73)	13:1
2-ClC_6H_4	(77)	10:1
4-ClC_6H_4	(80)	6:1
3,4-$Cl_2C_6H_3$	(70)	100:0
2,4-$Cl_2C_6H_3$	(76)	9:1
3-$O_2NC_6H_4$	(55)	7:1
4-$O_2NC_6H_4$	(80)	3:1
4-MeC_6H_4	(57)	100:0
Bn	(16)	100:0

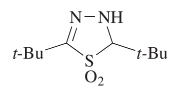
TABLE 5. ALKENES AND THIIRANE DIOXIDES VIA EXTRUSIONS OF NITROGEN AND/OR SULFUR DIOXIDE (*Continued*)

N-Substrate	*S*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		Et_3N, THF, 0°, 1h	 (46)	255
		Et_3N, Et_2O, –5°, 1 h[b]	 (75), isomer ratio = 2:1[f]	28, 37
		1. Et_3N, Et_2O, –10° 2. 80°, 10 min	 (64)	37
C_5				
	SO_2	Solvent, 5 min	 **I** +  **II** +  **III** +  **IV**	31

Solvent	Temp (°)	**I**:**II**:**III**:**IV**[g]
pentane	–95	27:55:18:2
pentane	–25	16:63:21:4
pentane	25	18:62:20:16
Et_2O	–8	29:63:4:4
Et_2O	–25	25:61:14:4
THF	–25	47:43:10:14
CH_2Cl_2	–25	58:32:10:4
MeCN	–45	77:20:3:11
MeCN	–25	73:22:5:18
EtOH	–25	63:20:7:7
2-propanol	–25	58:34:8:8
MeOH	–25	71:27:2:43



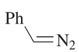
Et_3N, MeCN, – 25°, 1 h

I + **II** + **III** + 

IV **I**:**II**:**III**:**IV**[h] = 32:63:4

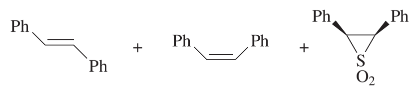
31

C_7



SO_2

SO_2, solvent

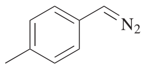
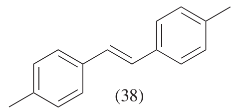
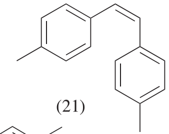
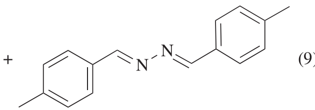
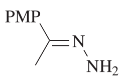
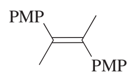
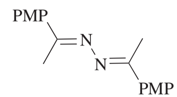
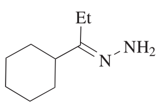
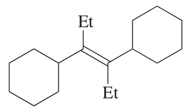
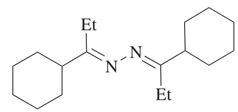
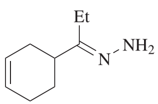
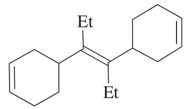


I **II** **III**

Solvent	Temp (°)	**I**	**II**	**III**
Et_2O	–20	(77)	(trace)	(23)
n-hexane	–20	(40)	(trace)	(60)
benzene	0	(59)	(trace)	(41)
Et_2O–H_2O	0	(65)	(trace)	(10)

24

TABLE 5. ALKENES AND THIIRANE DIOXIDES VIA EXTRUSIONS OF NITROGEN AND/OR SULFUR DIOXIDE (*Continued*)

N-Substrate	*S*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8				
	SO_2	SO_2, 20°, 1 h	 (38) +  (21) +  (9)[h]	27
	SO_2	1. HgO, hexanes, 20 h 2. SO_2, 3. H_2O, reflux, 2 h	 **I** (2) +  **II** (16)	88
	SO_2	1. PbO, benzene, 5 h 2. SO_2, 5–10°, 0.5 h	**I** (9) + **II** (32)	256
C_9				
	SO_2	1. HgO, KOH, petroleum ether, 0°, 1 h 2. SO_2, rt 3. 240°	 (2) +  (16)	257
	SO_2	1. HgO, KOH, petroleum ether, –5°, 2–3 h 2. SO_2, –50° 3. Cu-bronze, 250°	 **I** (4)	33
	SO_2	1. HgO, KOH, petroleum ether, –5°, 2–3 h 2. SO_2, –50° 3. FVP, 350–500°	**I** (2–6)	33

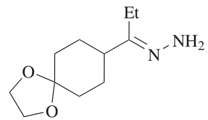
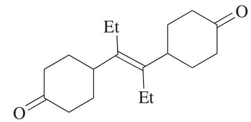
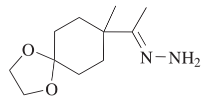
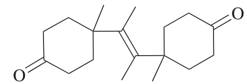
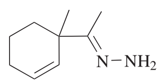
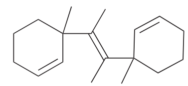
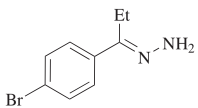
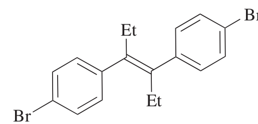
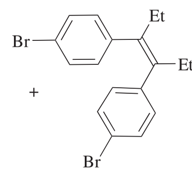
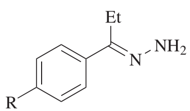
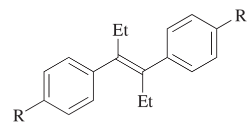
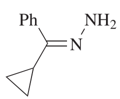
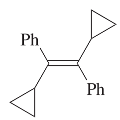
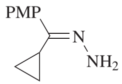
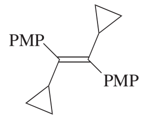
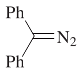
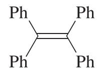
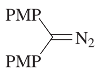
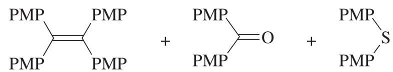
	SO_2	1. HgO, KOH, Et_3N, ether 35°, 45 min 2. SO_2, –20° 3. H_2SO_4, MeOH 4. FVP, 550°	 (5)	33
	SO_2	1. HgO, petroleum ether, 40°, 10 min 2. SO_2, –20° 3. H_2SO_4, MeOH 4. FVP, 550°	 (5)	33
	SO_2	1. HgO, petroleum ether, 40°, 10 min 2. SO_2, –20° 3. H_2SO_4, MeOH 4. FVP, 510–530°	 (1)	33
	SO_2	1. HgO, petroleum ether, <10° 2. SO_2, petroleum ether, 0° 3. 80–100°	 (70–80) +  (15–20)	258
C_{9-15}				
	SO_2	1. HgO, petroleum ether, <10° 2. SO_2, petroleum ether, 0° 3. 80–100°	 R: MeO (34); Ph (33)	258
C_{10}				
	SO_2	1. HgO, hexanes, 20 h 2. SO_2, 3. H_2O, reflux, 2 h	 (52)	88

TABLE 5. ALKENES AND THIIRANE DIOXIDES VIA EXTRUSIONS OF NITROGEN AND/OR SULFUR DIOXIDE (*Continued*)

	N-Substrate	*S*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}		SO_2	1. HgO, hexanes, 20 h 2. SO_2 3. H_2O, reflux, 2 h	 (52)	88
C_{13}		SO_2	1. SO_2, petroleum ether 2. 150°	 (20)	11
		SO_2	Solvent[b]	 **I** **II** **III**	27

Solvent	**I**	**II**	**III**
benzene	(61)	(3)	(6)
CCl_4	(64)	(18)	(12)
THF	(69)	(21)	(—)
DMF	(56)	(35)	(8)
MeCN	(11)	(67)	(—)
MeOH	(—)	(59)	(35)
EtOH	(—)	(35)	(30)

[a] The amount of SO_2 used in this reaction was 0.5 equivalents.

[b] The reaction was allowed to proceed until nitrogen evolution ceased.

[c] The excess diazomethane acted as the base.

[d] This is the yield obtained from isolated, crystalline *cis*-thiirane dioxide. The total yield of thiirane dioxides was not given.

[e] This product was obtained from residual, crude *trans*-thiirane dioxide.

[f] The configurations were not determined.

[g] The product ratios were determined by ^1H NMR spectroscopy.

[h] The yields were determined by ^1H NMR spectroscopy.

TABLE 6. ALKENES AND THIIRANE OXIDES VIA EXTRUSIONS OF NITROGEN AND/OR SULFUR MONOXIDE

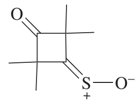
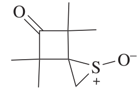
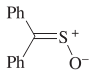
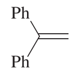
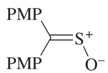
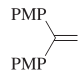
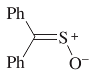
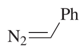
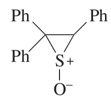
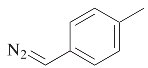
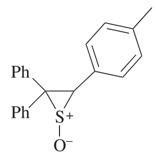
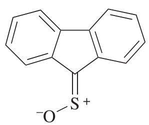
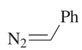
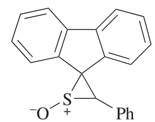
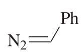
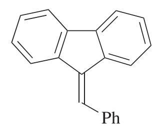
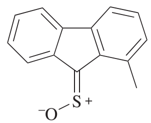
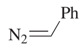
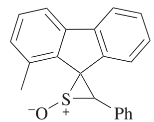
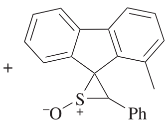
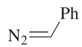
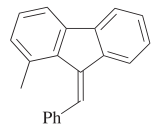
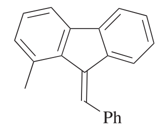
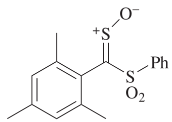
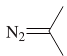
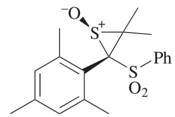
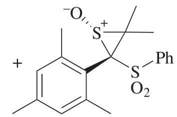
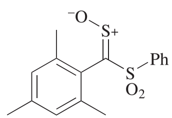
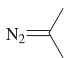
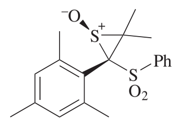
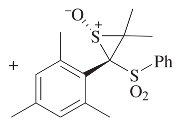
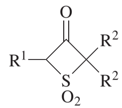
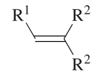
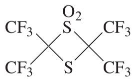
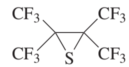
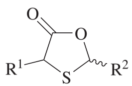
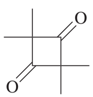
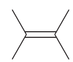
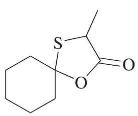
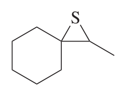
S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8 	CH_2N_2	1. Et_2O, 3°, 24 h 2. –20°, 3 d	 (29)	25
C_{13} 	CH_2N_2	Et_2O, rt, 48 h	 (60)	259
	CH_2N_2	Et_2O, rt, 48 h	 (35)	259
		Pentane, rt, 4 h	 (21)[a]	21
		Pentane, rt, 4 h	 (22)[a]	21
		Et_2O, 0°, 1 h	 (65)[a]	21
		1. Et_2O, 0°, 1 h 2. Benzene, reflux	 (65)	21

TABLE 6. ALKENES AND THIIRANE OXIDES VIA EXTRUSIONS OF NITROGEN AND/OR SULFUR MONOXIDE (*Continued*)

	S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			Et_2O, 0°, 24 h	 (35)[a] +  (4)[a]	21
			1. Et_2O, 0°, 24 h 2. CCl_4, rt	 (20)[b] +  (20)[b]	21
C_{16}			Et_2O, benzene, 0°	 (36) +  (36)	22
			Et_2O, benzene, 0°	 (36) +  (36)	22

[a] A mixture of stereoisomers was obtained.
[b] The yields were determined by ^{1}H NMR spectroscopy.

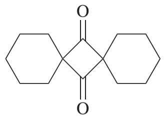
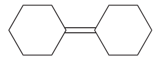
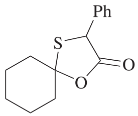
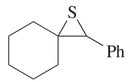
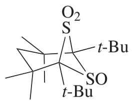
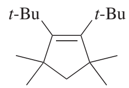
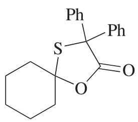
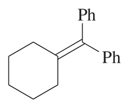
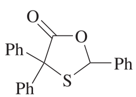
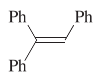
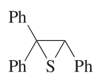
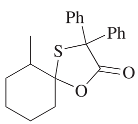
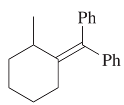
TABLE 7. ALKENES VIA MISCELLANEOUS EXTRUSIONS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{3-9} 	FVP, 930–950°		92
		R1 R2: H H (96–98); H Me (96–98); Ph H (96–98)	
C_6 	hν, benzene	 (—)	260
C_{7-15} 	FVP	 I + II	40
C_8 	hν, benzene	 (80)	261
C_9 	FVP, 750°	 (94)	40

R^1	R^2	*cis*/*trans*	Temp (°)	**I + II**	**I:II**
Me	*n*-Pr	63:37	750	(95)	38:62
Me	Ph	59:41	650	(93)	42:58
Ph	Me	67:33	650	(89)	33:67
Ph	Ph	62:38	600	(84)	35:65
Ph	Ph	40:60	600	(86)	63:37
Ph	Ph	10:90	600	(—)	92:8
Ph	Ph	89:11	600	(—)	14:86

R^1	R^2	Yield
H	H	(96–98)
H	Me	(96–98)
Ph	H	(96–98)

TABLE 7. ALKENES VIA MISCELLANEOUS EXTRUSIONS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14} 	$h\nu$, benzene–CH_2Cl_2	 (61)	90
	FVP, 700°	 (97)	40
C_{17} 	DMI, 224°, 1 h	 (69)	109
C_{20} 	$(Et_2N)_3P$, 160–200°, 5 h	 (82)	12
C_{21} 	$(Et_2N)_3P$, 150–160°, 2 h	 (95)	12
	Neat, 130°, 2 h	 (23)	39
	$(Et_2N)_3P$, 200–240°, 6 h	 (88)	12

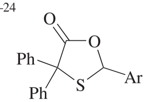
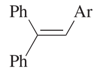
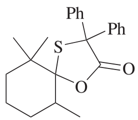
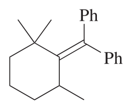
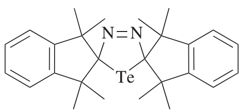
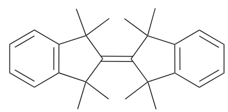
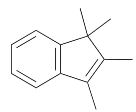
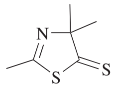
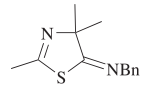
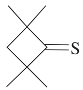
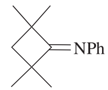
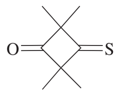
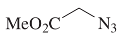
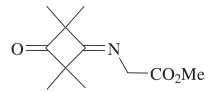
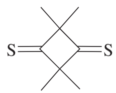
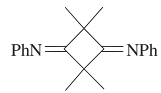
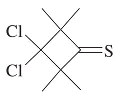
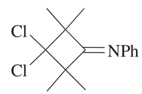
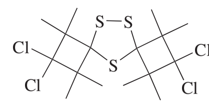
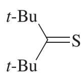
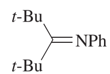
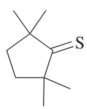
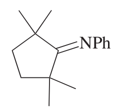
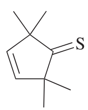
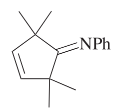
C_{21-24} 	Neat, 150°, 20 h	 Ar: Ph (78); C_6D_5 (69); 2-BrC_6H_4 (56); 3-BrC_6H_4 (59); 4-BrC_6H_4 (47); 3-ClC_6H_4 (57); 4-ClC_6H_4 (84); 2-$O_2NC_6H_4$ (55); 3-$O_2NC_6H_4$ (72); 4-$O_2NC_6H_4$ (60); 2-$MeOC_6H_4$ (49); 3-$MeOC_6H_4$ (55); 4-$MeOC_6H_4$ (73); 4-$BnOC_6H_4$ (59); (*E*)-PhCH=CH (85); 4-*i*-PrC_6H_4 (85)	39
C_{23} 	$(Et_2N)_3P$, 180–230°, 4 h	 (80)	12
C_{26} 	Melt, 160°, 6 h	 **I** (27) +  **II** (54)	262
	Melt, 200°, 6 h	**I** (15) + **II** (72)	262

TABLE 8. IMINES VIA TWOFOLD EXTRUSIONS OF NITROGEN AND SULFUR

	S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6		BnN_3	Neat, 80°, 24 h	 (68)	263
C_8		PhN_3	Neat, 100°, 10 h	 (47)	264
			Neat, 80°, 8 h	 (19)	41
		PhN_3	Benzene, 40–50°, 5 d	 (70)[a]	152, 13
		PhN_3	Neat, 80°, 10 h	 (—) +  (36)	265
C_9		PhN_3	Benzene, 40°, 6 d	 (55)[a]	152, 13
		PhN_3	Benzene, 40°, 6 d	 (82)[a]	152, 13
		PhN_3	Benzene, 40–50°, 6 d	 (35)[a]	152, 13

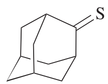
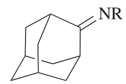
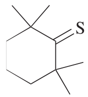
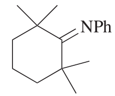
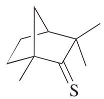
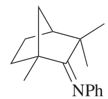
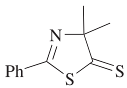
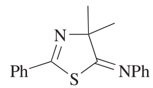
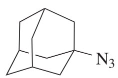
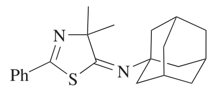
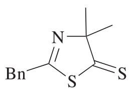
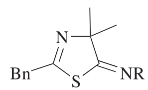
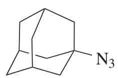
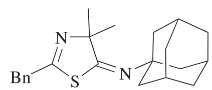
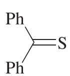
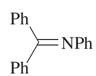
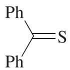
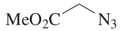
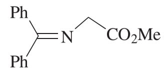
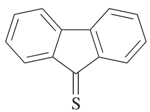
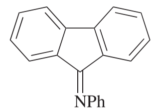
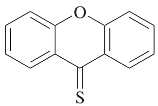
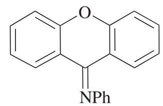
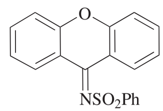
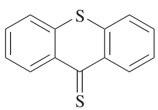
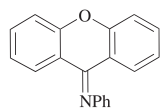
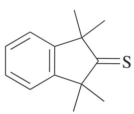
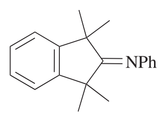
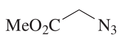
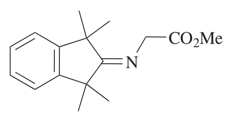
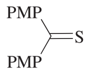
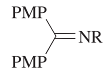
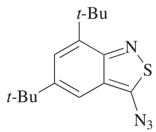
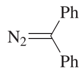
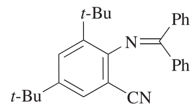
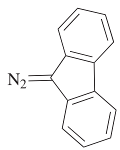
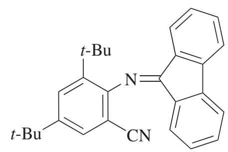
C_{10}		RN_3	Neat, 80°	 R / Time (h): MeO_2CCH_2 1.0 (17); *n*-Bu 1.5 (36); Ph 2.5 (34); Bn 2.5 (18)	266, 266, 266, 41
		PhN_3	Benzene, 40–50°, 5 h	 (52)[a]	152, 13
		PhN_3	Toluene, 60–80°, 1 wk	 (20)[b]	13
C_{11}		PhN_3	Neat, 80°, 18 h	 (61)	41
			Toluene, 90°, 8 h	 (71)	41
C_{12}		RN_3	Neat, 80°, 18 h	 R: Bn (65); MeO_2CCH_2 (76)	41, 263
			Toluene, 90°, 8 h	 (21)	263
C_{13}		PhN_3	80°, 35 min	 **I** (72)	264
		PhN_3	110°, 2 h	**I** (—)	267

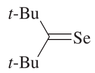
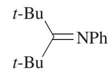
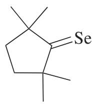
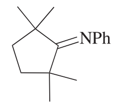
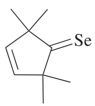
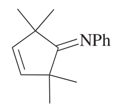
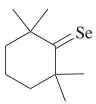
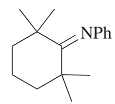
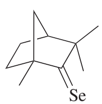
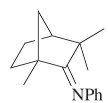
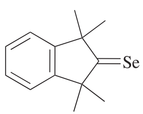
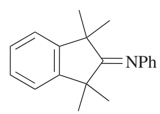
TABLE 8. IMINES VIA TWOFOLD EXTRUSIONS OF NITROGEN AND SULFUR (*Continued*)

	S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}			80°, 3 h	 (60)	41
		PhN_3	80°, 4 min	 (83)	264
		PhN_3	110°, 4 h	 (—)	267
		$PhSO_2N_3$	Xylene, reflux, 2 h	 (60)	267
		PhN_3	80°, 2 h	 (79)	264
		PhN_3	Benzene, 40–50°, 2 wk	 (70)[b]	152, 13
			Benzene, reflux, 9 h	 (64)[b]	41

	RN_3	Neat		R	Temp (°)	Time (h)		
				Ph	110	2	(—)	267
				Ph	80	1	(85)	264
				Bn	110	2.5	(82)	267
				1-$C_{10}H_7$	120	2.5	(63)	267
		Hexanes, rt, 3 d	 (78)					43
		Hexanes, rt, 3 d	 (80)					43

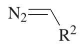
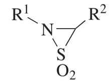
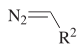
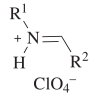
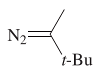
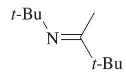
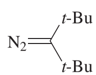
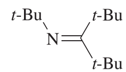
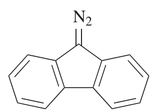
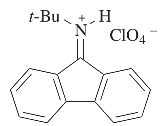
[a] The yield was determined by GC.
[b] The yield is based on recovered thione.

TABLE 9. IMINES VIA TWOFOLD EXTRUSIONS OF NITROGEN AND SELENIUM

	Se-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9		PhN_3	Benzene, 40–50°, 4 d	 (55)	152, 13
		PhN_3	Benzene, 40–50°, 1.5 d	 (82)	152, 13
		PhN_3	Benzene, 60°, 3 d	 (35)	152, 13
C_{10}		PhN_3	Benzene, rt, 12 h	 (52)	152, 13
		PhN_3	Toluene, 60–80°, 1 wk	 (94)[a]	152, 13
C_{13}		PhN_3	Benzene, reflux, 14 h	 (50)	152, 13

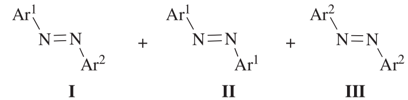
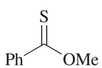
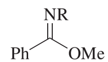
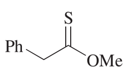
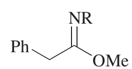
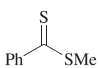
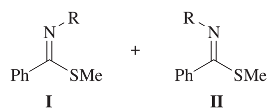
[a] The yield is based on recovered selone.

TABLE 10. IMINES AND THIAZIRIDINE-1,1-DIOXIDES VIA EXTRUSIONS OF NITROGEN AND SULFUR DIOXIDE

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{4-10}				
R^1NHSO_2Cl		Et_3N, Et_2O, –78°, 2.5 h	 R^1 / R^2 t-Bu / t-Bu (41–47) t-Bu / 1-adamantyl (35) 1-adamantyl / t-Bu (32) 1-adamantyl / 1-adamantyl (45)	106
		1. Et_3N, Et_2O, –78°, 2.5 h 2. $HClO_4$, HOAc	 R^1 / R^2 t-Bu / t-Bu (91) t-Bu / 1-adamantyl (—) 1-adamantyl / t-Bu (—) 1-adamantyl / 1-adamantyl (—)	106
C_4				
t-$BuNHSO_2Cl$		Et_3N, Et_2O, –78°, 2.5 h	 (7)[a]	106
		Et_3N, Et_2O, –78°, 2.5 h	 (30)[a,b]	106
		1. Et_3N, Et_2O, –60° to rt, 0.5 h 2. $HClO_4$, HOAc	 (47)	106

[a] The yield was determined by ^1H NMR spectroscopy.
[b] This product was characterized as the perchlorate salt.

TABLE 11. OTHER X=Y SYSTEMS VIA TWOFOLD EXTRUSIONS

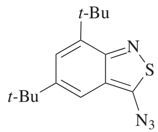
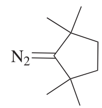
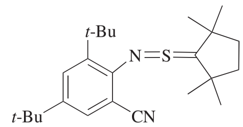
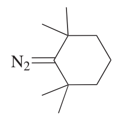
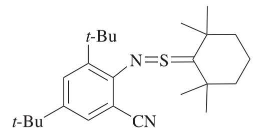
	S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{6-12}	$Ar^1N{=}S{=}O$	Ar^2N_3	Chlorobenzene, reflux, 72 h[a]		268
C_7		RN_3[d]	Neat, 110°, 6 h		105
C_8		RN_3[d]	Neat, 110°, 6 h		105
		RN_3[d]	Neat, 110°, 6–8 h		105

Ar^1	Ar^2	**I + II + III**
Ph	Ph	(~60)[b]
4-ClC_6H_4	Ph	(~60)[b,c]
4-$MeOC_6H_4$	4-ClC_6H_4	(~60)[b,c]
4-MeC_6H_4	4-$MeOC_6H_4$	(~60)[b,c]
2-PhC_6H_4	4-MeC_6H_4	(~60)[b,c]

R	
MeO_2CCH_2	(90)
Bn	(65)

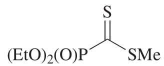
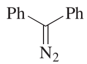
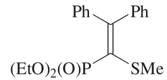
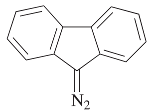
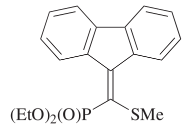
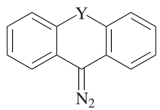
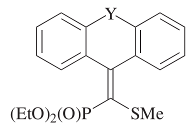
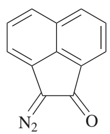
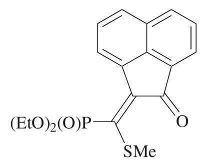
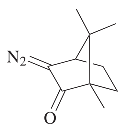
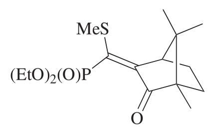
R	
Ph	(68)
MeO_2CCH_2	(41)[e]
Bn	(74)

R	**I + II**	**I:II**
MeO_2CCH_2	(30)	1:1
Bn	(82)	1:1

C_{15} 		Hexanes, rt, 3 d		(50)	43
		Hexanes, 30°, 2 d		(98)	43

[a] The same products were obtained by irradiation in benzene at room temperature.
[b] The yield was determined by GC.
[c] The unsymmetrical azo compound predominated. No further details were provided.
[d] An excess of the azide was used.
[e] The imidate was unstable and hydrolyzed to the corresponding amide upon workup.

TABLE 12. SUPPLEMENTAL TABLE ENTRIES 2008–2009:
ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES

	S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_1			1. THF, –60°, 30 min 2. $(Et_2N)_3P$, THF, reflux, 1.5 h	 (65)	269
			1. THF, –60°, 30 min 2. $(Et_2N)_3P$, THF, reflux, 1.5 h	 (58)	269
			1. THF, –60°, 30 min 2. $(Et_2N)_3P$, THF, reflux, 1.5 h	 Y / O (74) / S (54)	269
			1. THF, –60°, 30 min 2. $(Et_2N)_3P$, THF, reflux, 1.5 h	 (55)[a]	269
			1. THF, rt, 1 h 2. $(Et_2N)_3P$, THF, reflux, 1.5 h	 (70)[a]	269

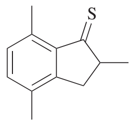
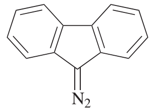
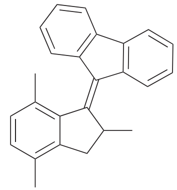
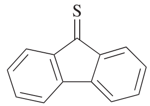
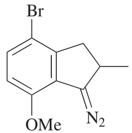
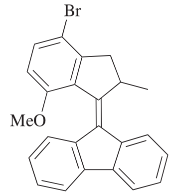
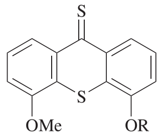
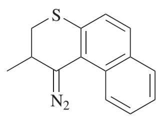
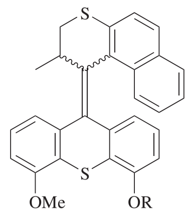
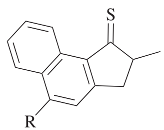
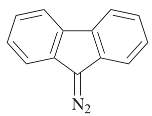
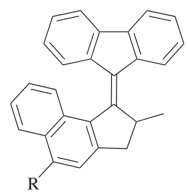
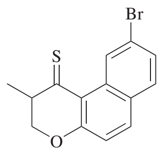
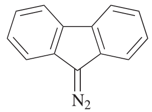
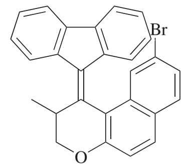
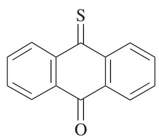
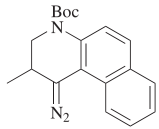
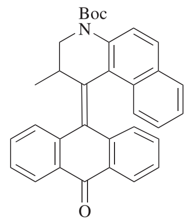
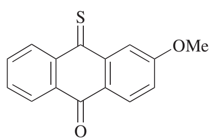
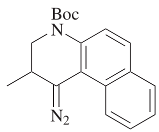
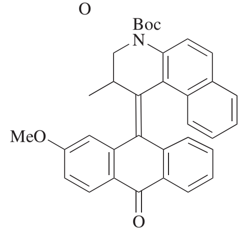
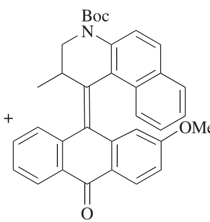
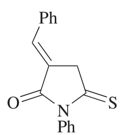
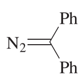
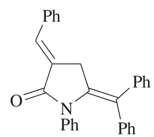
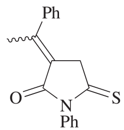
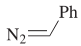
C_{12}			Toluene, 80°, 5 h		(18)	132
C_{13}			1. DMF, CH_2Cl_2, –50° to rt, o/n 2. Ph_3P, toluene, reflux, 60 h		(25)	270
			1. CH_2Cl_2, 0° to rt, 16 h 2. Reagent, *p*-xylene, reflux		R / Reagent / Time (h) Me / Cu-bronze / 16 / (45) Ac / Ph_3P / 16 / (65)[c] Bz / Ph_3P / 72 / (43)[c]	271
C_{14}			1. Benzene, reflux, 4 h 2. Ph_3P, toluene, reflux, 12 h		R MeO (71) Cl (30)	272

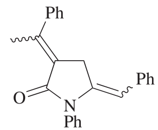
TABLE 12. SUPPLEMENTAL TABLE ENTRIES 2008–2009:
ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

	S-Substrate	*N*-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}			1. Toluene, reflux, o/n 2. Ph_3P, toluene, reflux, o/n	 (29)	273
			1. $CHCl_3$, rt, 30 min 2. Ph_3P, toluene, reflux, o/n	 (53)	274
			1. $CHCl_3$, rt, 30 min 2. Ph_3P, toluene, reflux, o/n	 (24) +  (16)	274
C_{17}			Toluene, reflux, o/n	 (93)	241





Toluene reflux, 6 h

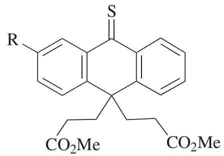


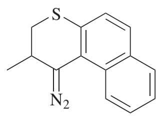
(38)

$(Z,Z)/(E,Z)/(Z,E)/(E,E)$ = 65:20:10:5

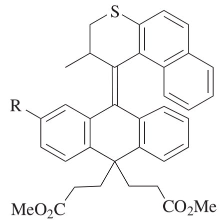
241

C_{20}





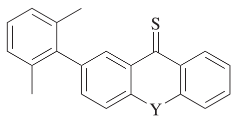
1. CH_2Cl_2, rt, 4 h
2. Cu bronze, *p*-xylene, reflux, time

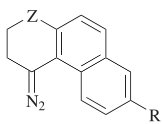


R	Time 2		
H	18 h	(77)	
OMe	1 d	(43)	(*Z*) + (*E*)

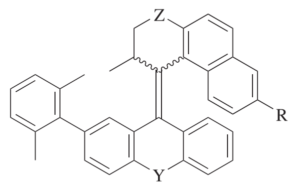
275

C_{21}





1. CH_2Cl_2, rt, 3 h
2. Cu powder, *p*-xylene, reflux, o/n



Y	Z	R		(*Z*)/(*E*)
S	CH_2	Me	(14)	1:1
S	O	H	(85)	—
O	S	H	(71)	—
O	CH_2	Me	(69)	—
O	O	H	(68)	—

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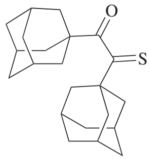
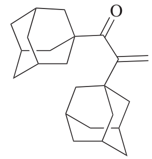
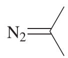
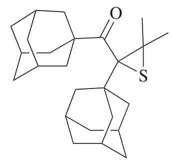
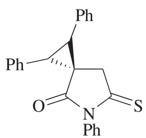
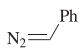
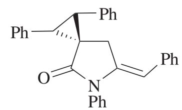
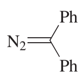
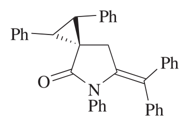
TABLE 12. SUPPLEMENTAL TABLE ENTRIES 2008–2009: ALKENES AND THIIRANES VIA EXTRUSIONS FROM IN SITU GENERATED THIADIAZOLINES (*Continued*)

S-Substrate	N-Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{22} 	CH_2N_2	1. Et_2O,THF, –65° to rt, 3 h; reflux, 2 h 2. $(Et_2N)_3P$, THF, reflux	 (84)	277
		Et_2O, THF, –65° to rt, 3 h; reflux, 1 h	 (64)	277
C_{24} 		Toluene, reflux, 7 h	 (53)	241
		Toluene, reflux, 4 h	 (82)	241

[a] Only the (*Z*) isomers was observed.

[b] Only the (*E*) isomers was observed.

[c] A mixture of (*E*) and (*Z*) isomers was obtained.

REFERENCES

[1] Smith, M. B.; March, J. In *Advanced Organic Chemistry VI*; Wiley: New York, 2007; pp 1553–1558.
[2] Smith, M. B.; March, J. In *Advanced Organic Chemistry V*; Wiley: New York, 2001; pp 937–941.
[3] Guziec, F. S., Jr.; SanFilippo, L. J. *Tetrahedron* **1988**, *44*, 6241.
[4] Paine, A. J.; Warkentin, J. *Can. J. Chem.* **1981**, *59*, 491.
[5] Stark, B. P.; Duke, A. J. *Extrusion Reactions*; Pergamon: Oxford, 1967.
[6] Paquette, L. *Org. React.* **1977**, *25*, 1.
[7] Taylor, R. J. K. *Org. React.* **2003**, *62*, 357.
[8] Shiosaki, K. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds., Pergamon: Oxford, 1991; Vol. 2, p. 865.
[9] Schaap, A. P.; Faler, G. R. *J. Org. Chem.* **1973**, *38*, 3061.
[10] Mlostoń, G.; Heimgartner, H. *Helv. Chim. Acta* **1996**, *79*, 1785.
[11] Staudinger, H.; Pfenninger, F. *Chem. Ber.* **1916**, *49*, 1941.
[12] Barton, D. H. R.; Willis, B. J. *J. Chem. Soc., Perkin. Trans. 1* **1972**, 305.
[13] Guziec, F. S., Jr.; Moustakis, C. A. *J. Chem. Soc., Chem. Commun.* **1984**, 63.
[14] Kellogg, R. M.; Wassenaar, S. *Tetrahedron Lett.* **1970**, *11*, 1987.
[15] Kellogg, R. M.; Wassenaar, S.; Buter, J. *Tetrahedron Lett.* **1970**, *11*, 4689.
[16] Kellogg, R. M. *Tetrahedron Lett.* **1976**, *32*, 2165.
[17] Mlostoń, G.; Heimgartner, H. *Pol. J. Chem.* **2000**, *74*, 1503.
[18] Guziec, F. S., Jr.; Murphy, C. J.; Cullen, E. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 107.
[19] Watanabe, S.; Kawashima, T.; Okazaki, R. *Chem. Lett.* **1994**, 1289.
[20] Woodward, R. B.; Hoffmann, R. *Angew. Chem. Int. Ed. Eng.* **1969**, *81*, 797.
[21] Bonini, B. F.; Capelli, A.; Maccagnani, G.; Mazzanti, G. *Gazz. Chim. Ital.* **1975**, *105*, 827.
[22] Thijs, L.; Wagenaar, A.; van Rens, E. M. M.; Zwanenburg, B. *Tetrahedron Lett.* **1973**, *14*, 3589.
[23] Bonini, B. F.; Maccagnani, G.; Wagenaar, A.; Thijs, L.; Zwanenburg, B. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2490.
[24] Tokura, N.; Nagai, T.; Matsumura, S. *J. Org. Chem.* **1966**, *31*, 349.
[25] Zwanenburg, B.; Wagenaar, A.; Thijs, L.; Strating, J. *J. Chem. Soc., Perkin Trans. 1,* **1973**, 73.
[26] Hartzell, G. E.; Paige, J. N. *J. Org. Chem.* **1967**, *32*, 459.
[27] Tanabe, T.; Nagai, T. *Tetrahedron Lett.* **1978**, *19*, 1545.
[28] Opitz, G.; Fischer, K. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 70.
[29] Opitz, G. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 107.
[30] Quast, H.; Kees, F. *Chem. Ber.* **1981**, *114*, 802.
[31] Quast, H.; Kees, F. *Chem. Ber.* **1981**, *114*, 787.
[32] Nazarov, A. M.; Nikolaev, A. I.; Serenko, S. Y.; Komissarov, V. D. *Bull. Acad. Sci. USSR* **1990**, *39*, 2257.
[33] Inhoffen, H. H.; Jonas, R.; Krösche, H.; Eder, U. *Liebigs Ann. Chem.* **1966**, *19*, 694.
[34] Neureiter, N. P. *J. Am. Chem. Soc.* **1966**, *88*, 558.
[35] Matsumura, S.; Nagai, T.; Tokura, N. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 635.
[36] Hesse, G.; Majmudar, S. *Chem. Ber.* **1960**, *93*, 1129.
[37] Fischer, N. H. *Synthesis* **1970**, 393.
[38] Barton, D. H. R.; Willis, B. J. *J. Chem. Soc., Chem. Commun.* **1970**, 1225.
[39] Pedersen, C. T. *Acta Chem. Scand. Ser. B* **1968**, *22*, 247.
[40] Cameron, T. B.; Pinnick, H. W. *J. Am. Chem. Soc.* **1980**, *102*, 744.
[41] Mlostoń, G.; Romański, J.; Linden, A.; Heimgartner, H. *Pol. J. Chem.,* **1996**, *70*, 880.
[42] Mlostoń, G.; Romański, J.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta,* **1993**, *76*, 2147.
[43] Takahashi, M; Okazaki, R.; Inamoto, N.; Sugawara, T.; Iwamura, H. *J. Am. Chem. Soc.* **1992**, *114*, 1830.
[44] Motoki, S.; Saito, T. *Sulfur Reports*, **1984**, *4*, 33.
[45] Collazo, R.; Guziec, F. S., Jr. *J. Org. Chem.* **1993**, *58*, 43.
[46] Buter, J.; Wassenaar, S.; Kellogg, R. M. *J. Org. Chem.* **1972**, 37, 4045.
[47] Talma, A. G.; Goorhuis, J. G. M.; Kellogg, R. M. *J. Org. Chem.* **1980**, *45*, 2544.
[48] Huisgen, R.; Langhans, E. *Tetrahedron Lett.* **1989**, *30*, 5369.

[49] Huisgen, R.; Langhans, E. *Heteroatom Chem.* **2006**, *17*, 433.
[50] Barton, D. H. R.; Guziec, F. S., Jr.; Shahak, I. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1794.
[51] Schönberg, A.; Sidky, M. M. *J. Am. Chem. Soc.* **1959**, *81*, 2259.
[51a] Beiner, J. M.; Lecadet, D.; Paquer, D.; Thuillier, A.; Vialle, J. *Bull. Soc. Chim. Fr.* **1973**, 1979.
[52] ter Wiel, M. K. J.; Vicario, J.; Davey, S. G.; Meetsma, A.; Feringa, B. L. *Org. Biomol. Chem.* **2005**, *3*, 28.
[53] Schönberg, A.; Frese, E. *Chem. Ber.* **1963**, *96*, 2420.
[54] Schönberg, A.; Frese, E. German Patent DE 1241438 (1967).
[55] Kägi, M.; Linden, A.; Mlostoń, G.; Heimgartner, H. *Helv. Chim. Acta* **1996**, *79*, 855.
[56] Whittingham, W. G. In *Comprehensive Organic Functional Group Transformations II*; Katritzky, A. R.; Taylor, R. J. K., Eds.; Elsevier: Oxford, 1995; Vol. 3, p 330.
[57] Cooper, N. J. In *Comprehensive Organic Functional Group Transformations II*; Katritzky, A. R.; Taylor, R. J. K., Eds.; Elsevier: Oxford, 1995; Vol. 3, p 309.
[58] Varma, R. S.; Kumar, D. *Org. Lett.* **1999**, 697.
[59] Back, T. G.; Barton, D. H. R.; Britten-Kelly, M. R.; Guziec, F. S., Jr. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2079.
[60] Krebs, A.; Rüger, W.; Nickel, W. *Tetrahedron Lett.* **1981**, *22*, 4937.
[61] Guziec, F. S., Jr.; Guziec, L. S. In *Comprehensive Organic Functional Group Transformations II*; Katritzky, A, R.; Taylor, R. J. K., Eds.; Elsevier: Oxford, 2005, Vol. 3, p 397.
[62] Guziec, F. S., Jr.; Guziec, L. S. In *Organoselenium Chemistry, A Practical Approach*; Back, T. G., Ed.; Oxford University Press, 1999; pp 193–206.
[63] Guziec, F. S., Jr.; Guziec, L. J. In *Comprehensive Organic Functional Group Transformations I*; Katritzky, A. R., Ed.; Pergamon: New York, 1995; Vol. 3, p 381.
[64] Cullen, E. R.; Guziec, F. S., Jr.; Hollander, M. I.; Murphy, C. J. *Tetrahedron Lett.* **1981**, *22*, 4563.
[65] Guziec, F. S., Jr.; Moustakis, C. A. *J. Org. Chem.* **1984**, *49*, 189.
[66] Okuma, K.; Kojima, K.; Kaneko, I.; Tsuijimoto, Y.; Ohta, H.; Yokomori, Y. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2151.
[67] Guziec, F. S., Jr.; San Filippo, L. J.; Murphy, C. J.; Moustakis, C. A.; Cullen, E. R. *Tetrahedron* **1985**, *41*, 4843.
[68] Staudinger, H.; Siegwart, J. *Helv. Chim. Acta* **1920**, *3*, 833.
[69] Rall, K.; Sundermeyer, W. *J. Fluorine Chem.* **1990**, *47*, 121.
[70] Latif, N.; Fathy, I. *Can. J. Chem.* **1966**, *44*, 1075.
[71] See ref. 51a.
[72] Hogeveen, H.; Kingma, R. F.; Kok, D. M. *J. Org. Chem.* **1982**, *47*, 1910.
[73] McCombie, S. W., swmcc.orxn@verizon.net, 28 Hanford Place, Caldwell, NJ, 07006, personal communication.
[74] Padwa, A.; Kinder, F. R.; Nadler, W. R.; Zhi, L. *Heterocycles* **1993**, *35*, 367.
[75] Takano, S.; Tomita, S.-I.; Takahashi, M.; Ogasawara, K. *Synthesis* **1987**, 1116.
[76] Egli, D. H.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **2006**, *89*, 1910.
[77] Kim, G.; Chu-Meyer, M. Y.; Danishefsky, S. J.; Schulte, G. K. *J. Am. Chem. Soc.* **1993**, *115*, 30.
[78] Fang, F. G., Prato, M.; Kim, G.; Danishefsky, S. J. *Tetrahedron Lett.* **1989**, *28*, 3625.
[79] Schönberg, A.; von Vargha, L. *Liebigs Ann. Chem.* **1930**, *483*, 176.
[80] Schönberg, A.; König, B.; Frese, E. *Chem. Ber.* **1965**, *98*, 3303.
[81] Choi, N.; Tokitoh, N.; Goto, M.; Ando, W. *Tetrahedron*. **1993**, *49*, 1189.
[82] Tokitoh, N.; Choi, N.; Ando, W. *Chem. Lett.* **1987**, 2177.
[83] Mohamed, Y. A.; Ammar, Y. A.; El-Sharief, A. M.; Aly, M. M. *J. Chin. Chem. Soc. (Taipei)* **1990**, *37*, 511.
[84] Mlostoń, G.; Heimgartner, H. *Helv. Chim. Acta* **1992**, *75*, 1825.
[85] Petit, M.; Linden, A.; Mlostoń, G.; Heimgartner, H. *Helv. Chim. Acta* **1994**, *77*, 1076.
[86] Mlostoń, G.; Petit, M.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **1994**, *77*, 435.
[87] Emayan, K.; English, R. F.; Kouentis, P. A.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3345.
[88] Bennett, J. G., Jr.; Bunce, S. C. *J. Org. Chem.* **1960**, *25*, 73.

[89] Cameron, T. B.; Pinnick, H. W. *J. Am. Chem. Soc*. **1979**, *101*, 4755.
[90] Leermakers, P.; Vesley, G.; Turro, N.; Neckers, D. *J. Am. Chem. Soc*. **1964**, *86*, 4213.
[91] Strating, J.; Zwanenburg, A.; Wagenaar, A; Udding, A. *Tetrahedron Lett*. **1969**, *10*, 125.
[92] McIntosh, C. L.; deMayo, P. *J. Chem. Soc., Chem. Commun*. **1969**, 32.
[93] Schönberg, A.; König, B.; Singer, E. *Chem. Ber*. **1967**, *100*, 767.
[94] Huisgen, R.; Mlostoń, G. *Pol. J. Chem*., **1999**, *73*, 635.
[95] Kalwinsch, I., Xingya, L.; Gottstein, J.; Huisgen, R. *J. Am. Chem. Soc*. **1981,** *103*, 7032.
[96] Krapcho, A. P.; Rao, D. R.; Silvon, M. P.; Abegaz, B. *J. Org. Chem*. **1971**, *36*, 3885.
[97] Krapcho, A. P.; Silvon, M. P.; Goldberg, I.; Jahngen, E. G. E. *J. Org. Chem*. **1974**, *39*, 860.
[98] Mlostoń, G.; Huisgen, R. *Tetrahedron Lett.* **1989**, *30*, 7045.
[99] Sustmann. R.; Sicking, W.; Huisgen, R. *J. Org. Chem.* **1993**, *58*, 82.
[100] Kägi, M.; Linden, A.; Mlostoń, G.; Heimgartner, H. *Helv. Chim. Acta* **1998**, *81*, 285.
[101] Mlostoń, G.; Romański, J.; Heimgartner, H. *Pol. J. Chem.* **2002**, *76*, 551.
[102] Guziec, F. S., Jr.; SanFilippo, L. J. *J. Org. Chem*. **1991**, *56*, 3178.
[103] Brooks, P. R.; Bishop, R.; Craig, D. C.; Scudder, M. L.; Counter, J. A. *J. Org. Chem.* **1993**, *58*, 5900.
[104] Guziec, F. S., Jr.; Guziec, L. J., unpublished results.
[105] Mlostoń, G.; Romański, J.; Heimgartner, H. *Pol. J. Chem.* **2001**, *75*, 975.
[106] Quast, H.; Kees, F. *Chem. Ber*. **1981**, *114*, 774.
[107] Cullen, E. R.; Guziec, F. S., Jr.; Murphy, C. J. *J. Org. Chem*. **1982**, *47*, 3563.
[108] Krebs, A.; Rüger, W.; Ziegenhagen, B.; Hebold, M.; Hardtke, I.; Müller, R.; Schutz, M.; Wietzke, M.; Wilke, M. *Chem. Ber.* **1984**, *117*, 277.
[109] Ishii, A.; Furusawa, K.; Omata, T.; Nakayama, J. *J. Org. Chem*. **2000**, *65*, 1799.
[110] Guziec, F. S., Jr.; Murphy, C. J. *J. Org. Chem.* **1980**, *45*, 2890.
[111] Krebs, A.; Kaletta, B.; Nickel, W.; Rüger, W.; Tikwe, L. *Tetrahedron* **1986**, *42*, 1693.
[112] Cullen, E. R.; Guziec, F. S., Jr. *J. Org. Chem*. **1986**, *51*, 1212.
[113] Feringa, B. L. *Acc. Chem. Res*. **2001**, *34*, 504.
[114] Jager, W. F.; de Jong, J. C.; de Lange, B.; Huck, N. P. M.; Meetsma, A.; Feringa, B. L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 348.
[115] Hoogesteger, F. J.; Havenith, R. W. A.; Zwikker, J. W.; Jenneskens, L. W.; Kooijman, H.; Veldman, N.; Spek, A. L. *J. Org. Chem*. **1995**, *60*, 4375.
[116] Xiao, S.; Tang, J.; Beetz, T.; Guo, X.; Tremblay, N.; Siegrist, T.; Zhu, Y.; Steigerwald, M.; Nuckolls, C. *J. Am. Chem. Soc*. **2006**, *128*, 10700.
[117] Belser, P.; Bernard, S.; Blum, C.; Beyeler, A.; De Cola, L.; Balzani, V. *Coord. Chem. Rev*. **1999**, *109*, 155.
[118] Maercker, A. *Org. React.* **1965**, *14*, 270.
[119] Wadsworth, W. S. *Org. React.* **1977**, *25*, 73.
[120] Maryanoff, B. E.; Reitz, A. B. *Chem. Rev*. **1989**, *89*, 863.
[121] Kelly, S. E. In *Comprehensive Organic Synthesis: Selectivity, Strategy and Efficiency in Modern Organic Chemistry*; Trost, B.; Fleming, I.; Schreiber, S. L., Eds.; Pergamon: Oxford, 1991; Vol. 1, p 729.
[122] Ager, D. J. *Org. React*. **1990**, *38*, 1.
[123] Pine, S. H. *Org. React*. **1993**, *43*, 1.
[124] Beadham, I; Mickelfield, J. *Curr. Org. Synth*. **2005**, *2*, 231.
[125] Lenoir, D. *Synthesis* **1989**, 883.
[126] McMurry, J. E.; Fleming, M. P. *J. Org. Chem.* **1976**, *41*, 896.
[127] McMurry, J. E.; Fleming, M. P.; Kees, K. I.; Krepski, L. R. *J. Org. Chem.* **1978**, *43*, 3255.
[128] Olah, G. A.; Prakash, G. K. S. *J. Org. Chem.* **1977**, *42*, 580.
[129] Lenoir, D.; Burghard, H. *J. Chem. Res. (S)* **1980**, 396.
[130] Villiers, C.; Vandais, A.; Ephritikhine, M. J. *Organomet. Chem*. **2001**, *617*, 744.
[131] Coe, P. L.; Scriven, C. E. *J. Chem. Soc., Perkin Trans. 1* **1986**, 475.
[132] Pollard, M. M.; Meetsma, A.; Feringa, B. L. *Org. Biomol. Chem.* **2008**, *6*, 507.
[133] Jager, W. F.; de Lange, B.; Schoevaars, A. M.; van Bolhuis, F.; Feringa, B. L. *Tetrahedron: Asymmetry* **1993**, *4*, 1481.

[134] Levy, A.; Biedermann, P. U.; Cohen, S.; Agranat, I. *J. Chem. Soc. Perkin. Trans. 2* **2000**, 725.
[135] Nelsen, S. F.; Kapp, D. L. *J. Am. Chem. Soc.* **1986**, *108*, 1265.
[136] Jones, G.; *Org. React.* **1967**, *15*, 204.
[137] Murphy, P. J.; Brennan, J. *Chem. Soc. Rev*. **1988**, *17*, 1.
[138] Bergmann, E. D.; Solomonovici, A. *Synthesis* **1970**, 183.
[139] Widequist, S., *Arkiv Kemi*. **1945**, *B20*, 7.
[140] Tsujikawa, T.; Nakagawa, Y.; Tsukamura, K.; Masuda, K. *Heterocycles* **1977**, *6*, 261.
[141] Tsujikawa, T.; Nakagawa, Y.; Tsukamura, K.; Masuda, K. *Chem. Pharm. Bull.* **1977**, *25*, 2775.
[142] Bates, H. A.; Farina, J. *J. Org. Chem*. **1985**, *50*, 3843.
[143] Roth, M.; Dubs, P.; Gotschi, E.; Eschenmoser, A. *Helv. Chim. Acta* **1971**, *54*, 710.
[144] Dayagi, S.; Degani, Y. In *The Chemistry of the Carbon-Nitrogen Double Bond*; Patai, S., Ed.; Wiley and Sons: New York, 1970.
[145] Love, B. E.; Ren, J. *J. Org. Chem*. **1993**, *58*, 5556.
[146] Weingarten, H.; Chupp, J. P.; White, W. A. *J. Org. Chem*. **1967**, *32*, 3246.
[147] Bee, L.; Beeby, J.; Everett, J.; Garratt, P. *J. Org. Chem*. **1975**, *40*, 2212.
[148] Smith, L. I.; Howard, K. L. *Org. Synth., Coll. Vol. 3*, **1955**, 351.
[149] Klages, C. P.; Voss, J. *Chem. Ber*. **1980**, *113*, 2255.
[150] Whitlock, H. W. *J. Am. Chem. Soc*. **1962**, *84*, 2807.
[151] Mlostoń, G.; Romański, J.; Schmidt, C.; Reisenauer, H. P.; Maier, G. *Chem. Ber.* **1994**, *127*, 2527.
[152] Moustakis, C. A. Ph. D. Dissertation, Tufts University, 1984.
[153] Seitz, G.; Hoffmann, H. *Synthesis* **1977**, 201.
[154] Seitz, G.; Hoffmann, H. *Arch. Pharm*. **1977**, *310*, 757.
[155] Middleton, W. J. *J. Org. Chem*. **1969**, *34*, 3201.
[156] Everett, J. W.; Garratt, P. J. *J. Chem. Soc., Chem. Commun*. **1972**, 642.
[157] Diebert, C. D. *J. Org. Chem*. **1970**, *35*, 1501.
[158] Woźnicka, M.; Rutkowska, M.; Mlostoń, G.; Majchrzak, A.; Heimgartner, H. *Pol. J. Chem*. **2006**, *80*, 1683.
[159] Krapcho, A. P.; Horn, D. E.; Rao, D. R.; Abegaz, B. *J. Org. Chem*. **1972**, *37*, 1575.
[160] Huisgen, R.; Mlostoń, G.; Giera, H.; Langhals, E.; Polborn, K.; Sustmann, R. *Eur. J. Org. Chem.* **2005**, 1519.
[161] Gierra, H.; Huisgen, R.; Langhals, E.; Polborn, K. *Helv. Chim. Acta.*, **2002**, *85*, 1298.
[162] Huisgen, R.; Mlostoń, G. *Tetrahedron Lett*. **1985**, *26*, 1049.
[163] Huisgen, R.; Mlostoń, G.; Pröbstl, A. *Tetrahedron Lett.* **1985**, *26*, 4331.
[164] Bachi, M. D.; Goldberg, O.; Gross, A.; Vaya, J. *J. Org. Chem.* **1980**, *45*, 1481.
[165] de Meijere, A.; Wenck, H.; Zöllner, S.; Merstetter, P.; Arnold, A.; Gerson, F.; Schreiner, P. R.; Boese, R.; Bläser, D.; Gleiter, R.; Kozhushkov, S. I. *Chem.—Eur. J.* **2001**, *7*, 5382.
[166] Romański, J.; Mlostoń, G.; Szynkiewicz, S. *Synthesis* **2003,** 2259.
[167] Pedersen, L. D.; Weiler, L. *Can. J. Chem.* **1977**, *55*, 782.
[168] Rupp, H.; Schwarz, W.; Musso, H. *Chem. Ber*. **1983**, *116*, 2554.
[169] Redlof, H.; Vögtle, F.; Puff, H.; Reuter, H.; Woller, P. *J. Chem. Res. (M)* **1984**, 2910.
[170] Bushby, R.; Mann, S.; Jesudason, M. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2457.
[171] Sauter, H.; Horster, H.; Prinzbach, H. *Angew. Chem., Int. Ed. Engl*. **1973**, *12*, 991.
[172] Kabe, Y.; Takata, T.; Ueno, K.; Ando, W. *J. Am. Chem. Soc*. **1984**, *106*, 8174.
[173] Bushby, R. J.; Pollard, M. D.; McDonald, W. S. *Tetrahedron Lett*. **1978**, *19*, 3851.
[174] Bushby, R. J.; Pollard, M. D. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2401.
[175] Shah, J. N. *Indian J. Chem., Sect. B* **1979**, *18*, 271.
[176] Garratt, P. J.; Payne, D.; Tocher, D. A. *J. Org. Chem*. **1990**, *55*, 1909.
[177] Krebs, A.; Rüger, W. *Tetrahedron Lett*. **1979**, *15*, 1305.
[178] Schweiker, O.; Netscher, T.; Knothe, L.; Prinzbach, H. *Chem. Ber*. **1984**, *117*, 2045.
[179] Loerzer, T.; Gerke, R.; Lüttke, W. *Tetrahedron Lett*. **1983**, *24*, 5861.
[180] McMurry, J. E.; Haley, G. J.; Matz, J. R.; Clardy, J. C.; Van Duyne, G.; Gleiter, R.; Schäfer, W.; White, D. H. *J. Am. Chem. Soc*. **1986**, *108*, 2932.

[181a]Kellogg, R. M.; Noteboom, M.; Kaiser, J. M. *Tetrahedron.* **1976**, 32, 1641.
[181b]Kellogg, R. M.; Noteboom, M.; Kaiser, J. M. *J. Org. Chem.* **1975**, 40, 2573.
[182] Sugihara, Y.; Noda, K.; Nakayama, J. *Bull. Chem. Soc. Jpn*. **2000**, *73*, 2351.
[183] Langhals, E.; Huisgen, R. *Heteroatom Chem*. **2006**, *17*, 443.
[184] Freund, W.; Hünig, S. *J. Org. Chem*. **1987**, *52*, 2154.
[185] McMurry, J. E.; Haley, G. J.; Matz, J. R.; Clardy, J. C.; Mitchell, J. *J. Am. Chem. Soc*. **1986**, *108*, 515.
[186] Hartke, K.; Kumar, A.; Koster, J.; Henssen, G.; Kissel, T.; Kampchen, T. *Chem. Ber*. **1982**, *115*, 3096.
[187] Beiner, J. M.; Lecadet, D.; Paquer, D.; Thuillier, A. *Bull. Soc. Chim. Fr.* **1973**, 1983.
[188] Middleton, W. J.; Sharkey, W. H. *J. Org. Chem*., **1965**, *30*, 1384.
[189] Paquer, D.; Vialle, J. *Bull. Soc. Chim. Fr*. **1969**, 3327.
[190] Bushby, R. J.; Pollard, M. D. *Tetrahedron Lett.* **1977**, 3941.
[191] Bushby, R.; Mann, S. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2497.
[192] Huisgen, R.; Mlostoń, G.; Fulka, C. *Heterocycles* **1985**, *23*, 2207.
[193] Huisgen, R.; Mlostoń, G. *Heterocycles* **1990**, *30*, 737.
[194] Kägi, M.; Mlostoń, G.; Heimgartner, H. *Pol. J. Chem*. **1998**, *72*, 678.
[195] Mlostoń, G.; Urbaniak, K.; Lesniak, S.; Wasiak, P.; Heimgartner, H. *Heterocycles* **2007**, *72*, 541.
[196] Bernard, S.; Belser, P. *Synth. Commun*. **1996**, *26*, 3559.
[197] Kang, K.-T.; U, J.-S.; Yoon, I.-N.; Park, C. H. *J. Korean Chem. Soc*. **1991**, *35*, 292.
[198] Egli, D. H.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **2007**, *90*, 86.
[199] Egli, D. H.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **2006**, *89*, 3041.
[200] Metzer, P. *Bull. Soc. Chim. Fr*. **1973**, 2297.
[201] Kägi, M.; Linden, A.; Heimgartner, H.; Mlostoń, G. *Helv. Chim. Acta* **1993**, *76*, 1715.
[202] Huisgen, R.; Mlostoń, G.; Pröbstl, A. *Heteroatom Chem*. **2001**, *12*, 136.
[203] Bernard, S.; Belser, P. *Synthesis* **1996**, 192.
[204] Kägi, M.; Mlostoń, G.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **1994**, *77*, 1299.
[205] Shimasaki, T.; Kato, S.-I.; Shinmyozu, T. *J. Org. Chem*. **2007**, *72*, 6251.
[206] El-Kateb, A. A.; Hennawy, I. T; Shabana, R.; Osman, F. H. *Phosphorus and Sulfur* **1984**, *20*, 329.
[207] Staudinger, H.; Siegwart, J. *Helv. Chim. Acta* **1920**, *3*, 833.
[208] Kalwinsch, I.; Huisgen, R. *Tetrahedron Lett.* **1981**, *22*, 3941.
[209] Lesniak, S.; Mlostoń, G.; Urbaniak, K.; Wasiak, P.; Linden, A.; Heimgartner, H. *Tetrahedron* **2006**, *62*, 7776.
[210] Mlostoń, G.; Gendek, T.; Heimgartner, H. *Helv. Chim. Acta* **1996**, *79*, 1537.
[211] Mlostoń, G.; Celeda, M.; Linden, A.; Heimgartner, H. *Heterocycles* **2006**, *68*, 33.
[212] Schönberg, A.; Brosowski, K.; Singer, E. *Chem. Ber.* 1**962,** *95*, 1910.
[213] Schönberg, A.; Junghans, K. *Chem. Ber*. **1962**, *95*, 2137.
[214] Schönberg, A.; Frese, E. *Chem. Ber*. **1962**, *95*, 2811.
[215] Latif, N.; Fathy, I. *J. Org. Chem*. **1962**, *27*, 1633.
[216] Schönberg, A.; Frese, E. *Chem. Ber*., **1968**, *101*, 701.
[217] Schönberg, A.; Frese, E. *Chem. Ber*., **1968**, *101*, 694.
[218] Schönberg, A.; Fateen, A. E. K.; Sammour, A. E. M. A. *J. Am. Chem. Soc.* **1957**, *74*, 6020.
[219] Levy, A.; Cohen, S.; Agranat, I. *Org. Biomol. Chem*. **2003**, *1*, 2755.
[220] Vicario, J.; Walko, M.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc*. **2006**, *128*, 5127.
[221] Levy, A.; Pogodin, S.; Cohen, S.; Agranat, I. *Eur. J. Org. Chem*., **2007**, 5198.
[222] Mataka, S.; Ishi-i, S.; Tashiro, M. *J. Org. Chem*. **1978**, *43*, 3730.
[223] Schönberg, A.; Nickel, S. *Chem. Ber*. **1931**, *64*, 2323.
[224] See ref. 218.
[225] Levy, A.; Biedermann, P. U.; Agranat, I. *Org. Lett*. **2000**, *2*, 1811.
[226] Koumura, N.; Geertsema, E. M.; van Gelder, M. B.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc*. **2002**, *124*, 5037.
[227] Feringa, B. L.; Jager, W. F.; de Lange, B. *Tetrahedron Lett*. **1992**, *33*, 2887.

[228] Biedermann, P. U.; Stezowski, J. J.; Agranat, I. *Chem.—Eur. J.* **2006**, *12*, 3345.
[229] van Delden, R. A.; ter Weil, M. K. J.; de Jong, H.; Meetsma, A.; Feringa, B. L. *Org. Biomol. Chem.* **2004**, *2*, 1531.
[230] Feringa, B. L.; Jager, W. F.; de Lange, B.; Meijer, E. W. *J. Am. Chem. Soc.* **1991**, *113*, 5468.
[231] Oosterling, M. L. C. M., Schoevaars, A. M.; Haitjema, H. J.; Feringa, B. L. *Israel J. Chem.* **1996**, *36*, 341.
[232] Morin, J.-F.; Shirai, Y.; Tour, J. M. *Org. Lett.,* **2006**, *8*, 1714.
[233] van Delden, R. A.; Hurenkamp, J. H.; Feringa, B. L. *Chem.—Eur. J.* **2003**, *9*, 2845.
[234] van Delden, R. A.; Koumura, N.; Schoevaars, A.; Meetsma, A.; Feringa, B. L. *Org. Biomol. Chem.* **2003**, *1*, 33.
[235] Levy, A.; Biedermann, P. U.; Cohen, S.; Agranat, I. *J. Chem. Soc., Perkin Trans. 2* **2001**, 2329.
[236] Latif, N.; Zeid, I.; Assad, F. *Indian J. Chem. Sect. B* **1981**, *20*, 432.
[237] Mills, N. S.; Malandra, J. L.; Burns, E. E.; Green. A.; Unruh, K. E.; Kadlecek, D. E.; Lowery, J. A. *J. Org. Chem.* **1997**, *62*, 9318.
[238] Schönberg, A.; Elkaschef, M.; Nosseir, M.; Sidky, M. M. *J. Am. Chem. Soc*, **1958**, *80*, 6312.
[239] Mustafa, A.; Latif, N.; El-Namaky, H. *Recl. Trav. Chim. Pays-Bas* **1965**, *84*, 1386.
[240] Feringa, B. L.; Jager, W. F.; de Lange, B. *J. Chem. Soc., Chem. Commun.* **1993**, 288.
[241] Seyfried, M. S.; Linden, A.; Mlostoń, G.; Heimgartner, H. *Helv. Chim. Acta* **2009**, *92*, 1800.
[242] Kawashima, T.; Watanabe, S.; Okazaki, R. *Chem. Lett.* **1992,** 1603.
[243] Schoevaars, A. M.; Kruizinga, W.; Zijlstra, R. W. J.; Veldman, N.; Spek, A. L.; Feringa, B. L. *J. Org. Chem.* **1997**, *62*, 4943.
[244] ter Weil, M. K. J.; van Delden, R. A.; Meetsma, A.; Feringa, B. L. *Org. Biomol. Chem.* **2005**, *3*, 4071.
[245] Okuma, K.; Kojima, K., Oyama, K.; Kubo, K.; Shioji, K. *Eur. J. Org. Chem.* **2004**, 820.
[246] Okuma, K.; Izaki, T.; Kubo, K.; Shioji, K.; Yokomori, Y. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1121.
[247] Okuma, K.; Kubo, K.; Yokomori, Y. *Heterocycles* **2003**, *60*, 299.
[248] Okuma, K.; Kojima, K.; Ohta, H. *Phosphorus, Sulfur Silicon Relat. Elem.* **1993**, *80*, 259.
[249] Ishii, A.; Tsuchiya, C.; Shimada, T.; Furusawa, K.; Omata, T.; Nakayama, J. *Heteroatom Chemistry*, **2002**, *13*, 351.
[250] Ishii, A.; Ding, M.-X.; Nakayama, J.; Hoshino, M. *Chem. Lett.* **1992**, 2289.
[251] Hesse, G.; Reichold, E.; Majmudar, S. *Chem. Ber.* **1957**, *90*, 2106.
[252] Bordwell, F. G.; Williams, J. M.; Hoyt, E. B.; Jarvis, B. B. *J. Am. Chem. Soc.* **1968**, *90*, 429.
[253] Rossi, S.; Maiorana, S. *Tetrahedron Lett.* **1966**, *4*, 263.
[254] Carpino, L. A.; Rynbrandt, R. H. *J. Am. Chem. Soc.* **1966**, *88*, 5682.
[255] Aoyama, T.; Toyama, S.; Tamaki, N.; Shioiri, T. *Chem. Pharm. Bull.* **1983**, *31*, 2957.
[256] Brophy, G. C.; Collins, D. J.; Hobbs, J. J. *Aust. J. Chem*, **1975**, *28*, 151.
[257] Hesse, G.; Reichold, E. *Chem. Ber.* **1957**, *90*, 2101.
[258] Vargha, L.; Kovacs, E. *Chem. Ber.* **1942**, *75*, 794.
[259] Vernier, C. G.; Gibbs, C. G. *Tetrahedron Lett.* **1972**, *13*, 2293.
[260] Middleton, W. J. U.S. Patent 3,136,781 (1963).
[261] Turro, N.; Byers, G. W.; Leermakers, P. *J. Am. Chem. Soc.* **1964**, *86*, 955.
[262] Minoura, M.; Kawashima, T.; Okazaki, R. *Tetrahedron Lett.* **1997**, *38*, 2501.
[263] Mlostoń, G.; Romański, J.;. Linden, A.; Heimgartner, H. *Helv. Chim. Acta,* **1995**, *78*, 1067.
[264] Mlostoń, G.; Heimgartner, H. *Helv. Chim. Acta* **1995**, *78*, 1298.
[265] Mlostoń, G.; Majchrzak, A.; Rutowska, M.; Woznicka, M.; Linden, A.; Heimgartner, H. *Helv. Chim. Acta* **2005**, *88*, 2624.
[266] Mlostoń, G.; Romański, J.; Heimgartner, H. *Pol. J. Chem.* **1996**, *70*, 437.
[267] Schönberg, A.; Urban, W. *J. Chem. Soc.* **1935**, 530.
[268] Benati, L.; Deluca, G.; Maccagnani, G.; Tundo, A. *J. Chem. Soc., Chem. Commun.* **1972**, 702.
[269] Mlostoń, G.; Urbaniak, K.; Linden, A.; Heimgartner, H. *Tetrahedron* **2009**, *65*, 8191.
[270] Cnossen, A.; Pijper, D.; Kudernac, T.; Pollard, M. M.; Katsonis, N.; Feringa, B. L. *Chem.—Eur. J.* **2009**, *15*, 2768.
[271] Pollard, M. M.; ter Weil, M. K. J.; van Delden, R. A.; Vicario, J.; Koumura, N.; van den Brom, C. R.; Meetsma, A.; Feringa, B. L. *Chem.—Eur. J.* **2008**, *14*, 11610.

[272] Pollard, M. M.; Wesenhagen, P. V.; Pijper, D.; Feringa, B. L., *Org. Biomol. Chem.* **2008**, *6*, 1605.
[273] Pijper, D.; Jongejan, M. G. M.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc*. **2008**, *130*, 4541.
[274] Pijper, D.; van Delden, R. A.; Meetsma, A.; Feringa, B. L. *J. Am. Chem. Soc*. **2005**, *127*, 17612.
[275] Pollard, M. M.; Lubomska, M.; Rudolf, P.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 1278.
[276] ter Weil, M. K. J.; Feringa, B. L. *Tetrahedron* **2009**, *65*, 4332.
[277] Mlostoń, G.; Urbaniak, K.; Nomura, T.; Nakayama, J.; Heimgartner, H. *Pol. J. Chem.* **2009**, *83*, 1945.