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Sulfur Ylides

Emerging Synthetic Intermediates

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Sulfur Ylides

Emerging Synthetic Intermediates

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Preface

The construction of molecular architecture continues as one of the most exciting challenges to the practicing chemist. Real advances in establishing methodology for the development of the synthetic plan have been made. Most noteworthy is the systematization of transformations under the concept of functional group equivalents (synthons) which forms the basis for computer-designed syntheses. This approach is limited by the available synthetic reactions. Thus, real strides in synthesis require the discovery of new methodology. Of the various reaction types in organic synthesis, none is more basic than the formation of carbon–carbon bonds, i.e., alkylation reactions. A powerful addition to this arsenal is sulfur ylides (π-sulfuranes).

This monograph represents a survey of the chemistry of sulfur ylides with emphasis on their use as synthetic intermediates. Those aspects of the subject which relate directly to their synthetic applications have been covered in detail. Aspects of sulfur ylide chemistry which do not relate to synthesis have been treated only cursorily.

This book is intended for the modern synthetic organic chemist who must face the problem of constructing complex molecules. As the most extensive treatment of this important area of sulfur chemistry, it is also intended for the expert who must keep abreast of rapid developments. Finally, it is intended to stimulate new research in this exciting area. Potential for new reagents and new applications abounds. Structural and mechanistic questions have only just been broached.

While an attempt has been made to provide comprehensive coverage of the field to 1974 within the scope of synthesis, difficulties in searching such a subject may have led to some omissions. For these, we apologize. Because of the synthetic emphasis, a brief survey of alternative methods to carry out similar transformations and representative experimental procedures have been included.

We want to express our thanks to the many individuals who have contributed their comments and unpublished work and to Mrs. Grace Legler for typing this manuscript.

Barry M. Trost
Lawrence S. Melvin, Jr.

Sulfur Ylides

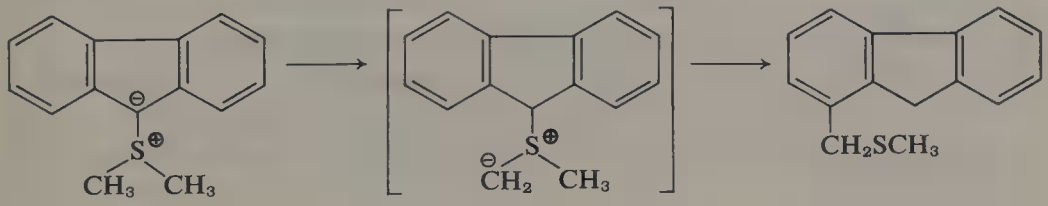
Emerging Synthetic Intermediates

1

Introduction

The usefulness of ylides in organic synthesis captured the imagination of organic chemists with the introduction of the Wittig olefin synthesis. Such success clearly required the study of families of ylides other than those related to phosphorus. Considering the documentation of proton abstraction from carbon-bearing sulfur both in sulfides[1] and sulfonium salts,[2,3] attention was directed toward utilization of these anions in synthesis.

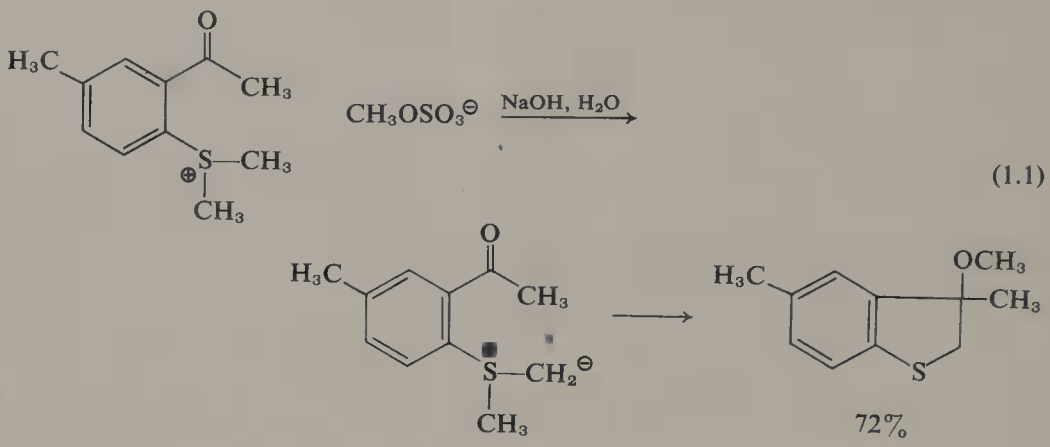
Sulfur ylides, formally zwitterions in which a carbanion achieves stabilization by interaction with an adjacent sulfonium center, have been known for over forty years since the report of Ingold and Jessop on the isolation of dimethylsulfonium fluorenylide **1**.[3,4,4a] However, little was known about the



1

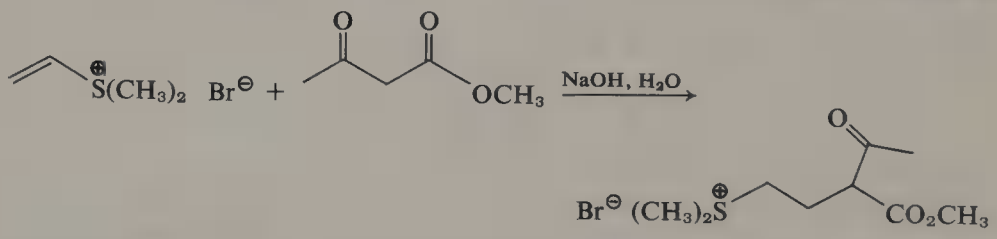
chemistry of such a species. It had been found that the treatment of **1** in protonic solvents leads to 1-methylthiomethylfluorene by a sulfur analog of the Sommelet–Hauser rearrangement.[5,6] Nevertheless, exploitation of this result did not occur until the late 1960's. A base-catalyzed ring closure of

dimethyl(*o*-aceto-*p*-tolyl)sulfonium methylsulfonate necessitates invoking the first addition of a sulfur ylide to a carbonyl group [see Eq. (1.1)].[7]



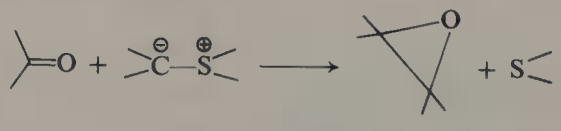
(1.1)

Subsequent studies led to the conclusion that a sulfonium center provides "unusual" stabilization of an adjacent negative charge when compared to a model system, e.g., an ammonium center. Most noteworthy are the observations that trimethylsulfonium iodide undergoes 98% deuterium incorporation at 62° after 3 hr, whereas tetramethylammonium iodide shows no appreciable incorporation after 504 hr under the same conditions, and that dimethylvinylsulfonium bromide serves as a Michael acceptor whereas the



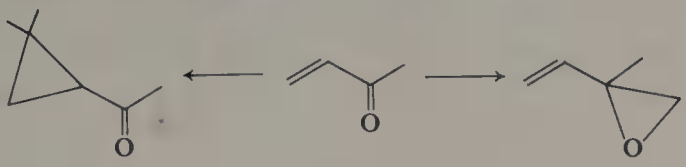
corresponding ammonium salt does not.[2] Sporadic reports of other ylides, in particular in the context of base-catalyzed rearrangements or eliminations of sulfonium salts, have appeared over the years.[8] However, not until the excellent work of the groups of Corey[9] and Franzen[10] has this class of intermediates found its practical application in organic synthesis.

Because sulfur ylides are nucleophilic alkylidene transfer agents in contrast to carbenes which are electrophilic alkylidene transfer agents, they react with electron-deficient functional groups. With carbonyls, epoxides are formed.

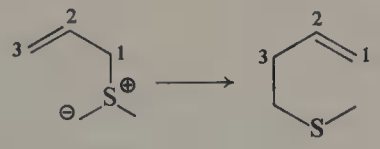


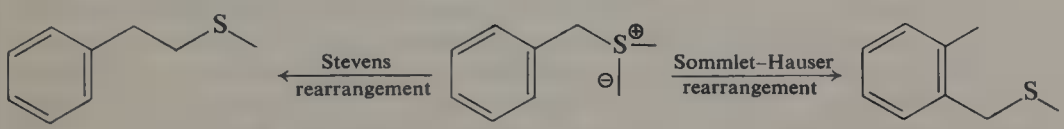
With Michael acceptors, either carbonyl addition with epoxide formation or conjugate addition with cyclopropanation occurs depending on the structure

of the Michael acceptor and, more important, the ylide. Allyl- and benzylsulfonium alkylides undergo isomerization reactions with formation of



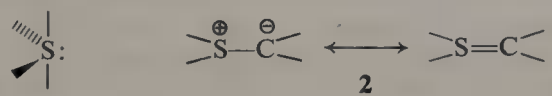
new carbon–carbon bonds. The ability to desulfurize readily either by elimination or reduction procedures also makes this reaction a valuable synthetic





transformation in which sulfur is used as a template. Thus, these reagents allow generation of new carbon–carbon bonds in a variety of fashions making them invaluable synthetic intermediates.

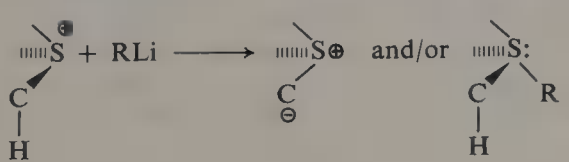
Systematization of the nomenclature of sulfur ylides is lacking. Johnson proposed considering these species as derivatives of the hypothetical sulfurane molecule, H_4S:.[4a] Utilizing such a premise, there are two classes of sulfuranes to be considered. The first, which may be called σ-sulfuranes, possesses four single bonds to sulfur in addition to the lone pair. Such species have been



2

σ-Sulfurane π-Sulfurane

characterized as reaction intermediates and have been isolated when the ligands are strongly electronegative.[11] The second, for which the term π-sulfuranes is proposed, possesses two single bonds and one double bond to sulfur in addition to the lone pair. Only to the extent that delocalization of electron density from carbon to sulfur in the zwitterion **2** occurs does sulfur expand its valence shell and give significance to the double bond structure. The major synthetic approach to ylides (π-sulfuranes), deprotonation of a sulfonium salt with base, relates the two classes of sulfuranes. Organolithiums are typical bases; however, they are also nucleophiles.



A sulfonium salt is an ambident electrophile. An organolithium may abstract a proton to give the ylide, but it may also react at the most electron-deficient site in the molecule, sulfur, to give the σ-sulfurane. In fact, it is now clear that low yields of ylides in some cases have their roots in this ambivalency in reaction.[12]

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2

Synthesis of Sulfonium Salts

The most common method of ylide generation consists of proton abstraction from the corresponding sulfonium salt. This fact is particularly true of the nonstabilized ylides. Thus, the availability of a variety of such salts determines the general utility of sulfur ylides.

Dimethylsulfonium salts are available by the direct alkylation of dimethyl sulfide. Normally, an active alkylating agent is required. Thus, primary,[1,2] allyl,[2,3] and benzyl halides[2,4] (usually bromides) or α-halocarbonyl[5] compounds produce the corresponding salts upon allowing an acetone, benzene, acetonitrile, methylene chloride, or nitromethane solution to stand at room

$$(CH_3)_2S + BrCH_2CO_2C_2H_5 \xrightarrow{(CH_3)_2CO,\ 25^\circ} (CH_3)_2\overset{\oplus}{S}CH_2CO_2C_2H_5\ Br^{\ominus} \quad \text{(Ref. 6)} \quad (2.1)$$

temperature [e.g., Eq. (2.1)]. In some cases, elevated temperatures and either no solvent or a solvent such as alcohol or water are employed.

$$(CH_3)_2S + CH_2{=}CHCH_2Cl \xrightarrow{H_2O} (CH_3)_2\overset{\oplus}{S}CH_2CH{=}CH_2\ Cl^{\ominus} \quad \text{(Ref. 2)}$$

A serious side reaction accompanying this method involves dealkylation of the salt by the nucleophilic dimethyl sulfide or halide ion.[7] Thus, alkylation of iodoacetonitrile with dimethyl sulfide produces exclusively a 1:1 mixture of methylthioacetonitrile and trimethylsulfonium iodide.[8] Subsequent alkylation of methylthioacetonitrile with a methylating agent possessing a nonnucleophilic anion produces the desired salt as its fluoroborate in

$$(CH_3)_2S + ICH_2CN \xrightarrow{(CH_3)_2CO} CH_3SCH_2CN + (CH_3)_3S^{\oplus}\ I^{\ominus}$$

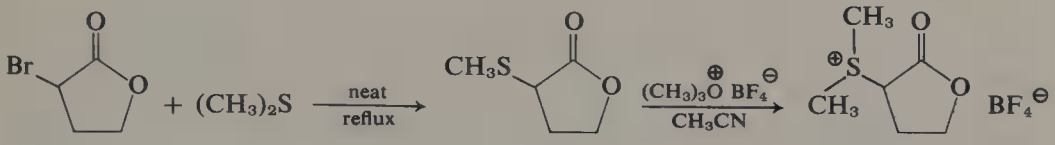
88%

$$\downarrow \; CH_3CN \mid (CH_3)_3O^{\oplus}\ BF_4^{\ominus}$$

$$(CH_3)_2\overset{\oplus}{S}CH_2CN\ BF_4^{\ominus}$$

100%

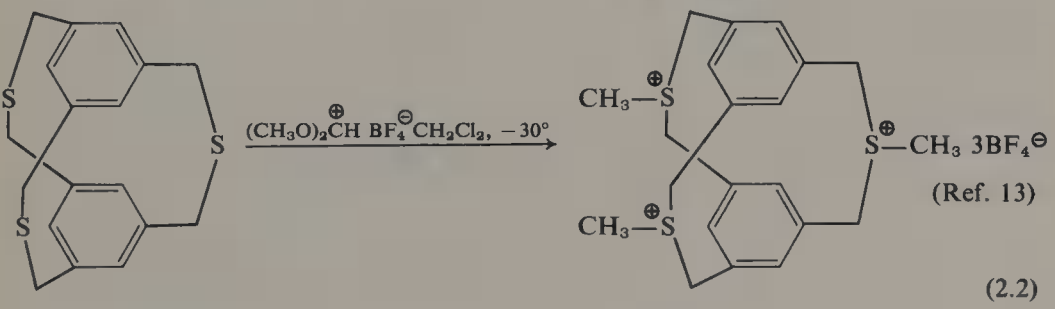
quantitative yield. In order to minimize this disproportionation reaction, use of excess alkylating agent and silver ion (to remove halide ion) is beneficial. However, examples exist in which these precautions fail to eliminate some disproportionation. In these instances, facilitation of the disproportionation by use of a large excess of dimethyl sulfide followed by methylation of the formed sulfide is the preferable synthetic approach. The preparation of the lactone salt **1** from α-bromo-γ-butyrolactone requires this approach.[9]



1

0.35 mole 1.37 moles 96% 47%

Generation of the salt precursors of many stabilized ylides frequently entails the alkylation of a sulfide. Methylations utilizing trimethyloxonium fluoroborate,[10] methyl fluorosulfate,[11] or dimethoxycarbonium fluoroborate[12] have been the preferred approach. Formation of a carbocation in the presence



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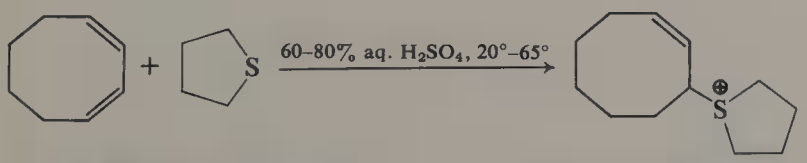
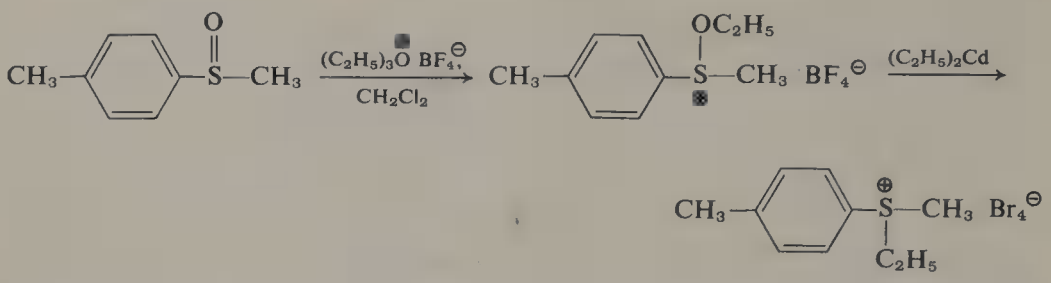
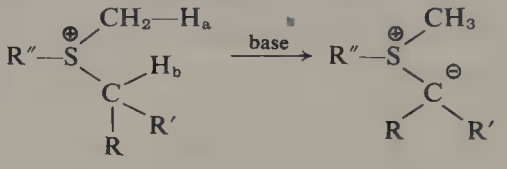


of a sulfide serves as an effective alkylation method [Eq. (2.2)].[14] A novel nonalkylative approach to sulfonium salts entails the addition of an organocadmium to an alkoxysulfonium salt.[15] This latter method has been used to prepare optically active sulfonium salts.

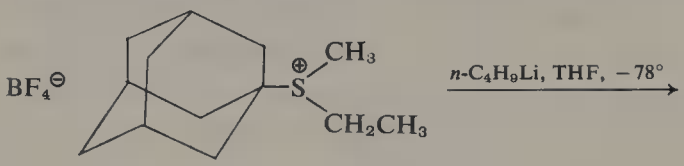


The suitability of the *S*-methylsulfonium salts as precursors for substituted ylides depends on the acidity of the hydrogen to be removed. In a mixed salt

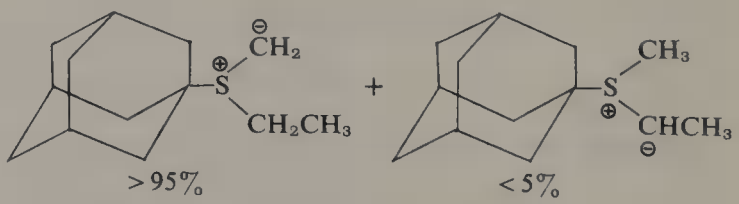


2

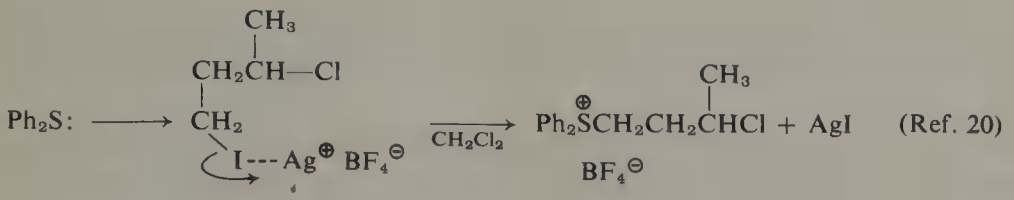
such as **2**, the kinetic and/or thermodynamic acidity of H_b must be greater than that of H_a to be able to generate the substituted ylide. If R and/or R′ is an anion stabilizing group such as cyano, carbonyl, aryl, or even vinyl, methylide formation does not interfere. On the other hand, if R and/or R′ are alkyl groups, methylide formation predominates. For example, adamantylethylmethylsulfonium fluoroborate generates a > 19:1 mixture of the methylide and ethylide, respectively, under conditions of kinetic deprotonation.[16]



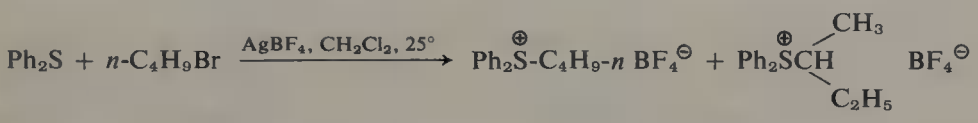
THF = tetrahydrofuran



The use of diphenylsulfonium salts precludes such ambiguities; however, the lower nucleophilicity of diphenyl sulfide prevents its direct condensation with alkylides. Such alkylations do succeed in the presence of a silver salt, almost invariably silver fluoroborate,[17,17a] or a mercuric salt, usually mercuric iodide.[18,19] For example, equivalent amounts of diphenyl sulfide and silver fluoroborate react with excess halides (usually bromide or iodide) in acetone, acetonitrile, nitromethane, or methylene chloride (the reaction mixture is best protected from light). The course of the reaction remains

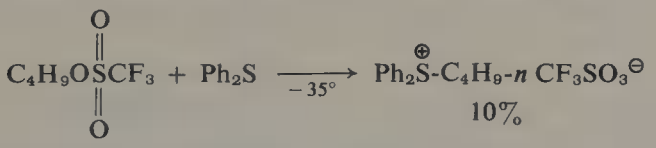


somewhat obscure. Two observations support the view that the reaction involves S_N2 displacement by sulfide on silver-complexed halide. First, no precipitation of silver halide occurs until the addition of diphenyl sulfide. Second, in the case of 1-iodo-3-chlorobutane only the primary alkylsulfonium salt was isolated in agreement with consideration of factors governing S_N2 reactions, but not carbonium ion reactions.[20] On the other hand, the use of straight-chain primary halides has been claimed to lead to mixtures of primary and secondary alkylsulfonium salts.[21] This type of behavior is typical of



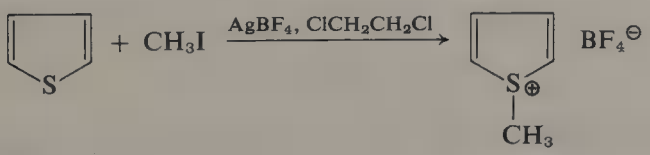
(3:2)

carbonium ion type reactions. The pure *n*-alkyldiphenylsulfonium salt was prepared, albeit in low yield, by alkylation with *n*-alkyl triflates (triflate = trifluoromethylsulfonate). This heretofore unrecognized difficulty requires

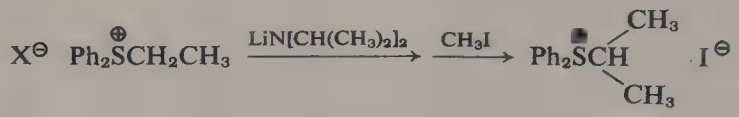


further examination since the silver-catalyzed alkylations constitute the most general route to alkyldiphenylsulfonium salts.

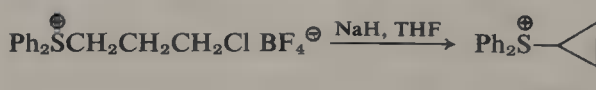
Because sulfides and silver fluoroborate can produce an insoluble complex,[17a] the reaction is normally carried out by portionwise addition of the silver salt to the solution of halide and sulfide (normal addition) or of the sulfide to the halide and the silver salt (inverse addition). Most of the diphenylsulfonium salts in Table 3.1 in Chapter 3 were prepared in this manner. The extreme reactivity under such conditions is indicated by the smooth alkylation of the very nonnucleophilic sulfur of thiophene.[22]



A second approach involves the alkylation of lower homolog ylides. Thus, diphenylisopropylsulfonium iodide was prepared by the direct alkylation of diphenylsulfonium ethylide.[23] On the other hand, attempted methylation of



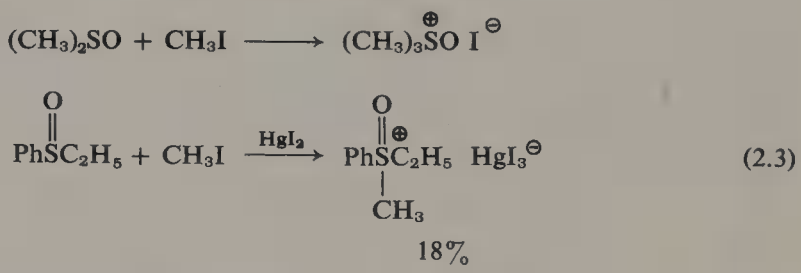
diphenylsulfonium allylide, a more stable ylide, led to recovered starting material.[3] Intramolecular alkylation of ylides appears facile. For example,



(79%)

cyclization of diphenyl-3-chloropropylsulfonium fluoroborate to cyclopropyldiphenylsulfonium fluoroborate proceeds at 25° via the intermediate ylide.[20] As a general route to sulfonium salts by intermolecular alkylation, this approach appears limited to the saturated alkylides and reactive alkylating agents.

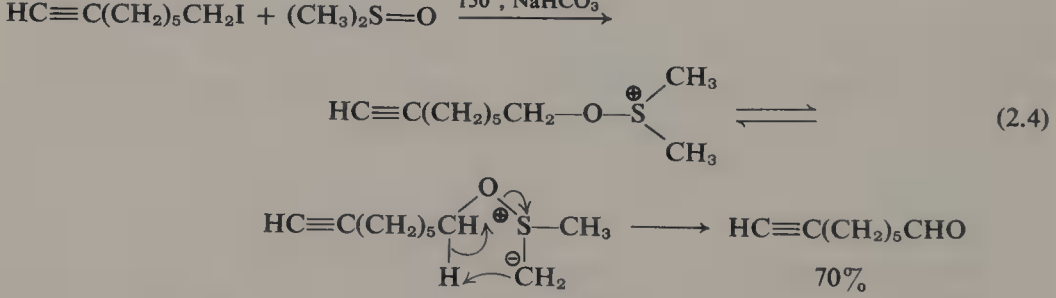
Oxosulfonium ylides require the availability of the corresponding salt. Direct alkylation of sulfoxides to generate the oxosulfonium salts is essentially limited to the reaction of methyl iodide with dimethyl sulfoxide.[1] In one



(2.3)

18%

case [e.g., Eq. (2.3)], a successful alkylation of a more substituted sulfoxide utilized a Lewis acid–alkyl halide complex although in only low yield.[24] The normal reaction is O- rather than S-alkylation. Indeed, this method has led to a general and mild method for oxidation as represented by Eq. (2.4).[25,26]

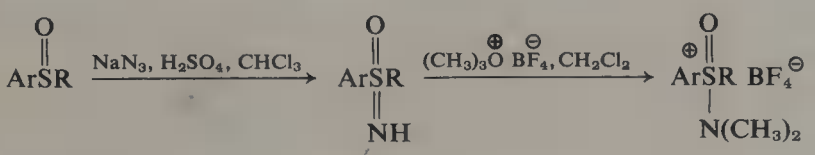


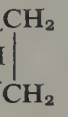
(2.4)

Oxidation of sulfonium salts has been achieved; however, the general applicability remains to be established.[27]

A practical alternative for structural variation in the oxosulfonium ylides involves aryl(dimethylamino)oxosulfonium alkylides.[28] The requisite salts

arise from sulfoxides by treatment first with hydrazoic acid followed by N-dialkylation with an oxonium salt (Meerwein's reagents). Better yields for



Ar = *p*-$CH_3C_6H_5$, R = C_2H_5	84%	79%
Ar = *p*-$CH_3C_6H_5$, R = $CH(CH_3)_2$	17%	35%
Ar = C_6H_5, R = 	68%	59%

the formation of the isopropyl ylide are obtained by *in situ* generation of the salt by methylation of aryl(dimethylamino)oxosulfonium ethylide.

Typical experimental procedures for the preparation of various types of sulfonium and oxosulfonium salts appear in Chapter 9.

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3

Synthesis and Structures of Sulfur Ylides

An understanding of the chemical behavior of sulfur ylides requires some knowledge of their structure. Such studies as well as applications in synthesis depend on the accessibility of various types of sulfur ylides. Two fundamentally distinct approaches to the generation of these ylides exist. The most common involves deprotonation of a salt that is either preformed or generated *in situ*. A less common, but exceedingly useful approach, involves the reaction of a sulfide with a carbene. The success of these methods determines, to a very large degree, the utility of these intermediates in synthesis.

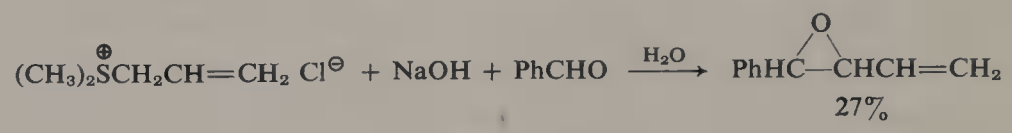
3.1. FORMATION BY DEPROTONATION OF PREFORMED SALT

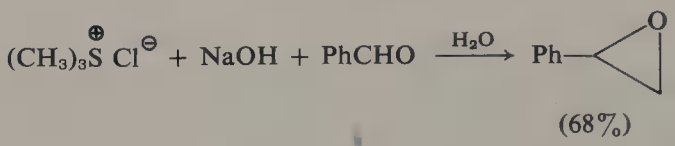
The relatively high acidity of methylsulfonium salts is illustrated by the complete deuteration of trimethylsulfonium iodide with sodium deuteroxide

$$(CH_3)_3S^{\oplus} \underset{}{\overset{^{\ominus}OD}{\rightleftharpoons}} (CH_3)_2\overset{\oplus}{S}\overset{\ominus}{C}H_2 \overset{D_2O}{\rightleftharpoons} (CH_3)_2\overset{\oplus}{S}CH_2D \rightleftharpoons \text{etc.}$$

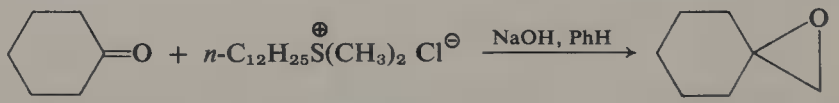
at 62° for 3 hrs.[1] If the ylide partner is stable to aqueous hydroxide such a method of ylide generation is useful. In some instances, it is the preferred method. For example, allyldimethylsulfonium chloride yields no allylide

derived product upon irreversible ylide generation conditions (see Chapter 7); whereas under reversible conditions the vinyl oxirane can be obtained.[2]





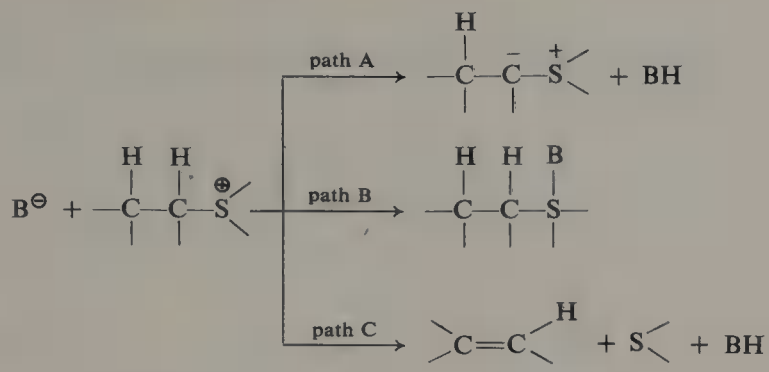
Conversion of cyclopropyldiphenylsulfonium fluoroborate to the cyclopropylide produced consistently higher yields of products utilizing a dimethyl sulfoxide suspension of potassium hydroxide than dimsylsodium (methylsulfinylmethylsodium) or an organolithium (see Appendix, Table A.III).[3] In this latter instance, the lower yields by the irreversible methods can be attributed to competing sulfur attack (see below) and E_2 elimination. The use of long-chain alkyldimethylsulfonium chlorides in an aqueous–benzene two-phase system has been recommended for good yields with a wide range of carbonyl partners.[4,4a] A very promising approach employs aqueous base–



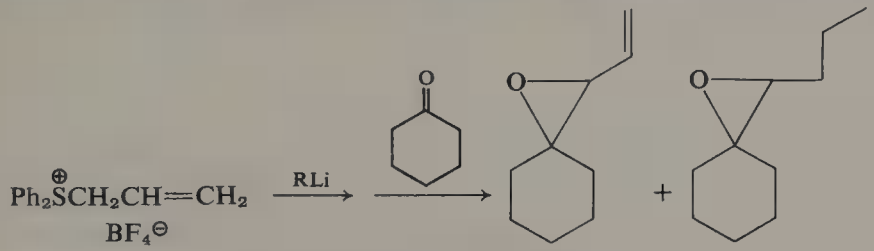
methylene chloride in the presence of tetraalkylammonium salts (phase transfer conditions).[4a]

The more common technique involves irreversible ylide generation. For the stabilized sulfonium ylides (see Table 3.I, part B) and oxosulfonium ylides (Table 3.II), the alkoxide bases in the corresponding alcohol or sodium hydride in dimethyl sulfoxide are preferable. In some instances, such as the carbonyl-stabilized ylides (Table 3.I, part B, cases 4, 5, 9, 13, 14, and 16), the ylide is isolable as an air-stable compound, frequently crystalline. For the nonstabilized ylides (see Table 3.I, part A), irreversible ylide generation requires the use of an organolithium, a lithium dialkylamide, or dimsylsodium as a base.

Choice of the exact base depends on each ylide being generated. σ-Sulfurane formation (path B) and E_2 elimination (path C) compete with the formation of the desired ylide (π-sulfurane) (path A). Corey and Oppolzer found that use of a nucleophilic organolithium (*n*-butyllithium, methyllithium, and phenyllithium) for generation of diphenylsulfonium ethylide gave many by-products; whereas use of the less nucleophilic but highly basic *t*-butyllithium or lithium diisopropylamide gave over 70% isolated yields of products

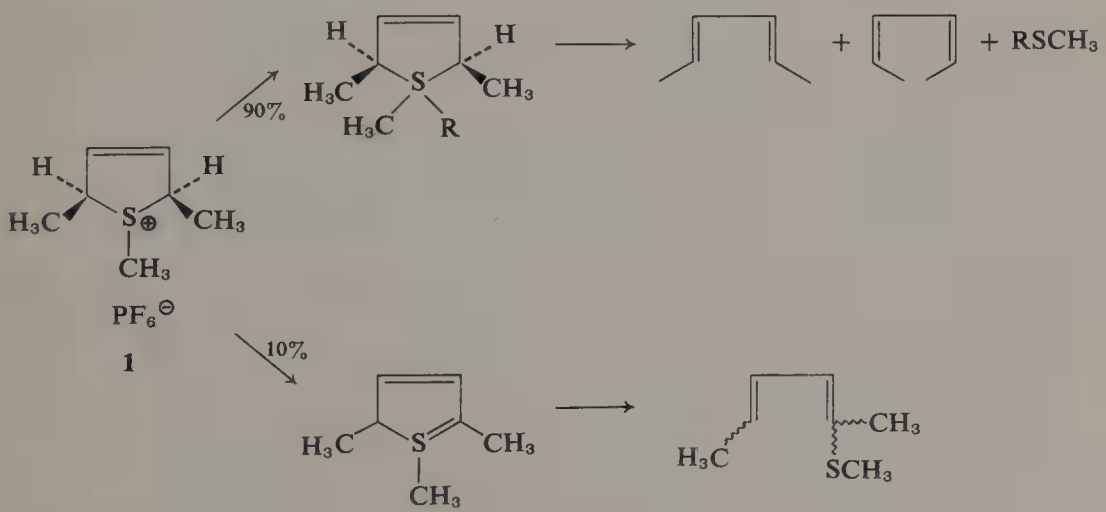


derived from the ethylide with very little by-product formation.[5] The by-products can be attributed to σ-sulfurane formation. LaRochelle, Trost, and Krepski found that generation of diphenylsulfonium allylide with *n*-butyllithium gave only a 52–56% yield of desired epoxide contaminated with propyloxirane.[6] The latter arises by sulfur attack leading to ligand exchange



R = *n*-C_4H_9	52–56%	5–7%
R = *t*-C_4H_9	80%	—

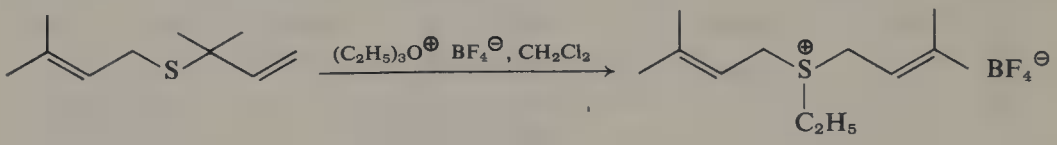
and ultimate formation of diphenylsulfonium butylide. Use of the sterically crowded *t*-butyllithium precludes sulfur attack and the desired epoxide is obtained in 80% yield. In the case of the sulfonium salt **1**, attack by organolithium leads to products which are 90% derived from the σ-sulfurane and



only 10% from the ylide.[7] For the best results clearly utilization of *t*-butyllithium, lithium dialkylamides, lithium dichloromethide, or dimsylsodium may be recommended.

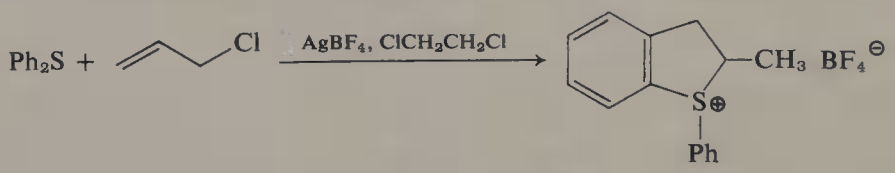
3.2 FORMATION BY DEPROTONATION OF *IN SITU* GENERATED SALT

The unavailability of many salts poses a limitation for the application of these reagents. For example, it has been pointed out that preparation of *n*-butyldiphenylsulfonium fluoroborate is complicated by the concurrent formation of *sec*-butyldiphenylsulfonium fluoroborate (see Chapter 2, p. 9).[8] Sulfide **2** is unstable to the alkylation conditions.[9,10] Only rearranged



2 **3**

salt **3** was obtained with triethyloxonium fluoroborate in methylene chloride. Attempted preparation of allyldiphenylsulfonium fluoroborate in 1,2-dichloroethane only led to the rearranged salt **4**, although the desired allyl

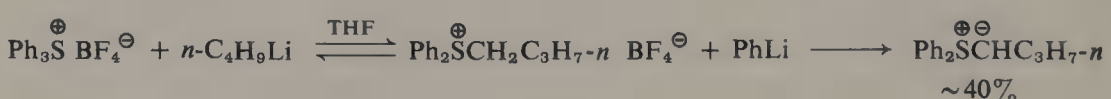


4

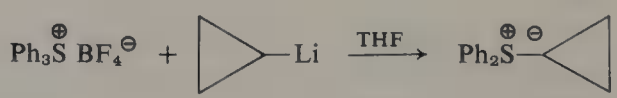
25%

salt was obtained in 85% yield utilizing allyl bromide as alkylating agent and acetone as solvent.[6] Such difficulties have led to the development of alternative *in situ* methods.

The occurrence of exchange of substituents between a triarylsulfonium salt and an aryllithium[11] suggested the applicability of this method as an *in situ* ylide formation procedure. Treatment of triphenylsulfonium fluoroborate



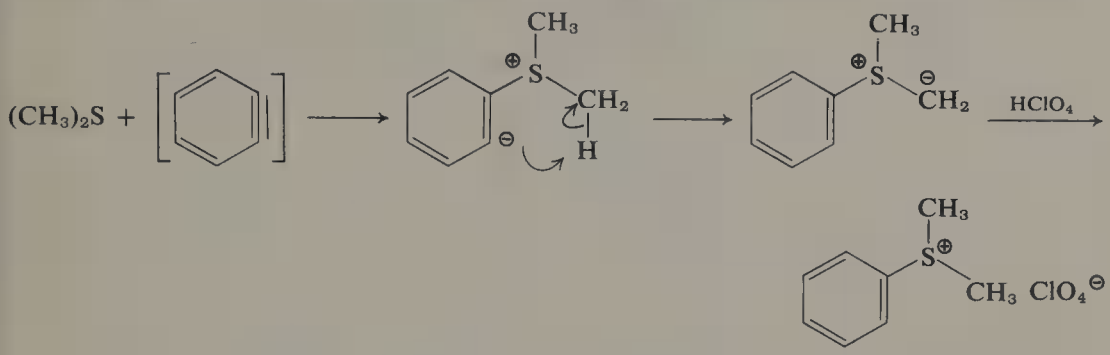
~40%

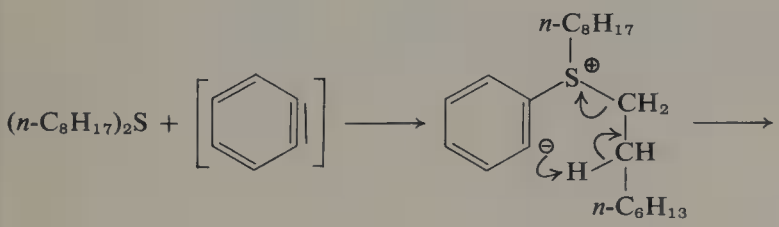


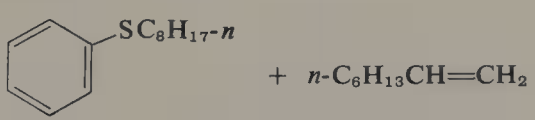
~20%

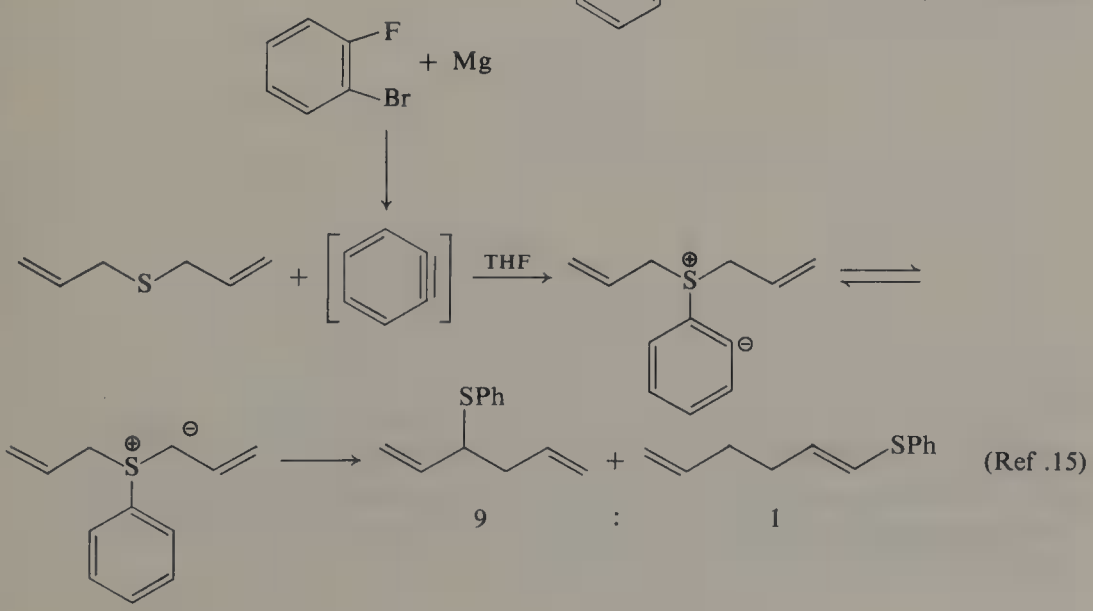
with *n*-butyllithium[12] or cyclopropyllithium[13] leads to the corresponding ylides in only fair to poor yields as determined by the yield of products isolated after quenching the reaction mixtures with cyclohexanone. Since the ylide yields are invariably inferior to the direct base abstraction technique, the method is recommended only where the salt is unavailable.

A somewhat more successful approach involves the treatment of a sulfide with benzyne. Methylphenylsulfonium methylide was prepared in about



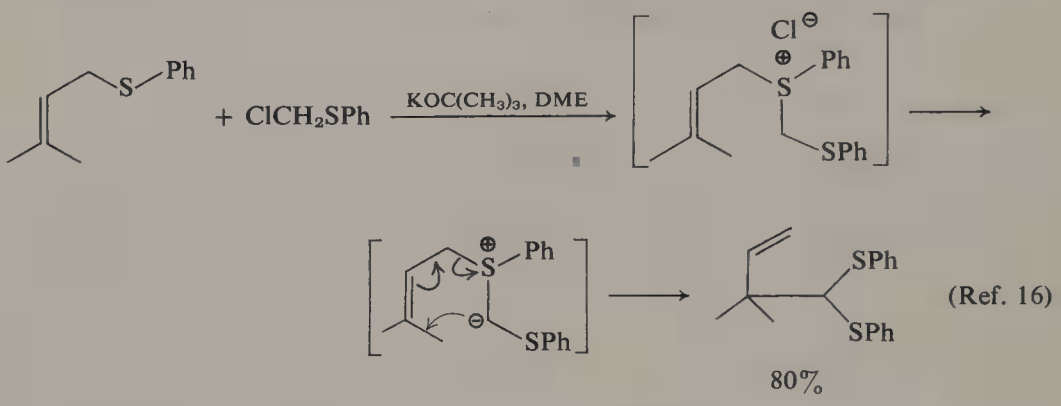






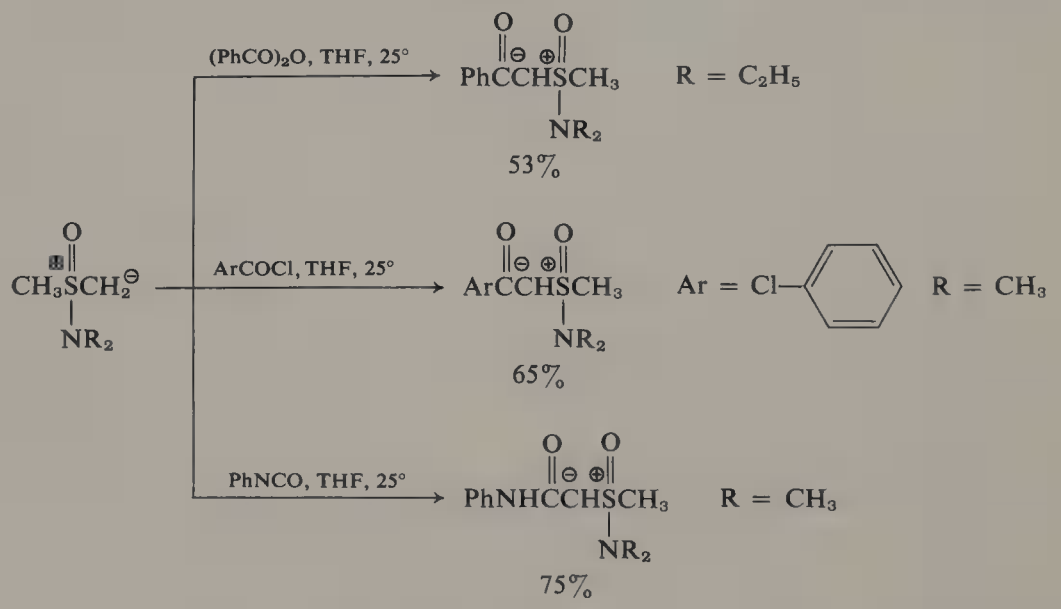
(Ref .15)

77% yield by this method.[14] However, attempts to extend the reaction to higher homologs of the sulfides, e.g., di-*n*-octyl sulfide, led only to elimination products. On the other hand, the method works for the generation of the ylide intermediates for the [2,3]sigmatropic rearrangement. The ylide intermediates for such rearrangements have also been successfully generated by the alkylation of an allyl sulfide in the presence of an external base.

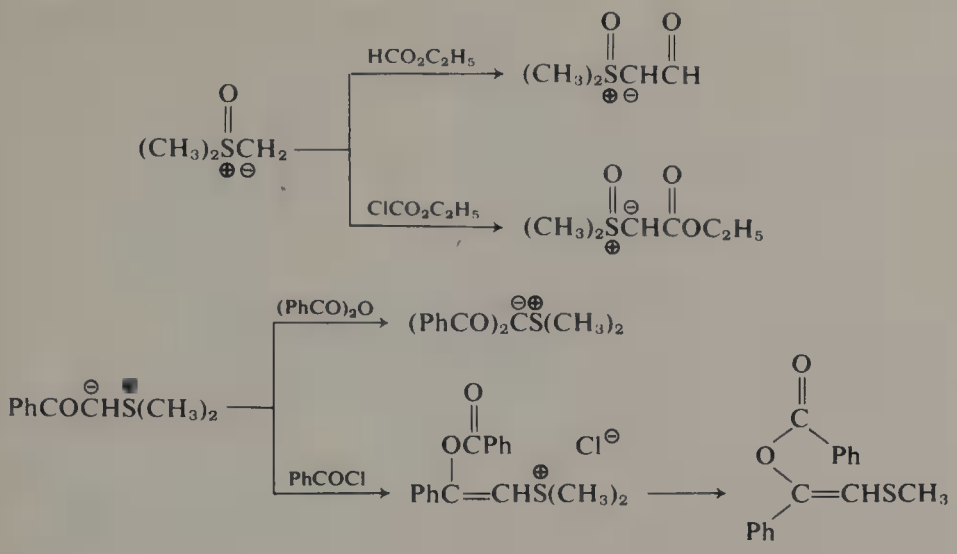


(Ref. 16)

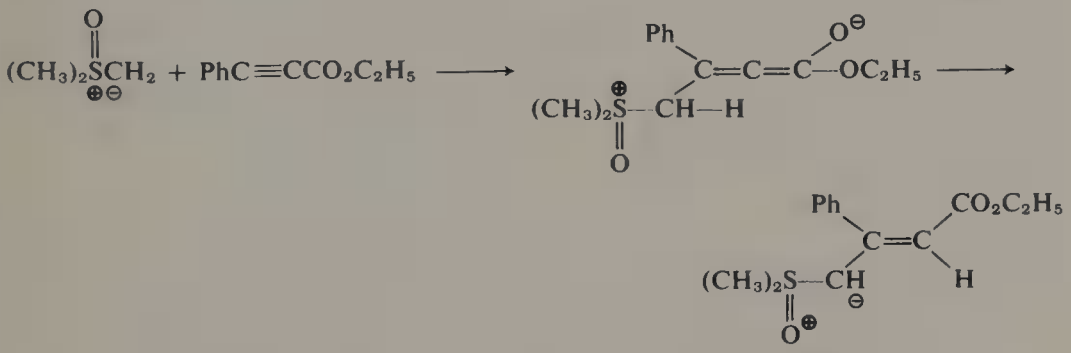
Alkylation or acylation of ylides has provided many substituted members mainly of the stabilized type. For example, the oxosulfonium ylides of Johnson produce carbonyl-stabilized ylides on condensation with acid



anhydrides, acid chlorides, or isocyanates.[17] Similarly, dimethyloxosulfonium methylide undergoes acylation with ethyl chloroformate[18] or ethyl formate.[19] Stabilized ylides also undergo such reactions quite readily; however, carbonyl stabilized ylides, e.g., dimethylsulfonium phenacylide, may behave as ambident nucleophiles.[20]



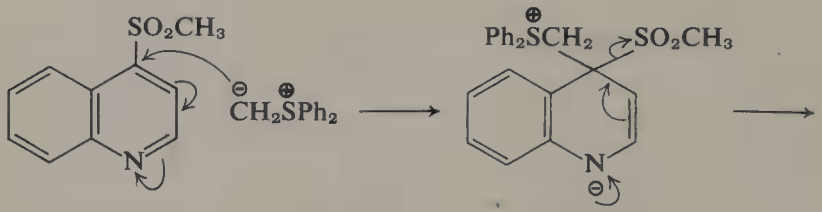
α,β-Acetylenic carbonyl systems or α,β-unsaturated carbonyl units possessing a leaving group on the β carbon condense with simple ylides to form more substituted and stabilized ylides. One of the first examples of such an approach involved the addition of dimethyloxosulfonium methylide to ethyl phenylpropiolate.[21,21a] A most interesting example arose in the treatment of

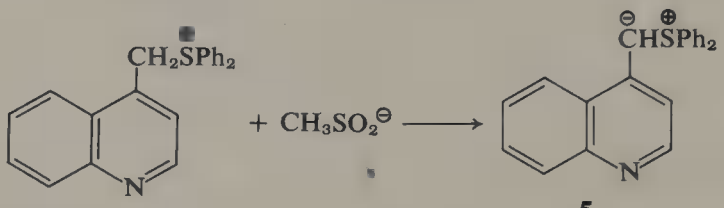


4-quinolylmethyl sulfone with diphenylsulfonium methylide in which ylide **5** utilized as an intermediate for the synthesis of quinine derivatives was produced.[22] [See Eq. (3.1).]

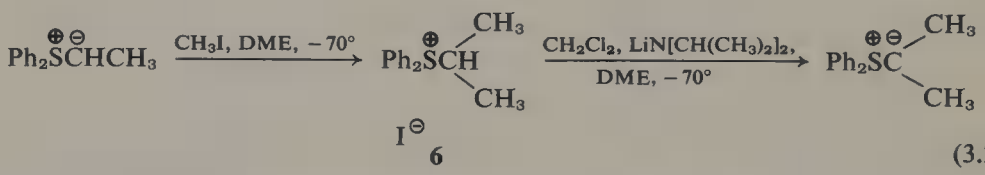
The most noteworthy nonstabilized ylide prepared by *in situ* alkylation methods is diphenylsulfonium isopropylide.[23] Because of the instability of the isopropylsulfonium salt **6**, generation by methylation of diphenylsulfonium ethylide followed by immediate base treatment to convert the salt to the isopropylide has been recommended. [See Eq. (3.2).]

The condensation of active methylene groups with sulfoxides or alkoxysulfonium salts provides an entry into highly stabilized ylides via intermediate salt formation.[24–26] The reaction with sulfoxides utilizes typical dehydration conditions. Acetic anhydride,[24] phosphorous pentoxide,[24] thionyl chloride,[24]



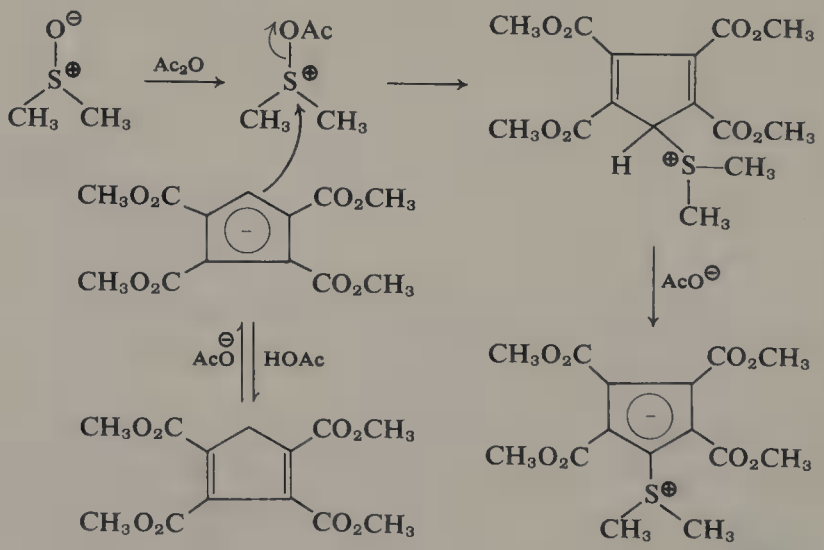


(3.1)



(3.2)

phenyl isocyanate,[26] and dicyclohexyl carbodiimide–phosphoric acid[25] have found use. For example, condensation of dimethyl sulfoxide and 1,2,3,4-tetracarbomethoxycyclopentadiene with acetic anhydride at elevated temperatures produces the corresponding ylide in 42% yield.[27] Facilitation

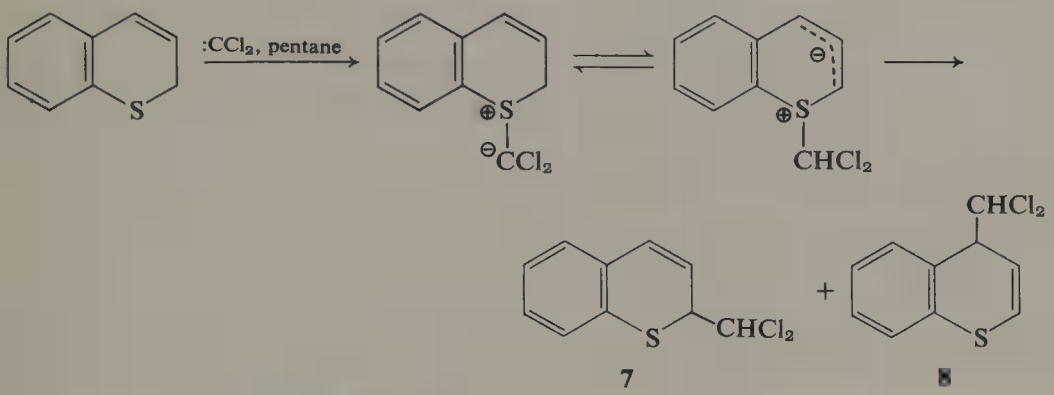


of attack of the anion of the active methylene partner on the sulfoxide is achieved by acylation to the acetoxysulfonium salt. The low yields frequently encountered with most sulfoxides except diphenyl sulfoxide may be attributable to the competing Pummerer reaction. Table 3.1, part B, provides further examples to illustrate the scope of the method.

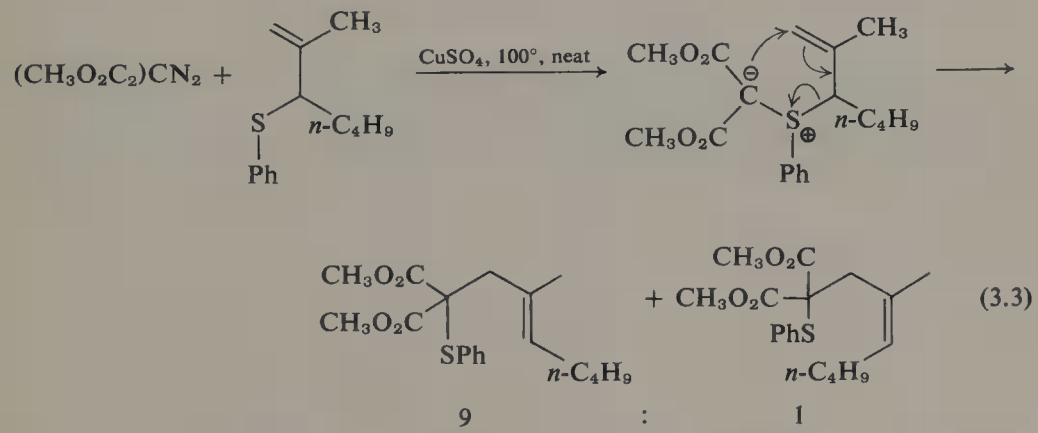
3.3 DIRECT FORMATION OF YLIDES

The addition of a carbene to a sulfide provides the most direct synthesis of sulfur ylides. Some of the earliest examples invoked such a pathway to

explain reaction products derived by thermal decomposition of ylide intermediates.[28] For example, the generation of dichlorocarbene in the presence of 2*H*-1-benzothiopyran produced the insertion products **7** and **8** explicable on the basis of an ylide intermediate.[28]

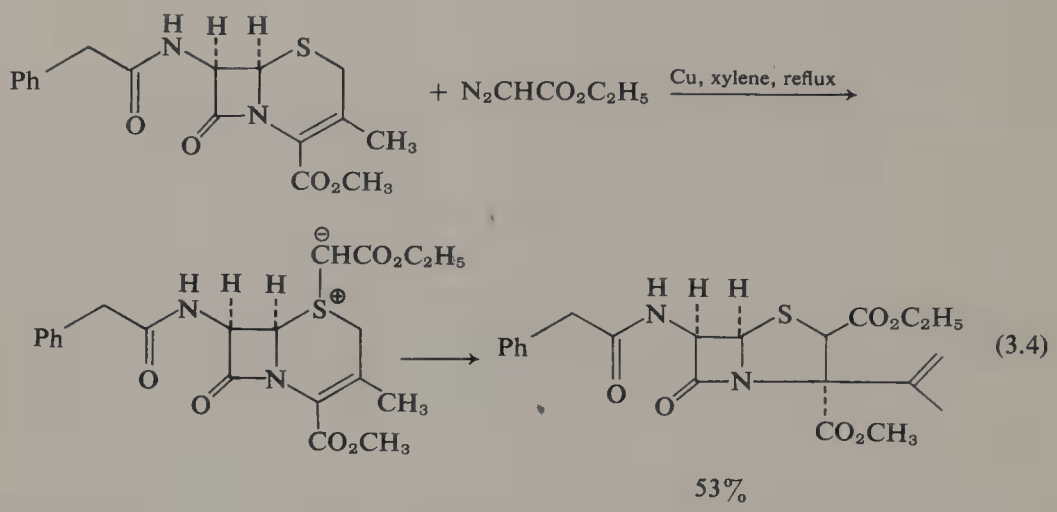


The application of this approach to the ylide intermediates for the [2,3]sigmatropic rearrangement has been the most fruitful.[29] Copper (or copper



(3.3)

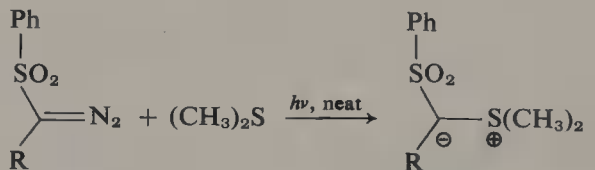
salt)-catalyzed thermal or photolytic decomposition of diazo compounds in the presence of an allyl or benzyl sulfide appears to be the most attractive synthetic technique; moreover, the thermal approach generates cleaner product mixtures. Disulfides have also been claimed to catalyze this reaction.[30] Diazoalkanes as well as α-diazocarbonyl compounds may be employed. The



(3.4)

novel conversion of the cephalosporin nucleus to a penicillin nucleus [Eq. (3.4)][31] and a rather highly stereospecific generation of a trisubstituted double bond [Eq. (3.3)][32] illustrate some of the potential of the method.

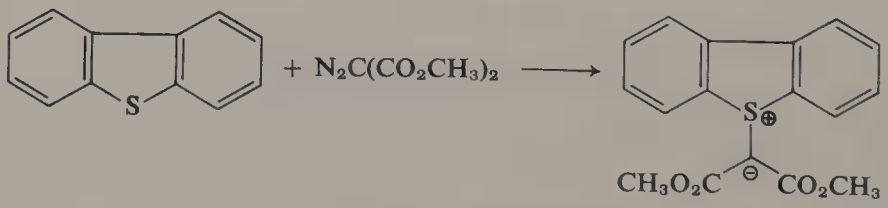
Stabilized ylides can be isolated by this technique. For example, diazo



9 **10**

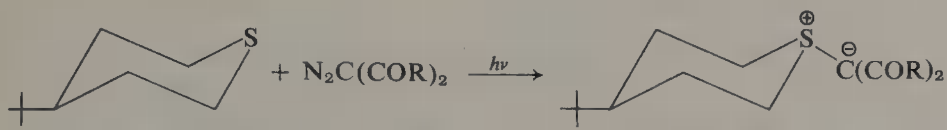
R = PhCO, CH_3CO, $PhSO_2$ 52–91%

compounds **9** produce good to excellent yields of the corresponding ylides **10** when irradiated in neat dimethyl sulfide.[33] Dialkyl or diaryl sulfides have both been employed with equal success. Even dibenzothiophene, in which



(1) *hν* (3660 Å) 75%
(2) $CuSO_4/\Delta$ 68%

the lone pair of sulfur is highly delocalized, is an efficient trap for the carbene.[34] A dialkyl sulfide appears to be four times more reactive than an olefin toward a carbene.[34] High stereoselectivity is observed with 4-*t*-butyltetrahydrothiopyran.[34a]



Stabilized oxosulfonium ylides, unavailable by the direct condensation of sulfoxides and α-halocarbonyl compounds,[35] are specially suited targets for

$$N_2CHCOR + (CH_3)_2SO \longrightarrow (CH_3)_2\overset{O}{\underset{\oplus}{S}}\underset{\ominus}{C}H\overset{O}{C}R$$

$$R = CH_3,\ Ph,\ OCH_3$$

the carbene approach.[36] Thermal methods utilizing silver oxide or cuprous cyanide catalysts as well as photolysis have been employed.

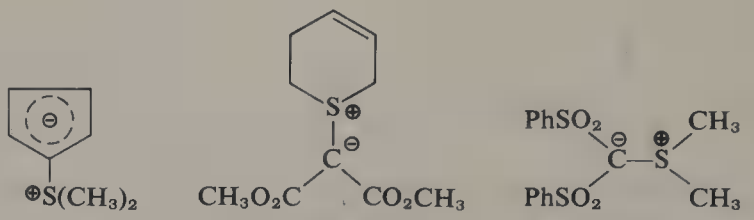
3.4 YLIDE STABILITY

The ylides listed in Table 3.I, part A, generally must be generated and utilized at or near −70°. Dimethylsulfonium methylide can be generated at 10° utilizing dimsylsodium in dimethyl sulfoxide–tetrahydrofuran; however, its half-life at this temperature is on the order of minutes.[37] The half-lives of diphenylsulfonium ethylide,[5] allylide,[6] and cyclopropylide[38] appear to be approximately 5 min (20°), 30 min (−15°) and 2.5 min (25°), respectively. The half-lives of the other ylides listed are not known, but generation has only been achieved at or near −70°. The products of thermolysis are discussed in Chapter 4.

In sharp contrast to ylides possessing only alkyl, vinyl, or aryl substituents, those possessing carbonyl, cyano, sulfonyl, and nitro substituents have enough stabilization so that they are isolable and storable. Several such ylides (e.g., **11–13**) have been distilled without decomposition. More frequently, stabilized

$CH_3\overset{O}{C}CHS(CH_3)_2$	$C_2H_5O_2CCHS(CH_3)_2$	$(CH_3)_3SiCHS(CH_3)_2$
b.p. 135°/0.8 mm	b.p. 40°/0.003 mm	b.p. 51°–53°/12 mm
11	**12**	**13**
(Ref. 39)	(Ref. 40)	(Ref. 41)

ylides are crystalline, sharp-melting solids (e.g., **14–16**). The shelf-life of these ylides depends on the nature and number of anion-stabilizing groups. With one anion-stabilizing group, as in the case of ylides **11–13**, slow decomposition at room temperature necessitates storing them in the cold. The stability also decreases in the order **11** > **12** > **13**, which reflects the delocalizing



m.p. 134° m.p. 103°–104° m.p. 214°–215°

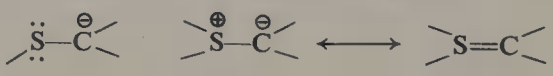
14 **15** **16**

(Ref. 42) (Ref. 29) (Ref. 43)

ability of the various substituents. On the other hand, ylides like **14–16** appear to be stable indefinitely at room temperature.

3.5 YLIDE STRUCTURE

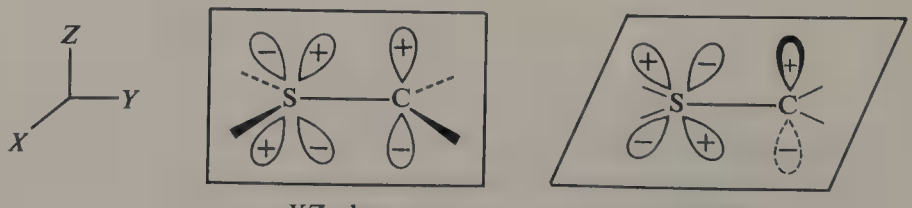
The ability of sulfur to stabilize an adjacent negative charge remains an interesting phenomenon. Whatever the cause in sulfides,[44] increasing the



17a **17b**

electronegativity of sulfur by converting a sulfide to a sulfonium salt should and does increase its anion-stabilizing ability. Comparison of the sulfur ylides to nitrogen ylides indicates that factors beyond electrostatic stabilization must be involved (also see Chapter 1). The simplest explanation invokes delocalization of electron density into "low-lying" *d* orbitals of sulfur.[45] It has been pointed out that a combination of only *s*- and *p*- type orbitals can also accommodate such a valence shell expansion.[46] In essence, the question revolves around the relative importance of structures **17a** and **17b** as resonance contributors to the ground state of sulfur ylides

Two major consequences might be envisioned if a double-bonded structure like **17b** makes a major contribution. To achieve maximum orbital overlap, both carbon and sulfur would tend to become planar (see Fig. 3.1). However,

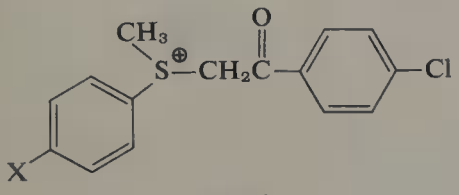


YZ plane *XY* plane

Fig. 3.1. p_π–d_π Orbital overlap.

no unusual barrier to rotation about the S–C bond need necessarily develop as a result of appreciable p_π–d_π overlap since rotation does not involve a transition state in which the carbon p orbital becomes orthogonal to the sulfur d orbitals. If overlap with the sulfur d_{YZ} orbital is envisioned initially, at 90° rotation there exists an equivalent d_{XY} orbital.

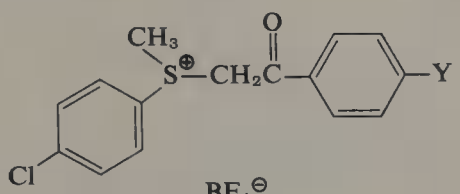
Most structural studies have been carried out on stabilized ylides. The importance of the electronegativity of sulfur is indicated by the dependence of the acidity of a series of arylsulfonium salts to electron-withdrawing groups on the aromatic ring.[47,48] Increasing the electron-withdrawing ability of the



$BF_4^\ominus$

18a

$pK_a = 6.40–1.13\sigma$



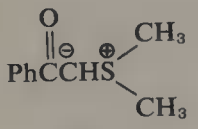
$BF_4^\ominus$

18b

$pK_a = 6.73–2.63\sigma$

X group in **18a** increases the acidity substantially. Nevertheless, delocalization by the carbonyl group is the predominant effect as reflected by the substantially greater dependence of the acidity of **18b** on substituents compared to **18a**.[47] Comparison of the pK_a's of a series of structurally related ammonium, phosphonium, and sulfonium salts establishes the order S > P > N. The enhancement of the acidity of sulfonium over ammonium salts by 2.6 pK_a units has been taken as strong evidence of charge delocalization into orbitals of sulfur,[47,49,49a] although this conclusion has been questioned.[48]

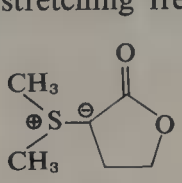
A large shift to lower energy ($\sim$110–170 cm^{-1}) in the "carbonyl" stretching frequency in the infrared spectrum of the ylides (e.g., **19**[49a] and **20**[50]) compared to the corresponding salts also demonstrates extensive delocalization of charge by such carbanion-stabilizing groups. A similar lowering of the π-bond order and consequently the stretching frequency of the nitrile is



19

Ylide 1520

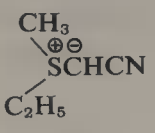
Salt precursor 1670



20

1647

1748



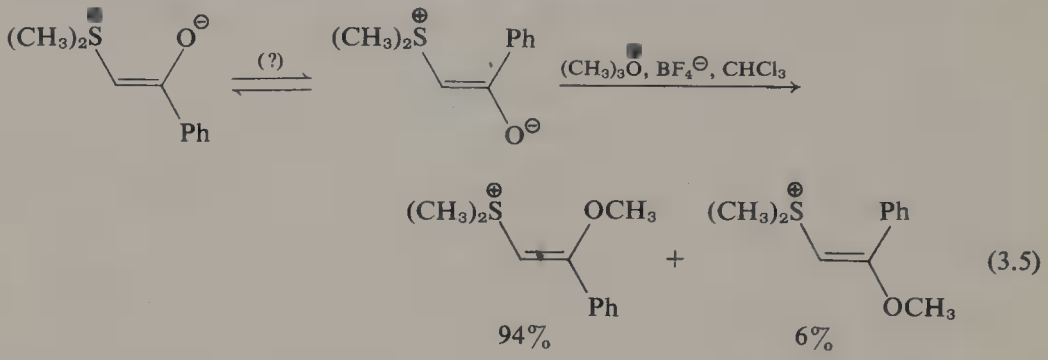
21

2130 cm^{-1}

2235 cm^{-1}

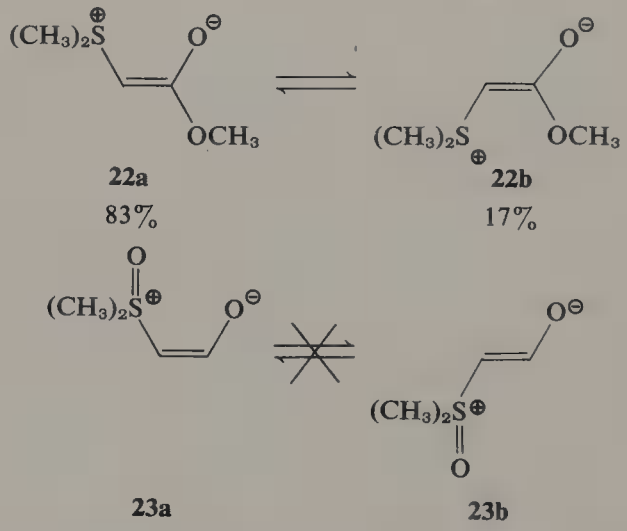
observed in the stabilized ylide **21**.[51] An increase in the ylide carbon–carbonyl carbon π-bond order accompanies the decrease in the π-bond order of the carbonyl group. The nmr spectrum of **19** which shows absorptions for only a single methine and a single *S*-methyl is invariant from $-30°$ to $+100°$.[52]

The fact that two forms must be present to at least a small extent as demonstrated by methylation studies [Eq. (3.5)], however, does not preclude a relatively high barrier to rotation. That the temperature invariance is likely



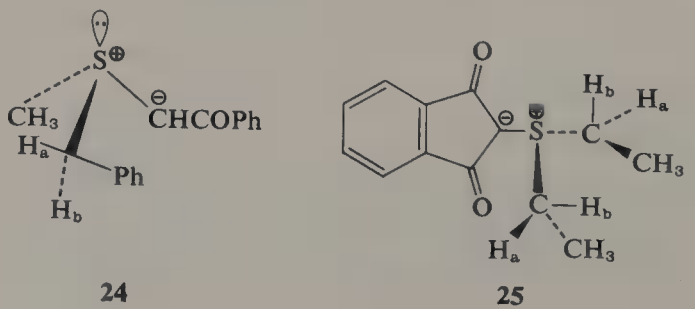
(3.5)

associated with a high barrier to rotation is the observation of two forms of the less delocalized ylide **22** at $-45°$.[53] Increasing electron delocalization

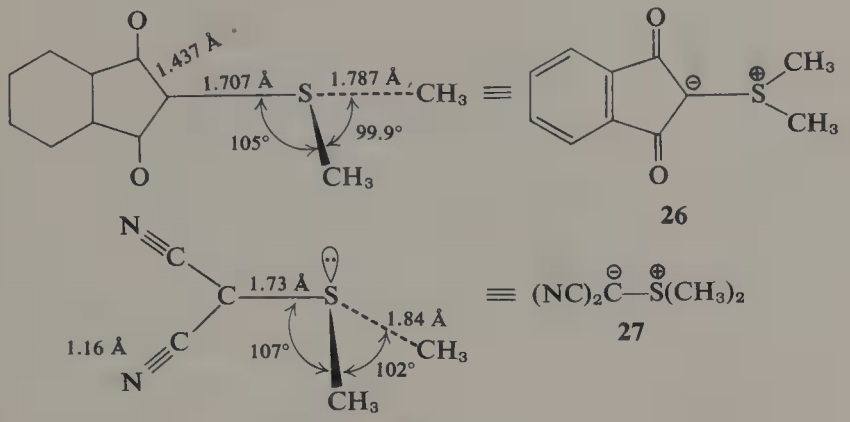


into the carbonyl substituent, as in the case of **23**, raises the barrier so that no interconversion is observed up to 70°.[19]

The tetrahedral nature of sulfur in these stabilized ylides is clearly indicated by nmr spectra of **24**[54] and **25**.[25] The appearance of the methylene group of



the benzyl and ethyl substituents, respectively, as AB patterns in their nmr spectra requires an asymmetric environment about sulfur. The crystal structures of ylides **26**[55] and **27**[56,56a] (see Fig. 3.2) also demonstrate nonplanarity

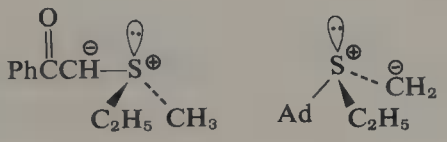


26

27

Fig. 3.2. X-Ray structure of stabilized ylides.

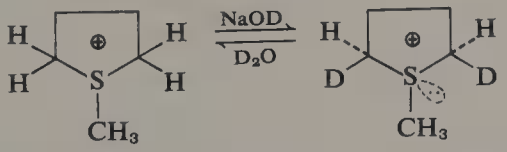
at sulfur. Darwish and Tomilson have succeeded in resolving the phenacylide **28** demonstrating a reasonable configurational stability at sulfur.[57] That the



28 **29**

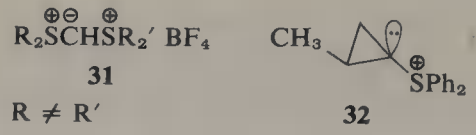
Ad = 1-adamantyl

nonplanarity at sulfur does not emanate from the presence of the electron-withdrawing substituent was demonstrated by the generation of the methylide **29** from optically active sulfonium salt.[58] Quenching of this ylide led to recovered sulfonium salt with no loss of optical purity. The cyclic sulfonium salt **30** shows a high stereochemical preference for H–D exchange of the diastereotopic protons of the ring methylenes.[59] This observation also supports the nonplanarity of the ylide system. It should be pointed out, however, that little or no specificity is seen with 6- or 7- membered rings.[59,59a]



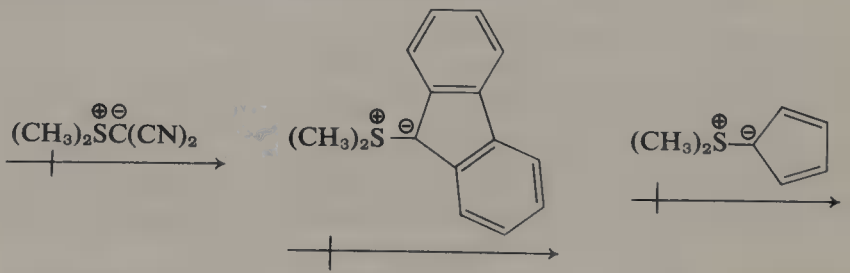
30

Wolfe recently claimed that the ylide **31** retains its asymmetry, too—a fact requiring a tetrahedral configuration at carbon as for most simple carbanions.[60] This structural question has been resolved for only one other



ylide, cyclopropylide **32**. It also retains its configuration at carbon relative to protonation in hydroxylic media or carbonyl condensation in aprotic media.[30] Such a geometry for **32** is not surprising considering the geometric constraints of the small ring.

Thus, the preferred geometry at sulfur and carbon does not lend support to appreciable double-bond character in sulfur ylides. Furthermore, the bond distances observed in the stabilized ylides **26** and **27** (Fig. 3.2) are difficult to interpret. The ylide carbon–sulfur bond length (1.71 to 1.73 Å) lies between that of a C–S single bond (1.81 Å) and a C–S double bond (1.64 Å). It is clear that charge effects determine these bond lengths to some extent. The change in the sulfur–methyl carbon single bond from 1.79 to 1.84 Å in going from **26** to **27** supports that contention. Furthermore, hybridization effects must also be taken into account. While no data exist to judge the inherent differences between an sp^3 carbon–sulfur and an sp^2 carbon–sulfur single bond, similar changes in hybridization of carbon–carbon bonds can lead to bond shortenings of 0.04–0.06 Å.[61] Without being able to make reasonable approximations of these effects, no significance can be attributed to the observed bond distances.[56a] The bond distances in the remaining portions of the molecule do indicate extensive charge delocalization by the carbonyl and cyano groups. Dipole moment studies also support a large amount of charge separation.[25,62,63] These structural studies combined with the chemical behavior of ylides fail to support the existence of appreciable double-bond character between the ylide carbon and sulfur.

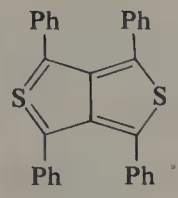


$\mu = 8.077$ (Ref. 25)

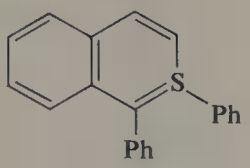
$\mu = 6.2$ (Ref. 62)

$\mu = 5.7$ (Ref. 63)

On the other hand, some double-bond character must be invoked to explain the unusual ability of sulfonium centers to stabilize an adjacent negative charge compared to ammonium centers. The fact that the unusual ylide **33**[64] appears to be aromatic reinforces this suggestion.[66] Compounds of the type **34** and **35**, while originally thought to be aromatic[65] appear to



33



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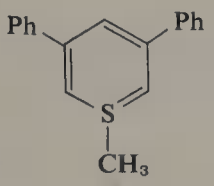


35

be "ylidelike."[65a,65b,66] Furthermore, ylide **28** racemizes 200 times faster than the corresponding sulfonium salt.[57] Several explanations may be brought forth[60,67]; however, an attractive possibility is the lowering of the activation energy for inversion at sulfur by more efficient Cp_π–Sd_π (or Cp_π–Sp_π) overlap in the planar transition state. On the other hand, Johnson and co-workers generated an optically active oxosulfonium ylide which appears to be optically stable indefinitely.[68]

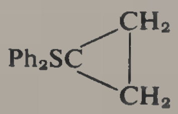
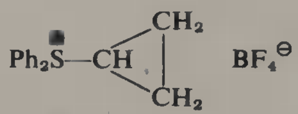
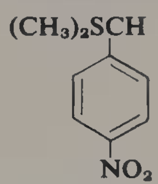
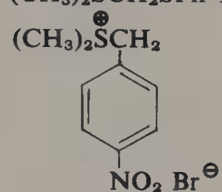
3.6 TABLES OF SELECTED YLIDES

The following tables provide a partial listing of the various ylides of synthetic value that have been prepared. On the whole, those ylides listed as nonstabilized must be generated at low temperatures and utilized *in situ*. Those that can be isolated have been listed under the heading stabilized ylides. For simplicity of presentation, the charges indicating the dipolar character of ylides have been omitted unless required for clarity. While an attempt has been made to make Table 3.I, part A comprehensive, Tables 3.I, part B and 3.II mainly contain representative examples to demonstrate the scope of the methods outlined in this chapter. Additional examples do appear in the text.

TABLE 3.I
Generation of Selected Sulfonium Ylides

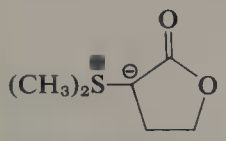
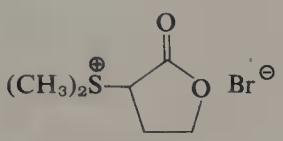
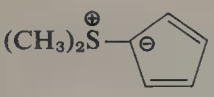
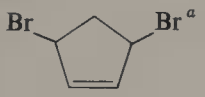
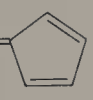
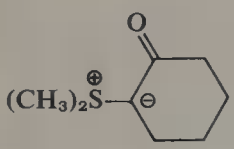
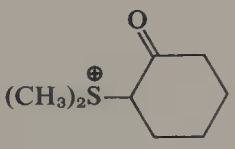
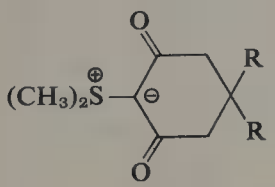
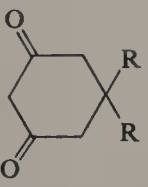
Ylide	Precursor	Base	Ref.
A. Nonstabilized			
1. $(CH_3)_2SCH_2$	$(CH_3)_3S^{\oplus}\ X^{\ominus}$	*n*-C_4H_9Li or $CH_3\overset{O}{\overset{\|}{S}}CH_2Na$, $KOC(CH_3)_3$, NaH, $NaNH_2$, NaOH	37, 69
	X = Cl, Br, I, BF_4		
2. Ph_2SCHCH_3	$Ph_2\overset{\oplus}{S}CH_2CH_3\ X^{\ominus}$ X = I, BF_4	$LiN(C_2H_5)_2$, *t*-C_4H_9Li, $LiN[CH(CH_3)_2]_2$	5
3. $(C_2H_5)_2SCHCH_3$	$(C_2H_5)_3S^{\oplus}\ I^{\ominus}$	$LiN(C_2H_5)_2$, NaOH	2, 5
4. $Ph_2SC(CH_3)_2$	$Ph_2\overset{\oplus}{S}CH(CH_3)_2\ I^{\ominus}$	$LiN[CH(CH_3)_2]_2$	23

TABLE 3.1 (*continued*)

Ylide	Precursor	Base	Ref.
5. 		$CH_3S(=O)CH_2Na$ or KOH	3, 38
6. $Ph_2SCHCH{=}CH_2$	$Ph_2\overset{\oplus}{S}CH_2CH{=}CH_2\ BF_4^{\ominus}$	*n*- or *t*-C_4H_9Li	6
7. $Ph_2SCH\text{-}C_3H_7\text{-}n$	$Ph_2\overset{\oplus}{S}CH_2\text{-}C_3H_7\text{-}n\ BF_4^{\ominus}$	*t*-C_4H_9Li, Ph_3CLi, $(C_2H_5)_2NLi$	5, 70
8. $Ph_2SC(CH_3)C_2H_5$	$Ph_2\overset{\oplus}{S}CH(CH_3)C_2H_5\ I^{\ominus}$	$LiN[CH(CH_3)_2]_2$	71
9. $Ph_2SCHCH(CH_3)_2$	$Ph_2\overset{\oplus}{S}CH_2CH(CH_3)_2\ BF_4^{\ominus}$	Ph_3CLi	69
10. $Ph_2SC(CH_3)CH_2CH{=}CH_2$	$Ph_2\overset{\oplus}{S}CH(CH_3)CH_2CH{=}CH_2\ BF_4^{\ominus}$	$LiN[CH(CH_3)_2]_2$	72
11. $Ph_2SC(CH_3)CH_2CH_2CH_3$	$Ph_2\overset{\oplus}{S}CH(CH_3)CH_2CH_2CH_3\ I^{\ominus}$	$LiN[CH(CH_3)_2]_2$	23
12. Ph_2SCHPh	$Ph_2\overset{\oplus}{S}CH_2Ph\ BF_4^{\ominus}$	*n*-C_4H_9Li	73
13. $(CH_3)_2SCHSPh$	$(CH_3)_2\overset{\oplus}{S}CH_2SPh\ Br^{\ominus}$	*n*-C_4H_9Li	70
14. 		NaH	74

Ylide	Precursor	Method	Ref.
B. Stabilized			
1. $(CH_3)_2SCH\overset{\oplus}{S}(CH_3)_2BF_4^{\ominus}$	$(CH_3)_2\overset{\oplus}{S}CH_2\overset{\oplus}{S}(CH_3)_2\ 2BF_4^{\ominus}$	Base, KOH	75
2. $(CH_3)_2SCHCO_2M$, M = Na, Li	$(CH_3)_2\overset{\oplus}{S}CH_2CO_2^{\ominus}$	Base, NaH, or *n*-C_4H_9Li	76
3. $(CH_3)_2SCHCO_2R$	$(CH_3)_2\overset{\oplus}{S}CH_2CO_2R\ Br^{\ominus}$	Base, $NaOCH_3$, or $NaOC_2H_5$	40, 49a 53
4. $(CH_3)_2SCHCON(C_2H_5)_2$	$(CH_3)_2\overset{\oplus}{S}CH_2CON(C_2H_5)_2\ Br^{\ominus}$	Base, NaH, or NaOH	49a
5. $(CH_3)(R)SCHCN$, R = CH_3, C_2H_5	$(CH_3)(R)\overset{\oplus}{S}CH_2CN\ BF_4^{\ominus}$	Base, NaOH, or *n*-C_4H_9Li	51, 77
6. $(CH_3)_2SCHSO_2C_{12}H_{25}\text{-}n$	$(CH_3)_2\overset{\oplus}{S}CH_2SO_2C_{12}H_{25}\text{-}n\ CH_3OSO_3^{\ominus}$	Base, NaOH	78

TABLE 3.I (*continued*)

Ylide	Precursor	Method	Ref.
7. $(CH_3)_2SC(CN)_2$	$(CH_3)_2S$ + $(NC)_2C$—  —$C(CN)_2$	Condensation	79
	$(CH_3)_2S{=}O'$ + $CH_2(CN)_2$	Condensation, P_2O_5, $SOCl_2$	79
8. $(CH_3)_2SC(CO_2CH_3)_2$	$(CH_3)_2S$ + $N_2C(CO_2CH_3)_2$	Condensation	30, 33, 34
9. 		Base, NaH	50
10. $(CH_3)_2SC(COCH_3)_2$	$(CH_3)_2S{=}O$ + $(CH_3CO)_2CH_2$	Condensation, P_2O_5	24
	$(CH_3)_2\overset{\oplus}{S}OC_2H_5$ $BF_4^{\ominus}$ + $(CH_3CO)_2CH_2$	Condensation, NaH	24
11. 	$(CH_3)_2S$ +  [a]	Condensation, NaOH	42, 63
	$(CH_3)_2S$ + 	Condensation, *hν*	80
12. 		Base, NaOH	81
13. 	$(CH_3)_2S{=}O$ + 	Condensation, Ac_2O, or DCC/H_3PO_4	25
14. $(CH_3)_2SCHCOAr$ Ar = Ph, *p*-$O_2NC_6H_4$, *p*-BrC_6H_4, *p*-ClC_6H_4, *p*-PhC_6H_4	$(CH_3)_2\overset{\oplus}{S}CH_2COAr$ $Br^{\ominus}$	Base, KOH, or $NaOC_2H_5$	20, 49a, 82, 83
15. $(CH_3)_2SC(COPh)_2$	$(CH_3)_2SCHCOPh$ + PhCOCl	Acylation, $(C_2H_5)_3N$	20
16. $(CH_3)_2SC(COPh)(COCH_2Ph)$	$(CH_3)_2SCHCOPh$ + $(PhCH_2CO)_2O$	Acylation, NaH	84

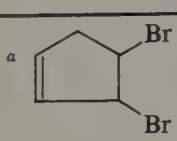
[a]  also present.

TABLE 3.II
Generation of Selected Oxosulfonium Ylides

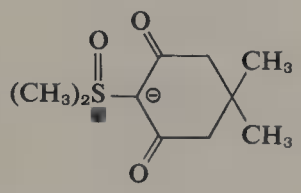
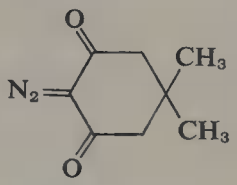
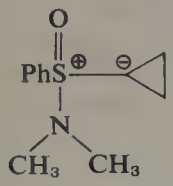
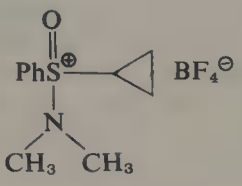
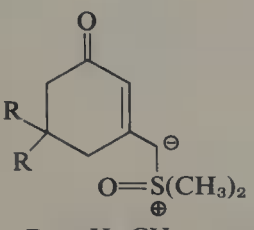
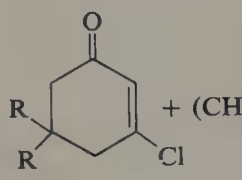
Ylide	Precursor	Method	Ref.
1. $(CH_3)_2\overset{\overset{O}{\|}}{S}CH_2$	$(CH_3)_3\overset{\oplus}{S}O\ I^{\oplus}$	Base, NaH	37
2. $RS(O)CH_2N(CH_3)_2$ R = Ph, CH_3	$RS(O)^{\oplus}CH_3\ BF_4^{\ominus}$ $N(CH_3)_2$	Base, NaH	85, 86
3. $PhS(O)(R)(R')N(CH_3)_2$ R = H, R′ = CH_3 R = R′ = CH_3	$PhS(O)^{\oplus}CHRR\ BF_4^{\ominus}$ $N(CH_3)_2$	Base, NaH	87
4. $(CH_3)_2\overset{\overset{O}{\|}}{S}CHCHO$	$(CH_3)_2\overset{\overset{O}{\|}}{S}CH_2 + HCO_2C_2H_5$	Condensation	19
5. $(CH_3)_2\overset{\overset{O}{\|}}{S}CHCO_2CH_3$	$(CH_3)_2S{=}O + N_2CHCO_2CH_3$	Condensation, *hν*, or CuCN	36, 88
6. $(CH_3)_2\overset{\overset{O}{\|}}{S}CHCONHPh$	$(CH_3)_2\overset{\overset{O}{\|}}{S}CH_2 + PhNCO$	Condensation	21a, 88
7. $(CH_3)_2\overset{\overset{O}{\|}}{S}CHCOCH_3$	$(CH_3)_2S{=}O + N_2CHCOCH_3$	Condensation, *hν*, or CuCN	89
8. 		Condensation, *hν*, or CuCN	88
9. $(CH_3)_2\overset{\overset{O}{\|}}{S}CHCOPh$	$(CH_3)_2S{=}O + N_2CHCOPh$	Condensation, *hν*, or CuCN	89
10. $(CH_3)_2\overset{\overset{O}{\|}}{S}CH\overset{\overset{Ph}{\|}}{C}{=}CHCO_2C_2H_5$	$(CH_3)_2\overset{\overset{O}{\|}}{S}CH_2 + PhC{\equiv}CCO_2C_2H_5$	Condensation	21, 21a

TABLE 3.II (*continued*)

	Ylide	Precursor	Method	Ref.
11.			Base, NaH	87, 90
12.	 R = H, CH_3		Condensation	91
13.	$(CH_3)_2SCHSi(CH_3)_3$	$(CH_3)_2SCH_2 + (CH_3)_3SiCl$	Condensation	92

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4

The Course of Alkylidene Transfers

4.1 INTRODUCTION

A comparison between sulfur ylides and diazo compounds is striking in terms of both structure and reactivity. Both species can condense with carbonyl partners to form epoxides. The sulfonium series reacts in this fashion with both saturated and α,β-unsaturated carbonyl partners; in

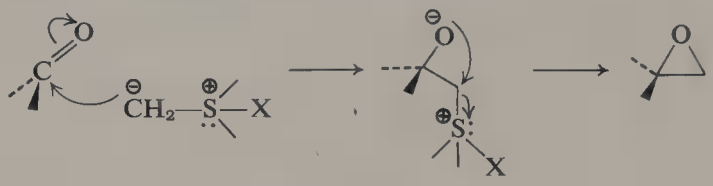
$$\overset{\ominus}{C}H_2—\overset{\oplus}{S}(CH_3)_2 \qquad \overset{\ominus}{C}H_2—\overset{\oplus}{\cdot}N_2$$

contrast, the oxosulfonium series requires aldehydes and ketones not susceptible to conjugate addition (Michael reaction). Both species cyclopropanate olefins. It is tempting to expand the analogy to mechanism. However, the available data suggest that virtually all reactions of the ylides are nucleophilic in nature.

4.2 EPOXIDATIONS

Although detailed mechanistic studies have not been carried out, the epoxidation reaction most simply can be envisioned as nucleophilic addition

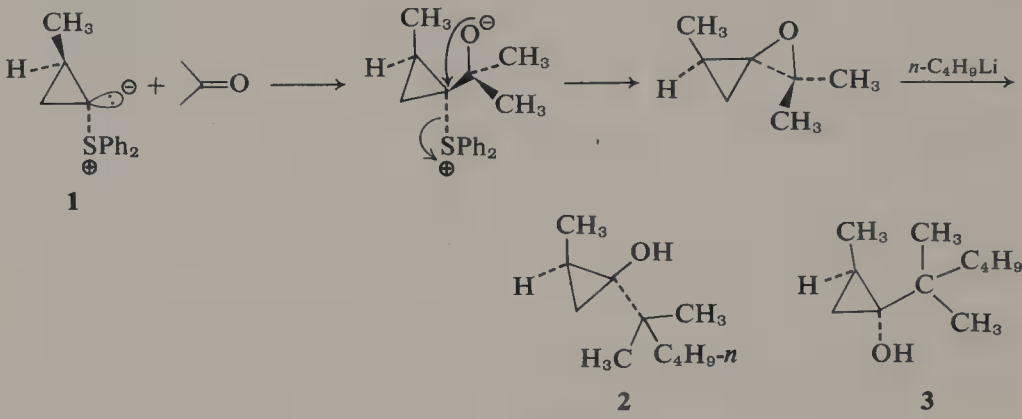
followed by 1,3-elimination [Eq. (4.1)]. The stereochemistry of the reaction supports this simple notion. Addition of the cyclopropylide **1** to acetone



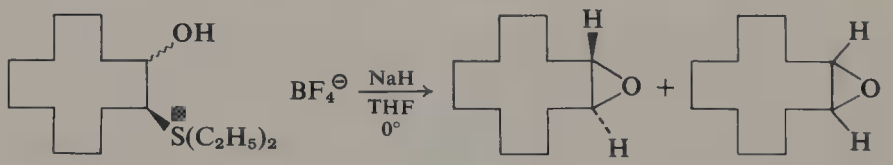
(4.1)

X = electron pair or O

followed by oxaspiropentane ring opening with *n*-butyllithium gave a cyclopropanol whose stereochemistry reflected the stereochemistry of the starting ylide.[1] Utilizing two mixtures of cyclopropylides differing in their trans-to-cis ratio (70:30 and 80:20) produces the cyclopropanols **2** and **3** in a ratio (70:30



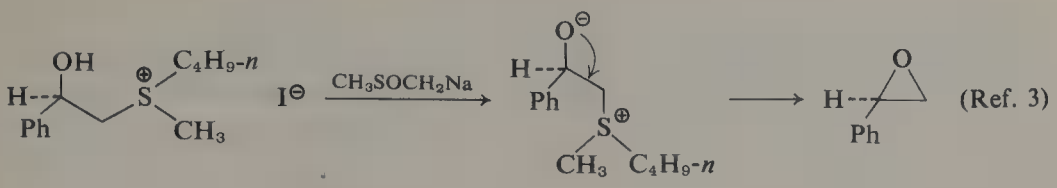
and 78:22, respectively) identical to that of the ylides. For simplicity, the stereochemical course for only the reaction of the *trans*-ylide is depicted. This result suggests retention of configuration at the ylidic carbon in the addition step followed by inversion of configuration at this carbon in the elimination step. The latter is further supported by the decompositions of the β-hydroxysulfonium salts **4a** and **4b** of known configuration.[2]



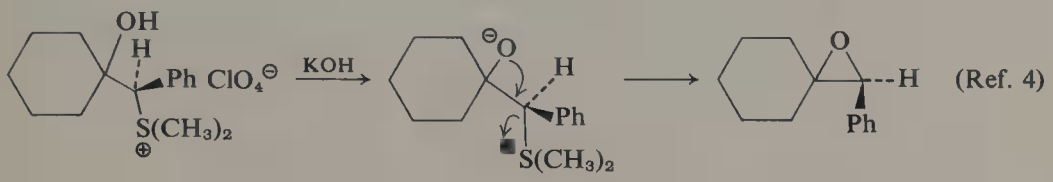
4a *cis*:*trans* 94:6 — 91% — 9%

4b *cis*:*trans* < 1:> 99 — 3% — 97%

In the case of "nonstabilized" sulfonium ylides, the formation of the betaine has been found to be irreversible. The optically active betaines **5** and **6** generated independently by deprotonation of the corresponding hydroxysulfonium salts underwent 1,3-elimination with essentially no loss of optical

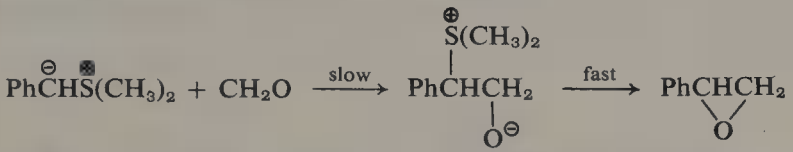


94% optically pure **5** 90% optically pure

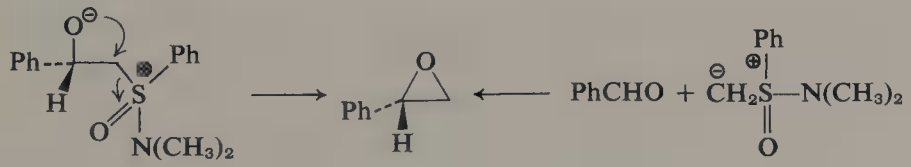


6

activity. Thus, dissociation of the betaines into carbonyl partners and ylides does not compete with elimination. Analysis of the reaction of formaldehyde with dimethylsulfonium benzylide led to a similar conclusion.[5] Independent generation of the betaine revealed that 1,3-elimination to product is at least 100 times faster than reversion to ylide and aldehyde.



On the other hand, the adducts from oxosulfonium and stabilized ylides with carbonyl partners revert to starting materials faster than they undergo 1,3-elimination. The optically pure betaine **7** produced styrene oxide with the same optical purity obtained when the chiral ylide reacted with benzaldehyde.[3]



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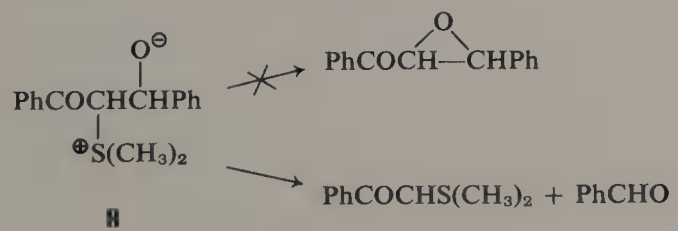
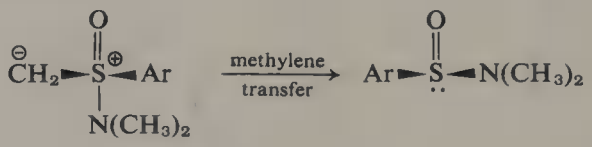
Dissociation of **7** to benzaldehyde and ylide was confirmed by performing the reaction in the presence of water or benzalacetophenone which diverts the ylide. Generation of the betaine **8** produced no epoxide, only the stabilized



8

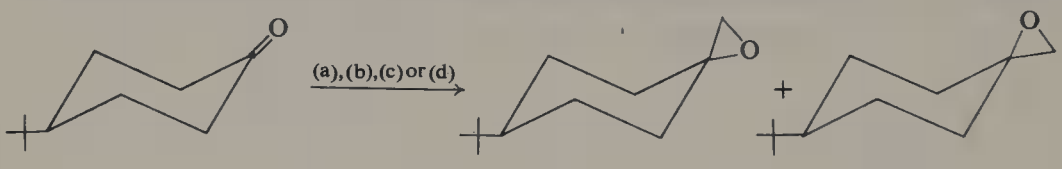
ylide and benzaldehyde were isolated.[6] The stereochemistry at sulfur during alkylidene transfer has also been established.[7] Methylene transfers with the oxosulfonium ylides **9a** and **9b** of the *R* configuration produce the



9a: Ar = 4-$CH_3C_6H_4$
9b: Ar = 2, 4, 6-$(CH_3)_3C_6H_2$

sulfinamide of the *R* configuration. This represents a retention of configuration at sulfur.

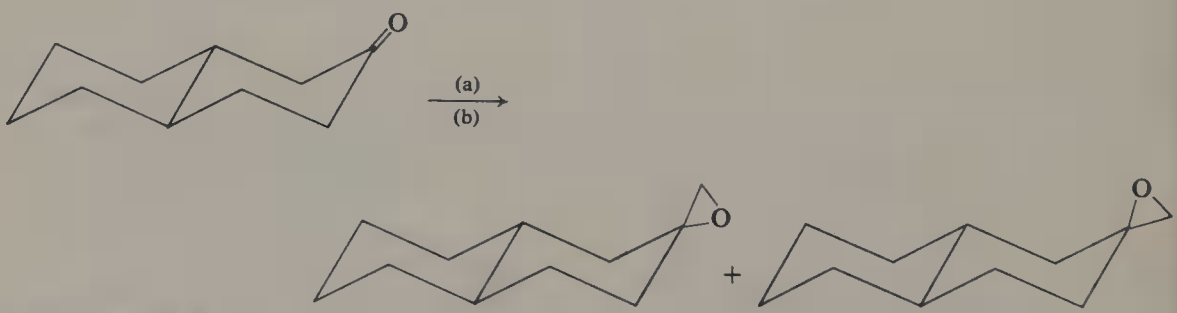
However, the dichotomy which exists between sulfonium methylides and oxosulfonium methylides in the stereochemistry of their addition to unsymmetrical ketones suggests that simple nucleophilic addition for both is



(a)	5	:	1
(b), (c), or (d)	—		only

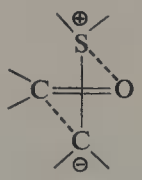
(a) = $(CH_3)_2SCH_2$ (b) = $(CH_3)_2\overset{\overset{O}{\|}}{S}CH_2$

(c) = $PhS(=O)(=NTs)CH_2$ (d) = $PhS(=O)(N(CH_3)_2)CH_2$



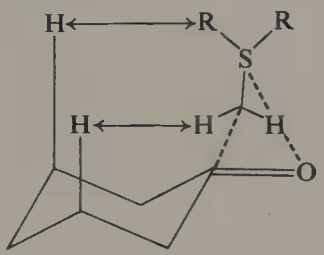
(a) = $(CH_3)_2SCH_2$	3	:	2
(b) = $(CH_3)_2\overset{\overset{O}{\|}}{S}CH_2$	1	:	9

unlikely. Thus, with 4-*t*-butylcyclohexanone[8] and *trans*-2-decalone,[9] dimethylsulfonium methylide showed a distinct preference for axial attack; whereas, the oxosulfonium methylides showed almost exclusive equatorial attack.[8–10] In steroids, the stereoselectivities appear to be even higher.[11,12] The origin of this difference must reside in the kinetic preference of the addition since the sulfonium betaines are known to collapse to epoxides faster than they revert. A possible explanation advances two orientations for the two classes of ylides in the addition step. Orbital symmetry suggests that a four-center

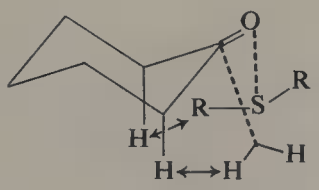


10

reaction is allowed in a $2a + 2s$ mode, i.e., **10**.[13] Such an orientation has been advocated to explain the stereochemistry of phosphorus ylide reactions.[14] If this mode of approach is assumed for the sulfonium ylide, for the axiallike approach steric interactions arise between the C-3 axial hydrogens and two

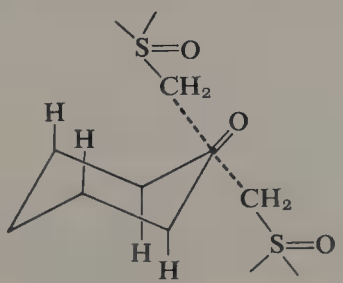


Axial approach



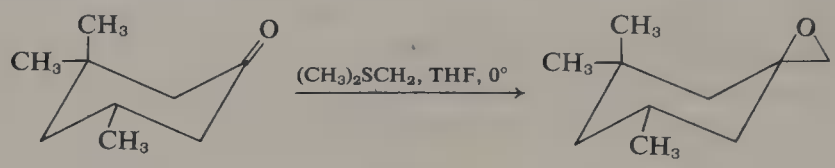
Equatorial approach

of the ylide substituents. On the other hand, equatoriallike approach involves steric interactions between C-2 axial hydrogens and these same ylide substituents. Molecular models suggest more severe steric crowding in this latter arrangement. In oxosulfonium ylides the electron-releasing oxygen and the dipole-dipole interactions diminish the importance of interaction between the ylide sulfur and carbonyl oxygen. Thus, such ylides favor end-on attack and exhibit stereochemical preferences akin to those of typical anions such as the

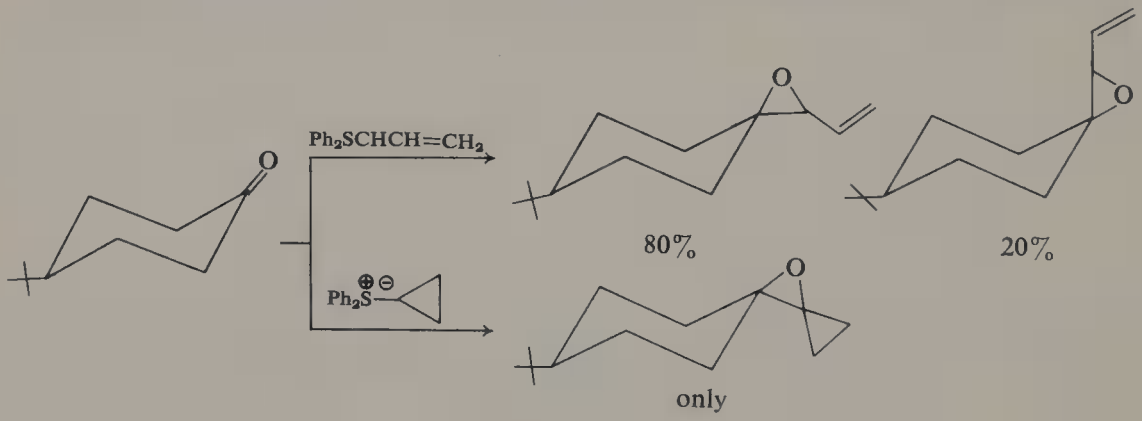


organomagnesium or organolithium reagents for which equatorial approach is known to predominate.[15]

This model predicts that axial substitution at C-3 would decrease the preference for the axiallike approach with the sulfonium ylides by increasing



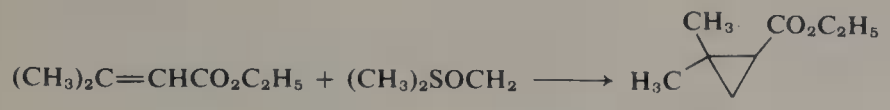
the nonbonded interactions. Indeed, 3,3,5-trimethylcyclohexanone produces only the epoxide arising from the equatorial approach regardless of the nature of the ylide.[16] As the methylene group and sulfur are substituted with bulkier substituents, the steric congestion created in the transition state for the four-center approach becomes so severe that only the equivalent of end-on attack can be accommodated. For example, the orientational preferences reverse in the additions of diphenylsulfonium allylide[17] and cyclopropylide[18] to carbonyl groups. The former exhibits an equatorial/axial ratio of attack of approximately four and the latter only produces the equatorial isomer.

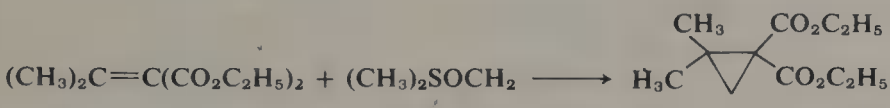


4.3 CYCLOPROPANATIONS

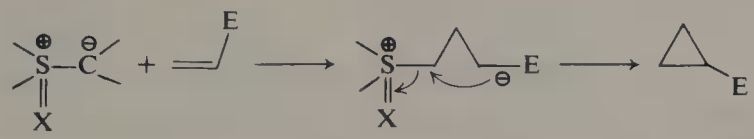
Cyclopropanation proceeds well only with systems normally susceptible to Michael addition. Furthermore, enhancement of the electron withdrawal from the double bond facilitates reaction. Thus, ethyl 3-methyl-2-butenoate underwent cyclopropanation only to the extent of 9% in 1 hr; whereas diethyl isopropylidenemalonate underwent cyclopropanation to the extent of 91% under identical conditions.[19]

Such findings stand in stark contrast to the carbene reactions whose rates are enhanced by electron-donating groups and retarded by electron-withdrawing groups. This requirement suggests stabilization of an incipent carbanion

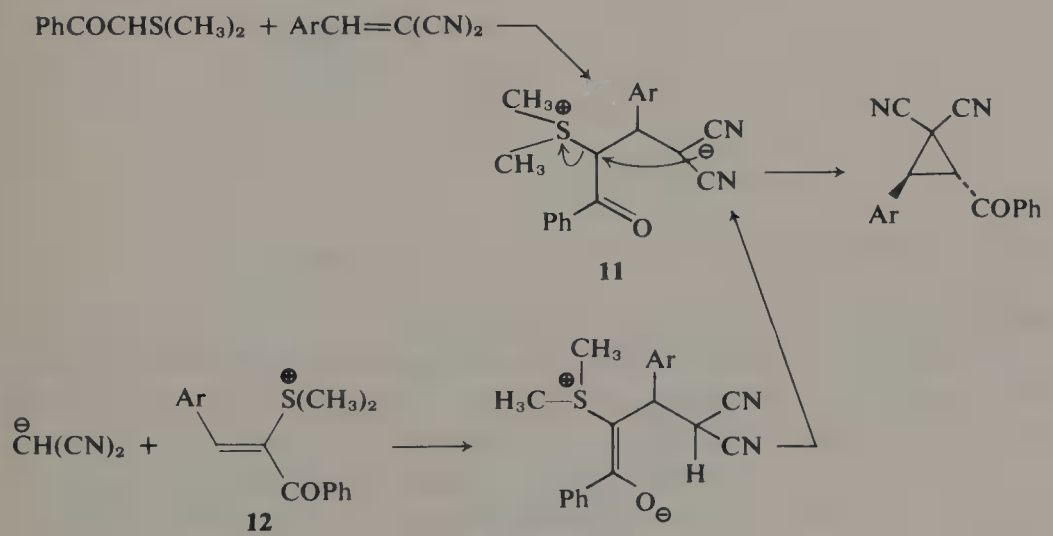




during the nucleophilic addition of the anionic center of the ylide to the Michael acceptor.

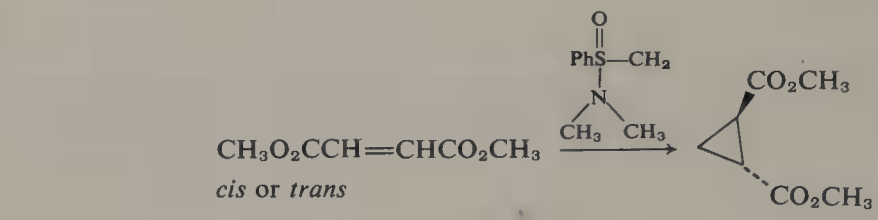


Independent generation of such intermediates confirms their facile collapse to cyclopropanes. The reaction of dimethylsulfonium phenacylide with arylidenemalononitrile produces the corresponding cyclopropane presumably via the intermediate **11**.[20] This intermediate can be synthesized by the addition of a malononitrile anion to the vinylsulfonium salt **12** followed by proton shift. In both instances the same cyclopropane is obtained in excellent yields (Scheme 4.1).

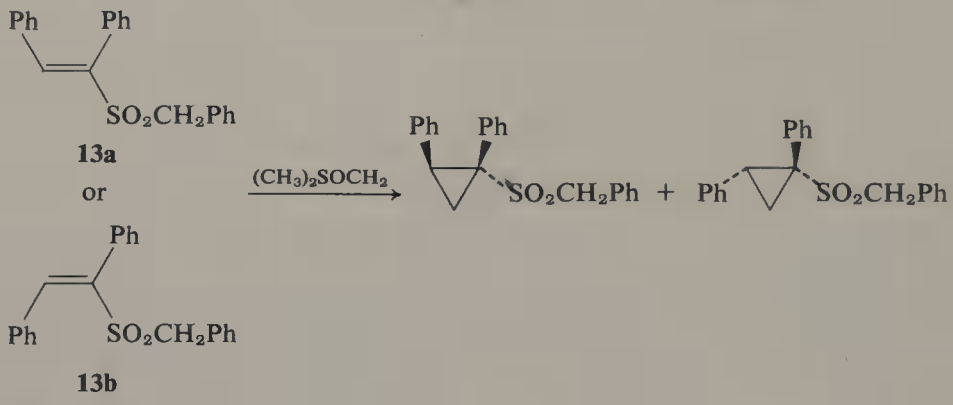


Scheme 4.1.

Further support for this interpretation arises in the stereochemistry of the reaction. Reaction of dimethyl maleate or dimethyl fumarate with phenyldimethylaminooxosulfonium methylide produced only *trans*-1,2-dicarbomethoxycyclopropane [Eq. (4.2)].[21] Similarly, both *cis*- and *trans*-sulfones **13a** and **13b** gave about a 1:1 mixture of the *cis*- and *trans*-cyclopropanes in 86 and 97% yields, respectively, with the oxosulfonium methylide.[22]

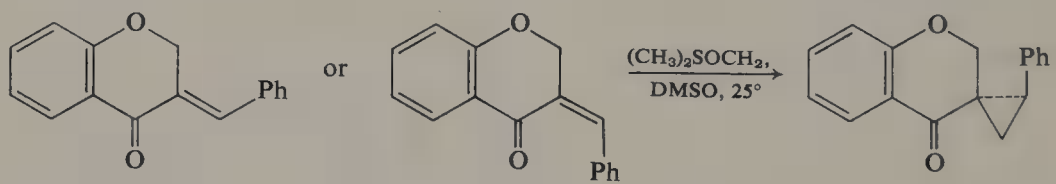


(4.2)



13a or **13b**

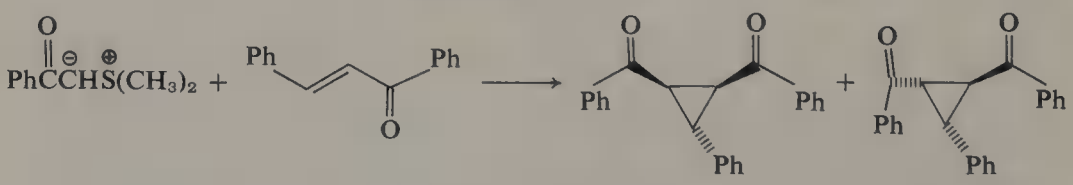
Additions to enones reveal similar behavior.[23,24] The arylidenechromanone **14** produces the cyclopropane **15** regardless of the geometry of the Michael



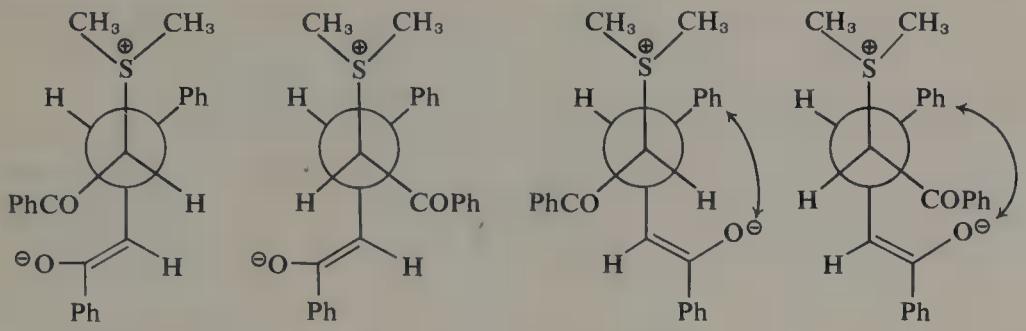
14a **14b** **15**

acceptor.[25] Suitable control and labeling studies exclude isomerization of starting materials and/or products. The formation of a 1,3-zwitterion as depicted earlier best accommodates these results.

Consideration of the nonbonded interactions in such an intermediate allows predictions of stereochemistry in the resultant cyclopropanes. Thus, the reaction of dimethylsulfonium phenacylide with *trans*-benzalacetophenone produces *cis*-1,2-dibenzoyl-*trans*-3-phenyl- and *trans*-1,2-dibenzoyl-3-phenylcyclopropane in which the former predominates.[26] Newman projections

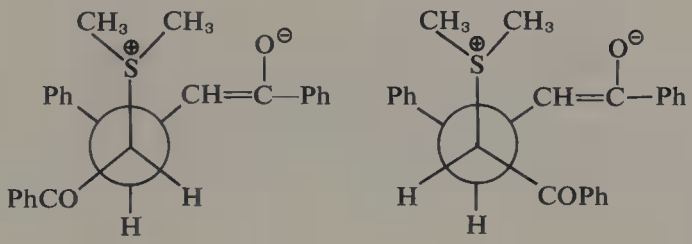


of the proposed intermediates in the conformation necessary for ring closure permit evaluation of the steric interactions. Diastereomers **16c** and **16d**



16a 16b 16c 16d

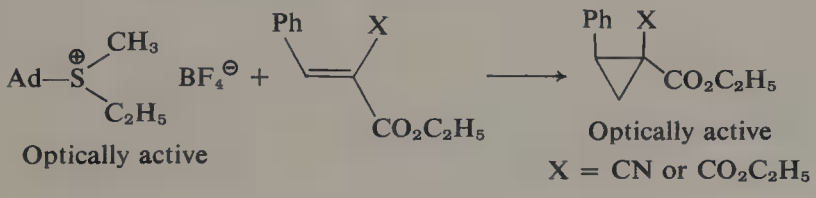
require eclipsing of the enolate and the bulky phenyl group for attainment of the desired conformation for 1,3-elimination and need not be considered further. Of the remaining conformations for diastereomers **16a** and **16b**, clearly that shown for **16a** minimizes the unfavourable eclipsing interactions. Thus, diastereomer **16a** should collapse to cyclopropane at a faster rate than diastereomer **16b**. Although the conformation depicted for **16a** is best for elimination, the relative thermodynamic stability of the two diastereomers **16a** and **16b** is reversed. The most stable conformations for these diastereomers, **16a′** and **16b′**, place the enolate close to the sulfonium center to minimize



16a′ 16b′

charge separation. Diastereomer **16b′** involves the least unfavorable eclipsing interactions. However, in this case, since the relative differences between the thermodynamic stabilities is probably not great because of eclipsing interactions of all bulky groups in both diastereomers, the higher rate of elimination of **16a** determines the product stereochemistry.

The involvement of sulfur in the elimination steps is demanded by the results obtained utilizing optically active ylides where the asymmetry resides at sulfur. Reaction of optically active adamantylethylsulfonium methylide with diethyl benzalmalonate or ethyl benzalcyanoacetate generates the



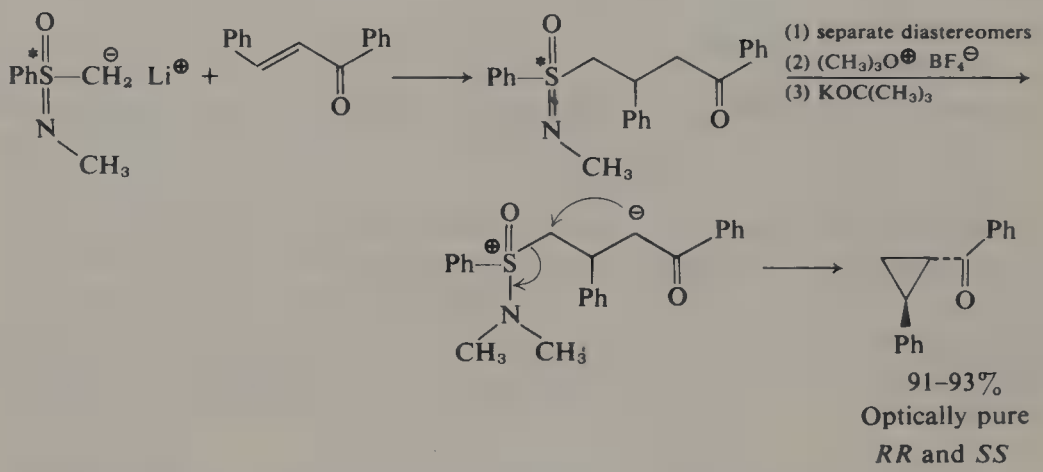
Optically active

Optically active

X = CN or $CO_2C_2H_5$

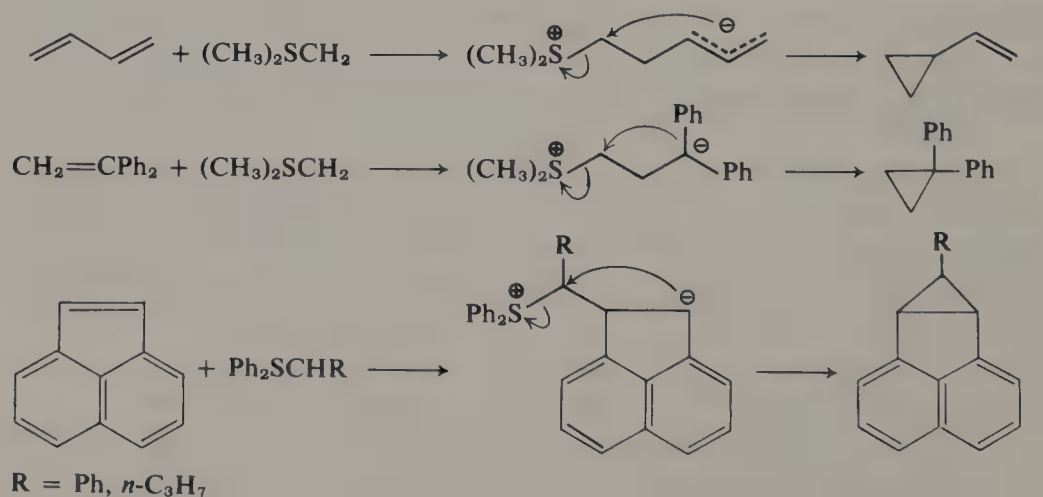
corresponding optically active cyclopropanes.[27] Optically pure phenyldimethylaminooxosulfonium methylide produces methyl *trans*-2-cyclopropyl-1-carboxylate with methyl *trans*-cinnamate in 30% optical yield.[7]

A modification of the ylide cyclopropanation allowed generation of the optically pure intermediate zwitterions.[3] Addition of lithium (*S*)-*N*-methylbenzenesulfonimidoylmethide to benzalacetophenone in dimethylformamide led to the Michael adduct as a diastereomeric mixture. Separation of the



diastereomers by column chromatography or recrystallization followed by alkylation (to the sulfonium salt) and base treatment generates the optically pure zwitterion intermediate. Its collapse produces each cyclopropane optically pure. The fact that no loss of optical purity accompanies 1,3-elimination indicates that reversal of the zwitterion to ylide and enone does not effectively compete.

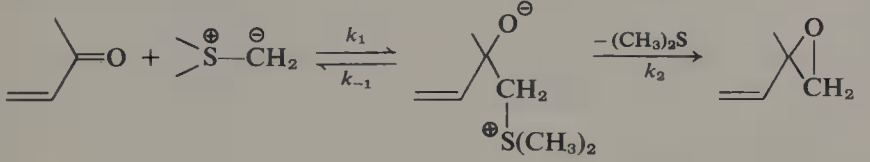
Although it seems firmly established that the cyclopropanation reaction proceeds by Michael addition followed by elimination, three exceptions to



the requirement for the presence of a strongly polarized double bond for reaction are known. It has been reported that dimethylsulfonium methylide cyclopropanates butadiene[28] and 1,1-diphenylethylene[8] in 30 and 61% yields, respectively, and that diphenylsulfonium benzylide and butylide cyclopropanate acenaphthylene.[29] Although it might be tempting to conclude that carbene reactions account for these reactions, more likely the same mechanism involving zwitterion intermediates operates. In each case, the required anion is stabilized by delocalization.

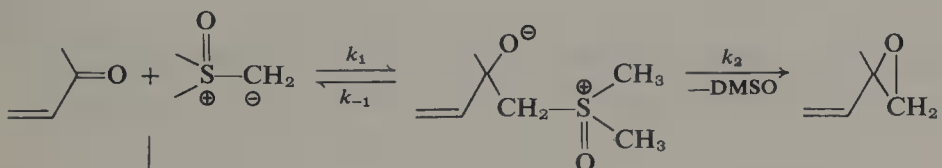
4.4 EPOXIDATION VS. CYCLOPROPANATION

There remains to establish the reasons for the discrepancy in reactions between dimethylsulfonium methylide and dimethyloxosulfonium methylide with α,β-unsaturated aldehydes and ketones in which the former forms epoxides and the latter cyclopropanes. The distinction can be attributed to 1,3-elimination being faster than reversion of carbonyl addition for the sulfonium methylide [Eq. (4.3), $k_2 > k_{-1}$]; whereas, the reverse is true of the oxosulfonium ylides [Eq. (4.4), $k_{-1} > k_2$]. In the latter case, the products,



(4.3)

17



(4.4)

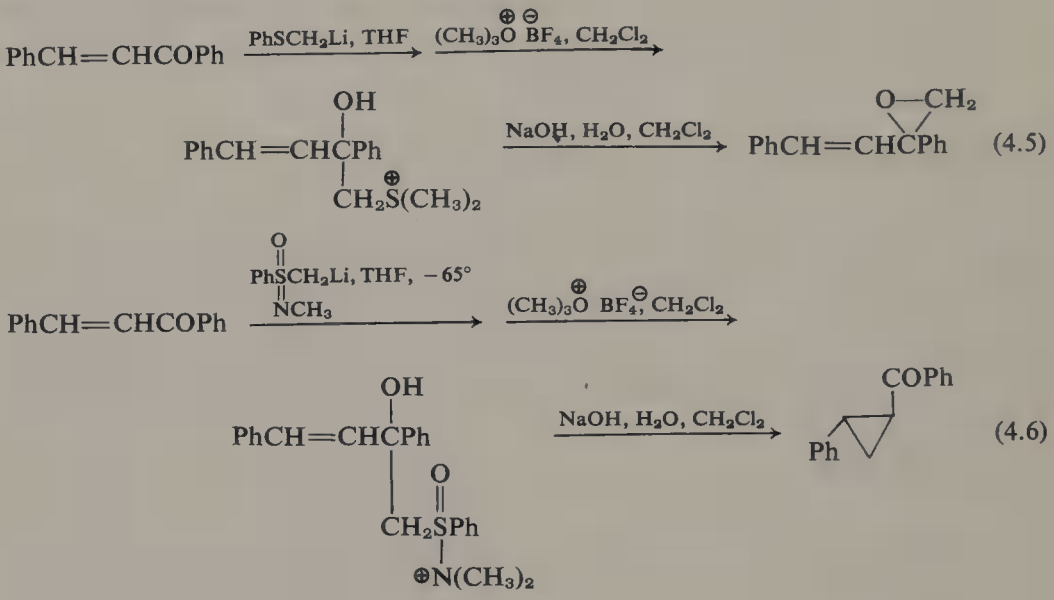
18

Conjugate addition

those of conjugate addition, are the result of thermodynamic control. Independent generation of the betaines **17** and **18** as outlined in Eq. (4.5) and Eq. (4.6) support this interpretation.[3]

Substituents which affect the relative rates of the elimination and reversal will alter the ratio of the two types of ylide products. Hindering 1,3-elimination by making the ylide carbon tertiary (e.g., isopropylide[30]) or part of a small ring (e.g., cyclopropylide[31]) leads to preference for thermodynamic control. Similarly, enhancing reversion of carbonyl addition by stabilizing the negative charge (e.g., allylide[17]) causes preferential cyclopropanation.

α-Keto ylides and others possessing similarly strongly stabilizing substituents most likely do not add to a carbonyl group even in a reversible fashion. Their failure to form epoxides with saturated aldehydes and ketones is a clear indication of this contention. Enhanced stabilization by resonance of the intermediate adduct obtained by conjugate addition is required for these ylides to react at all.

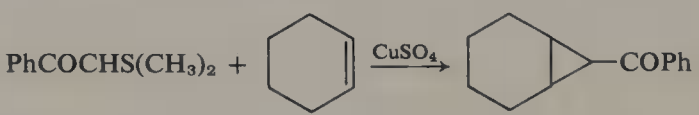


(4.5)

(4.6)

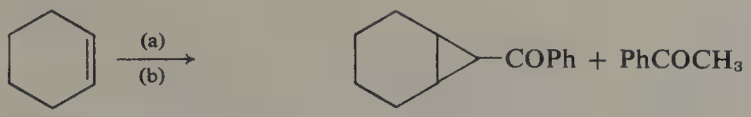
4.5 α-ELIMINATION

Can sulfur ylides form carbenes analogous to the related diazoalkanes? Evidence for thermal α-elimination is meager. Dimethylsulfonium phenacylide cyclopropanated cyclohexene in the presence of cupric sulfate, albeit



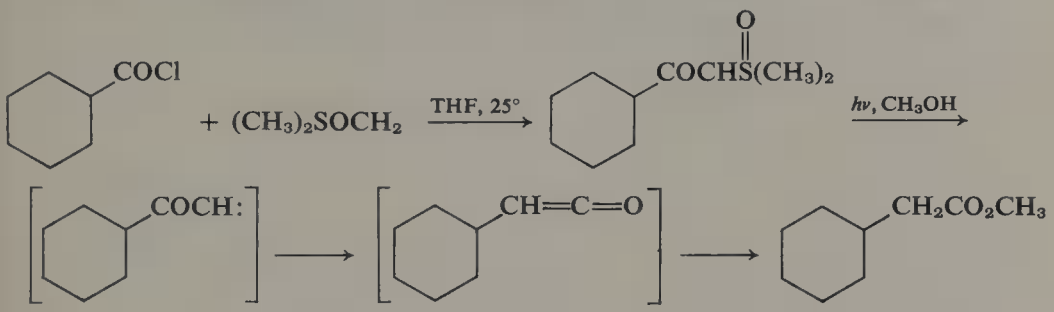
in low yield, and failed to do so in the absence of the copper salt.[26] This result suggests the intermediacy of a copper-complexed carbene.[26a] Other claims of thermal α-elimination remain even more speculative.[29,32,33]

On the other hand, a reasonable body of evidence exists for photolytic α-eliminations. The first case illustrated a striking resemblance between dimethysulfonium phenacylide and diazoacetophenone in their reactions with cyclohexene.[26] The ratio of cyclopropanation to hydrogen abstraction is identical within experimental error—a fact which suggests similar intermediates. This parallelism in behavior of the two classes of compounds



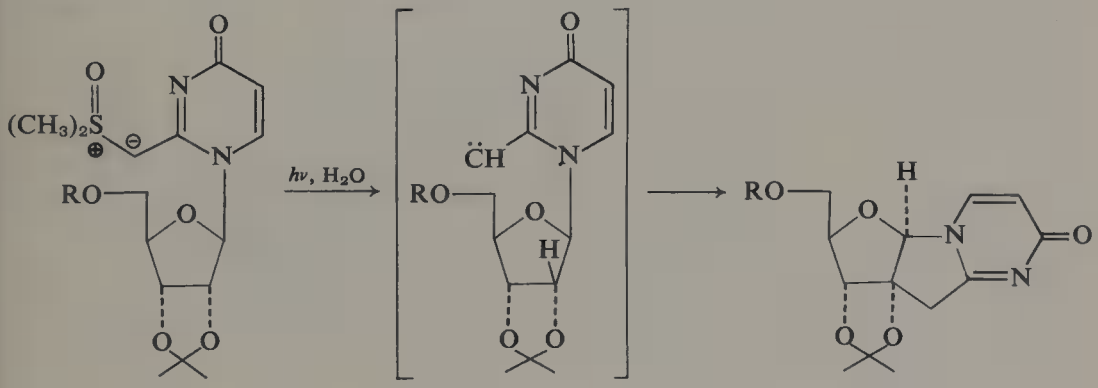
(a) = $PhCOCHS(CH_3)_2/h\nu$	1	:	8
(b) = $PhCOCHN_2/h\nu$	1	:	7

carries over to the photolytic decomposition of diphenylsulfonium allylide in which cyclopropene is isolated in 25% yield.[17] Corey and Chaykovsky developed an Arndt–Eistert type process by irradiation of β-ketooxosulfonium ylides prepared by acylation of the methylide.[34] Since the diazo



decompositions are believed to involve carbene intermediates, invocation of this same type of intermediate for the sulfur ylides appears most reasonable.

Insertion into C–H bonds serves as one of the most diagnostic reactions of carbenes. The fact that such a reaction occurs in good yields on irradiation of the ylide **19** provides further documentation for the α-elimination reaction.[35] The potential of sulfur ylides as general carbene precursors, although promising, remains to be exploited.



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5

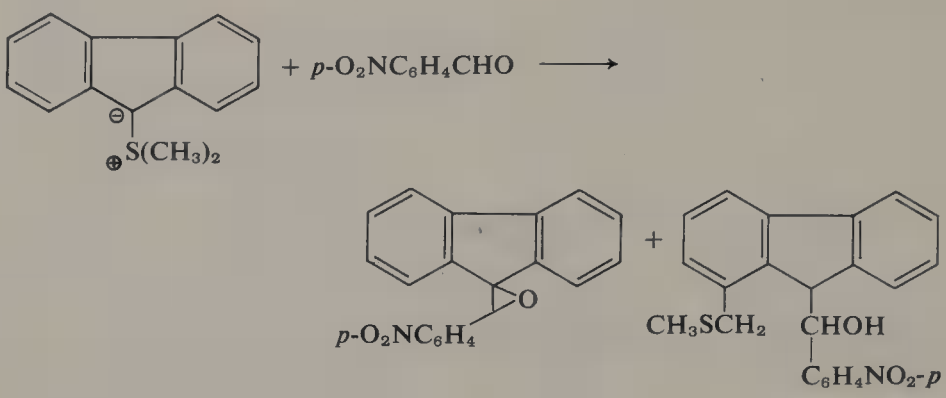
Carbonyl Additions

5.1 INTRODUCTION

One of the most widespread current uses of sulfur ylides is the synthesis of epoxides by condensation with aldehydes and ketones. The importance of epoxides per se as well as their versatility for conversion to many other structural units imparts special significance to this reaction. Prior to the introduction of sulfur ylides, epoxide formation generally involved olefin oxidation. The widespread occurrence of carbonyl groups in organic compounds made the discovery of a high-yield process for epoxide formation by carbonyl condensation essential. Normally, the condensation of diazo compounds[1] or stabilized α-haloanions[2] was utilized; however, side reactions are frequently predominant.

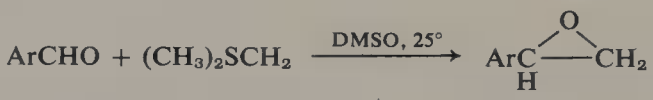
The first report of epoxide formation utilized the first reported stable ylide. Condensation of *p*-nitrobenzaldehyde with dimethylsulfonium fluorenylide produced the corresponding epoxide in addition to the product resulting from Sommelet–Hauser rearrangement of the intermediate betaine.[3] [See Eq. (5.1).]

Virtually all aldehydes and ketones examined serve as acceptors for either the oxosulfonium methylides or the more reactive dimethylsulfonium methylide. Aryl and alkyl aldehydes generate the corresponding oxiranes normally in 50–80% yields. As expected on the basis of nucleophilic addition to a carbonyl group, electron-withdrawing substituents facilitate reaction. Thus,



(5.1)

reaction of a series of aromatic aldehydes in which the electron-withdrawing effect of the aryl group was changed from 2-furanyl to 3,4-dichlorophenyl increased the yield of epoxide from 25 to 68% under a standard set of reaction conditions.[4–5a] In the one case examined, benzaldehyde, comparisons among



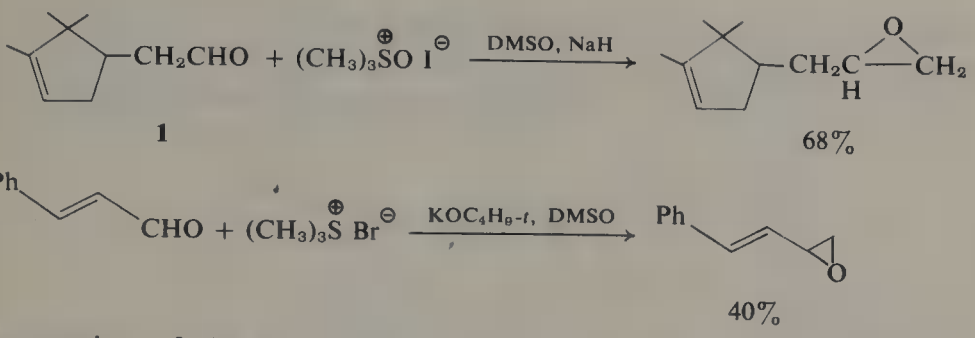
Ar = 2-furanyl	25%
Ar = 4-$CH_3OC_6H_4$	58%
Ar = C_6H_5	65%
Ar = 3, 4-$Cl_2C_6H_3$	68%

dimethylsulfonium methylide,[5–6] dimethyloxosulfonium methylide,[6] (dimethylamino)-*p*-tolyloxosulfonium methylide,[7] and (diethylamino)methyloxosulfonium methylide[8] revealed no appreciable differences in yields of epoxides (65–75, 56, 60, and 57%, respectively). The greater stability and availability of dimethyloxosulfonium methylide, however, would normally make it the reagent of choice. For simplicity, this reaction is referred to as nucleophilic epoxidation.

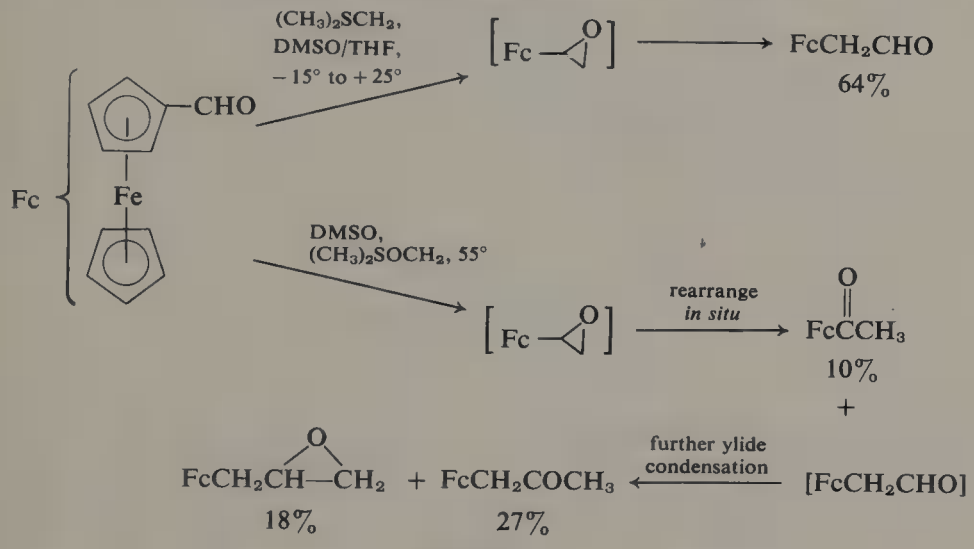
5.2 EPOXIDATIONS WITH METHYLIDES

No systematic study of the effect of various functional groups on carbonyl condensations of ylides has been made. Simple double bonds not conjugated to the carbonyl group do not interfere with epoxide formation with either the sulfonium or oxosulfonium ylides as in the case of aldehyde **1**.[9] On the other hand, α,β-unsaturated aldehydes exemplified by cinnamaldehyde require the use of the sulfonium ylides.[5] The oxosulfonium methylides generate only the corresponding cyclopropanes by conjugate addition.

In some cases, use of the more reactive sulfonium methylides precluded side reactions arising from decomposition of the initially produced epoxides.



The reaction of the two classes of ylides with ferrocene carboxaldehyde illustrates the phenomenon.[10] With the sulfonium methylide, condensation occurs smoothly at sufficiently low temperatures to allow formation of the

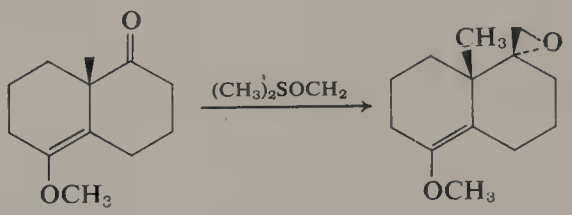


Scheme 5.1

expected epoxide. Rearrangement to the aldehyde, a net homologation sequence, presumably occurs during work-up (Scheme 5.1). On the other hand, the conditions required for condensation of this aldehyde with the oxosulfonium ylide also effect rearrangement of the sensitive epoxide. The major products arise by further ylide condensation with these intermediates.

Much more insight into the application of sulfur ylides arises in studying their reactions with ketones. Under normal conditions for methylide transfer, base-stable groups are inert. Thus, enol ethers [Eq. (5.2)][11] and acetals [Eq. (5.3)][12] remain intact. Hydroxyl and amino groups have been present without complications. Although other carbonyl functions like ester and amide are normally susceptible to nucleophilic addition, they react sufficiently more slowly so that they do not complicate epoxidation of ketones. For example, the keto ester **2** generates the desired epoxide in 61% yield.[13] However, in most instances, attack of the ylide on the ester would go un-

noticed except for lowering the yield of epoxide because the product of ester attack, a stabilized α-ketoylide, is normally water-soluble. Nitrile functions are also quite receptive toward nucleophiles, but the ketonitrile **3** was



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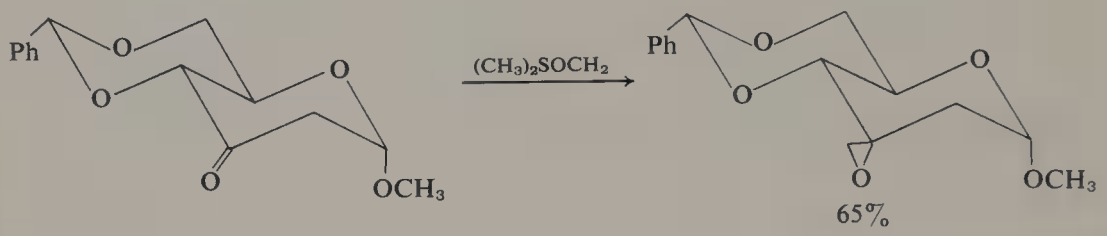

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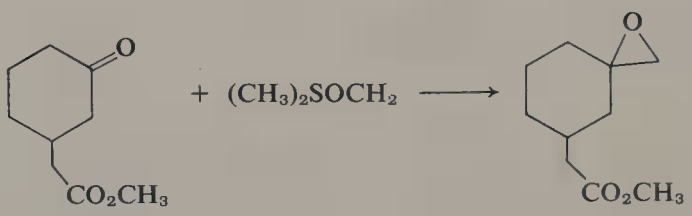

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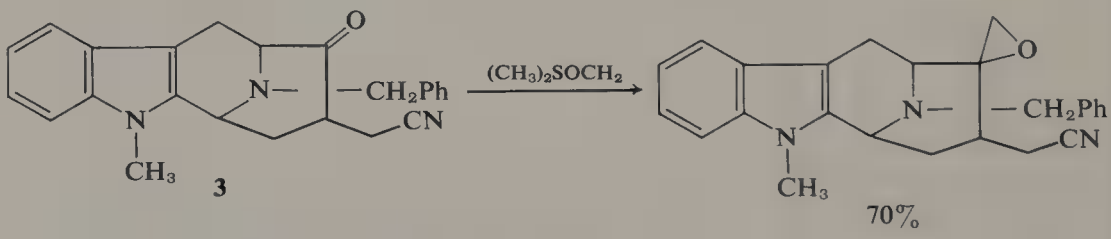
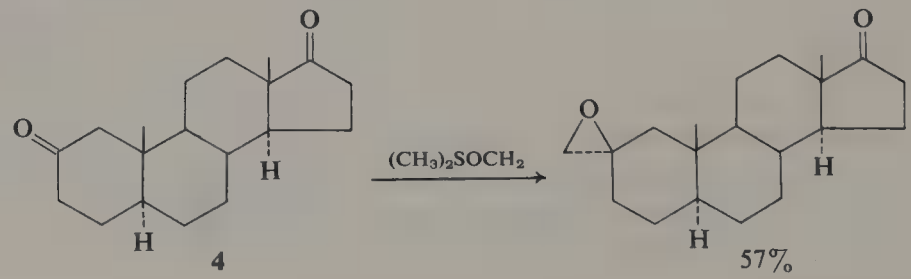


3

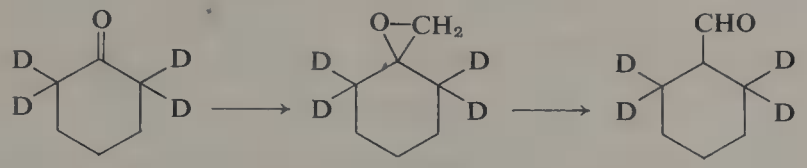
successfully epoxidized without interference as a key step in a total synthesis of ajmaline.[14,14a] A most interesting selectivity was demonstrated in condensation of the steroidal diketone **4** in which only the six-membered ring



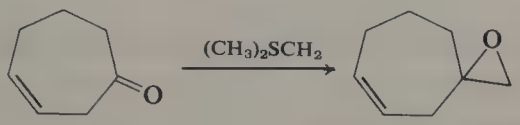
4

carbonyl group reacted. The generality of such discriminatory behavior remains to be established.

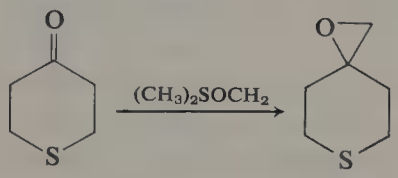
Enolization does not appear to compete with carbonyl addition. 2,2,6,6-Tetradeuterocyclohexanone undergoes methylene transfer with essentially no



deuterium loss as evidenced by the isolation of cyclohexanecarboxaldehyde-d_4



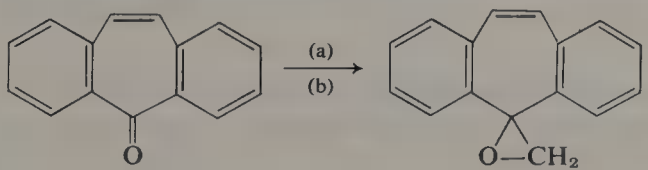
in 96% yield.[15] 3-Cycloheptenone undergoes methylene transfer with no evidence of double-bond migration.[16] 4-Thiacyclohexanone undergoes



65–75%

condensation without β-elimination.[17,17a] It appears that ketones possessing either a hydrogen isotope or asymmetry at the α-carbon atom will react without disturbance of that center. An exception occurs with ketones which show a high propensity for enolization or are very sterically hindered. Thus, deoxybenzoin[6] and hexahydrofluorenone[18] failed to react even with the methylides. In these instances, the ylide presumably serves as a base for enolization; the enolates are, of course, inert to condensation. Such problems potentially can be overcome by the reversible ylide generation technique. 4-Thiachromanones and dihydroquinolones appear also to be exceptions.[17a]

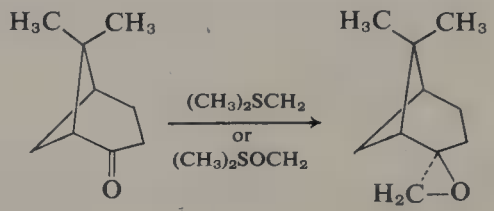
Many differences exist between the sulfonium methylides and the oxosulfonium methylides in their reactions with ketones. Normally, the more reactive sulfonium methylides give higher yields in shorter reaction times



(a) = $(CH_3)_2SCH_2$ 91%

(b) = $(CH_3)_2SOCH_2$ 42%

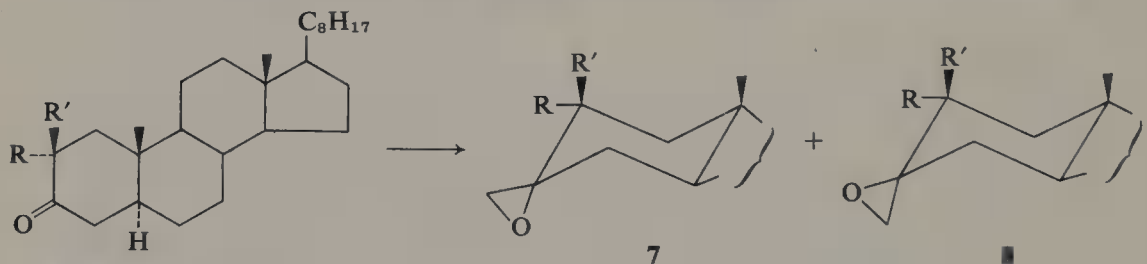
than do the oxoylide series. Thus, the sulfonium methylide at 0° for 30 min converts dibenzotropone into its epoxide in more than twice the yield as does the oxosulfonium ylide at 25° for 60 min.[19] Similarly, norpinone **5** is converted exclusively to the α-epoxide **6** in 80% yield with the sulfonium



5 **6**

methylide in only 1–2 h at −10°; whereas, this conversion proceeds only to the extent of 20% after 25 h at 25° with the oxosulfonium methylide.[20]

A second difference arises in the stereochemistry of addition. In general, the expectation that the sterically least hindered approach is taken is illustrated by the norpinone example above. However, specific exceptions must be cited. Cyclohexanones and condensed cyclohexanone systems (e.g., decalones, steroids, etc.) usually illustrate the complementary behavior of the two classes of ylides. 3-Cholestanone produces the β-epoxide **7a** (ratio 32:1) with the oxosulfonium methylide, but the α-epoxide preferentially with the sulfonium methylide (ratio of **7a** to **8a**, 1:2).[21] This axial preference for the

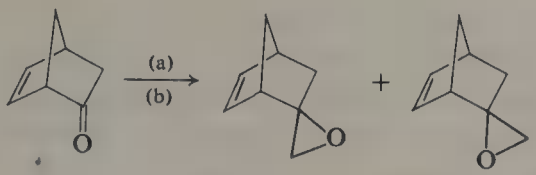


7 **8**

7a, 8a: R = R′ = H
7b, 8b: R = CH_3, R′ = H
7c, 7c: R = R′ = CH_3

sulfonium methylide is diminished by the incorporation of additional steric bulk on the α face of the molecule. Thus, reaction of the 2α-methyl-substituted cholestanone with the sulfonium ylide reverses the orientation giving a **7b**:**8b** ratio of 3:1. In this case, this ratio remains unchanged for the oxosulfonium methylide.

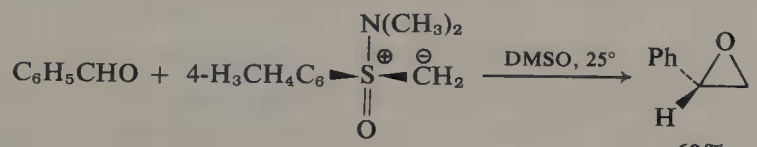
A similar reversal of stereochemistry has been observed with β,γ-unsaturated ketones suggesting a neighboring group effect for the proximate double bond. 5-Norbornen-2-one reacts with the oxosulfonium ylide to give mainly the product of more hindered attack, the *endo*-epoxide **9**; but, the sulfonium methylide generates the *exo*-epoxide **10** almost exclusively.[22] The fact that

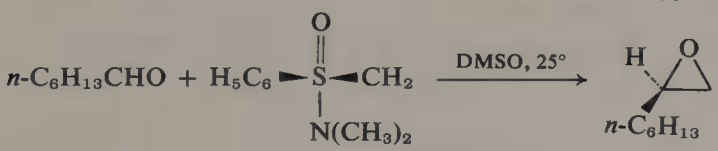


	9		10
(a) = $(CH_3)_2SOCH_2$	2.3	:	1
(b) = $(CH_3)_2SCH_2$	1	:	15.7

other carbanions react with 5-norbornen-2-one to give almost exclusive exo attack suggests that the stereochemistry of addition of the oxosulfonium ylide is the peculiar one. The rationale for the mechanism of carbonyl addition presented earlier accommodates these observations. Thus, in the end-on mode of attack of the oxosulfonium ylide, the positive sulfur is stabilized by interaction with the proximate double bond. A similar effect was observed with 2-norbornen-7-one[22,23] and 1-methylbicyclo[4.2.1]non-7-en-9-one[24] in which the oxosulfonium ylide added exclusively from the side syn to the double bond. Synthetically, the complementary behavior of the two ylides is exceedingly useful.

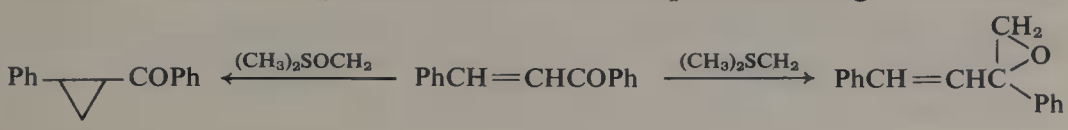
Asymmetric synthesis with optically active sulfoxamine ylides has been achieved with modest success; using an optically active sulfonium ylide has been unsuccessful. Condensation of benzaldehyde with optically pure adamantylethylsulfonium methylide leads to the corresponding epoxide with no observable rotation[25]; use of the sulfoxamine ylide of *R* configuration produces the same epoxide of *R* configuration with an optical purity of 20%.[26]



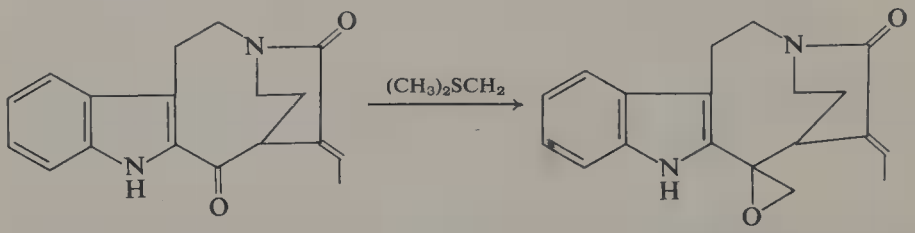


Use of an *S*-ylide with *n*-heptanal produces the *S*-epoxide of unknown optical purity.[26] The optical induction appears to exceed that normally observed in olefin epoxidations with optically active peracids.

The final major difference between the two classes of ylides arises in their behavior with Michael acceptor systems (α,β-unsaturated carbonyl compounds). Chalcone represents the classic example illustrating the contrast.

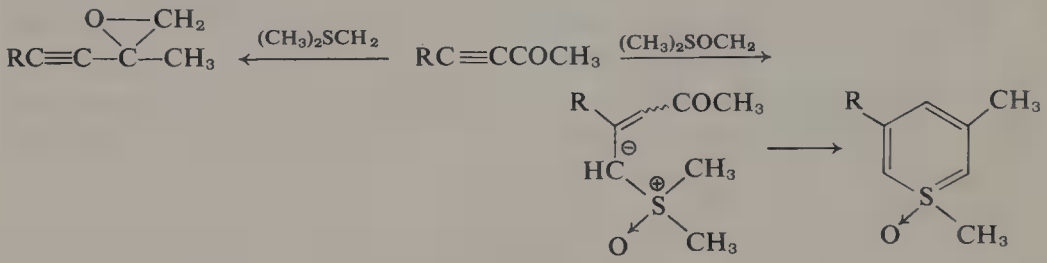


Dimethylsulfonium methylide condenses to form the epoxide exclusively in 87% yield; whereas the oxosulfonium methylide produced only the cyclopropane in 95% yield.[6] The reasons for these differences are discussed in Chapter 4. Dimethylsulfonium methylide is sufficiently selective so that even the unreactive ketone of a 2-acylindole reacts without cyclopropanation of the conjugated system.

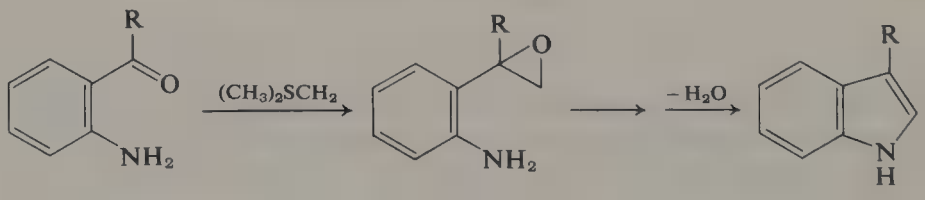


(Ref. 27)

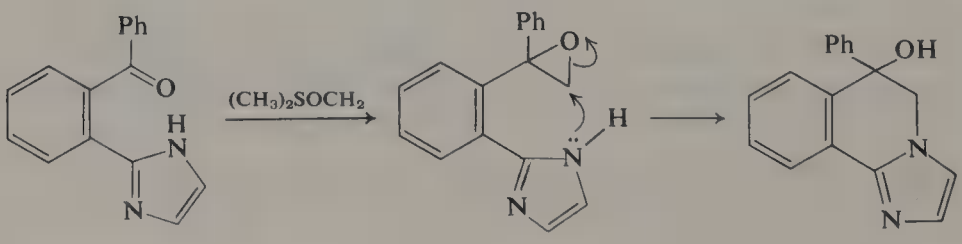
This discrepancy in behavior extends to α,β-acetylenic ketones. 2-Pentyn-4-one and 3-hexyn-5-one are epoxidized in 25–30% yield with dimethylsulfonium methylide,[28] but are converted into stabilized ylides with dimethyloxosulfonium methylide.[29] These stabilized ylides suffer thermal dehydration to generate the fascinating *S*-methylthiabenzene *S*-oxides.[29,30]



In cases where nucleophilic centers are situated close to the carbonyl group, epoxides are not the isolated products. Thus, phenyl ketones possessing an amino function ortho to the carbonyl generally produce heterocycles as the examples below illustrate. Although the epoxides have not been isolated from these reactions, their intermediacy is most reasonable.

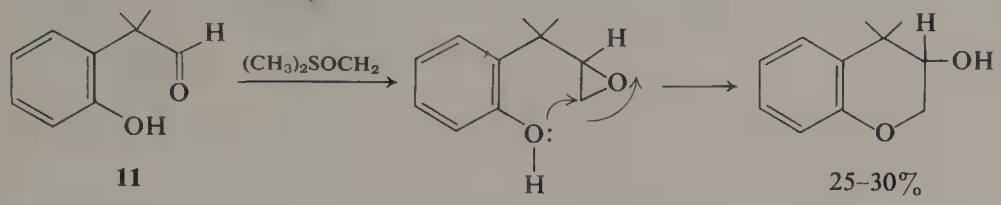


(Ref. 31)



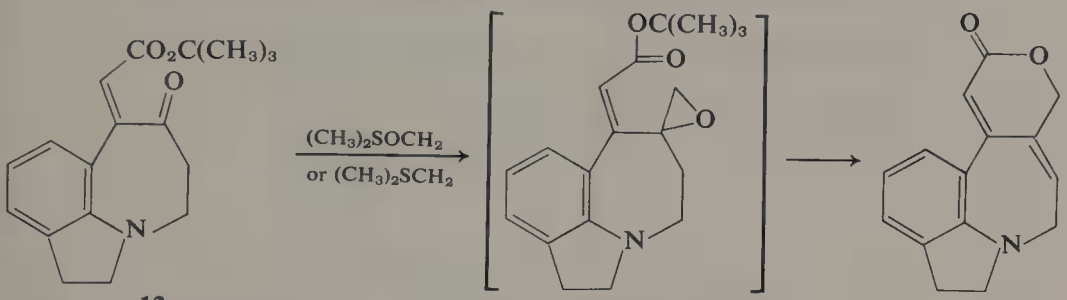
(Ref. 32)

A similar phenomenon has been observed with *o*-mercaptophenyl ketones from which benzothiophenes and 3-hydroxydihydrobenzothiophenes are isolated.[33] Participation by way of a six-membered ring transition state also occurs as the hydroxyketone **11** illustrates.[34] The ketone **12** did not furnish



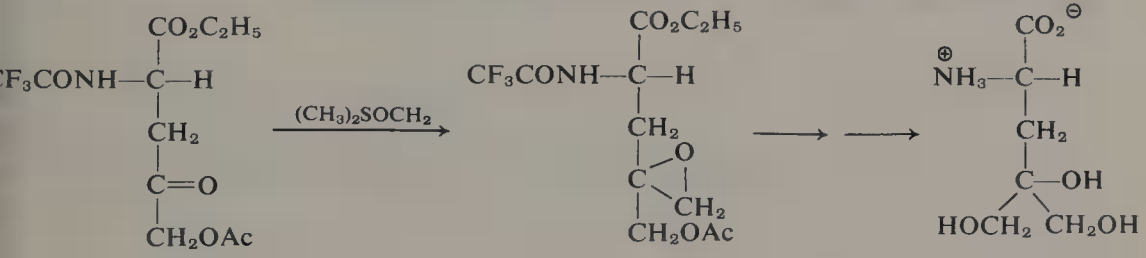
11 25–30%

an epoxide; instead an unusual participation of the proximate *t*-butyl ester led to ring opening and dehydration to generate an unsaturated lactone.[35]



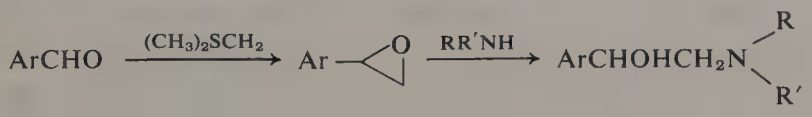
12

The intermolecular ring opening of epoxides with nucleophiles generates much of the interest in epoxidations. Thus, synthesis of the naturally occurring α,δ,δ′-trihydroxy-*L*-leucine involved aqueous basic work-up of the intermediate methylene oxide.[36] Amine cleavage of the epoxides derived



49%

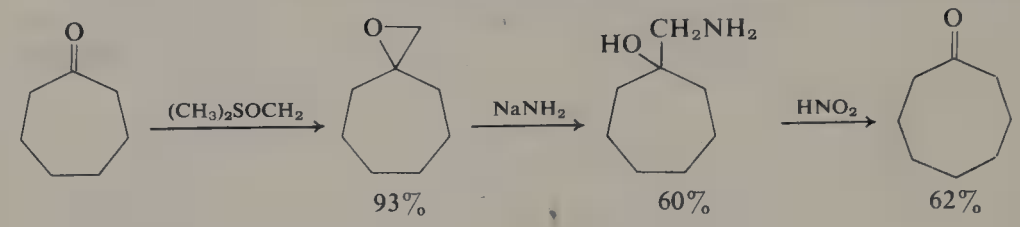
from aromatic aldehydes provides a convenient route to compounds of interest as adrenergic drugs.[4,37] Amide[6] or azide[38] (followed by reduction)

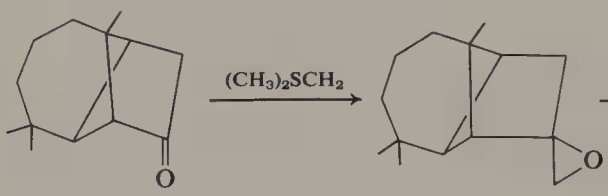


70–80%

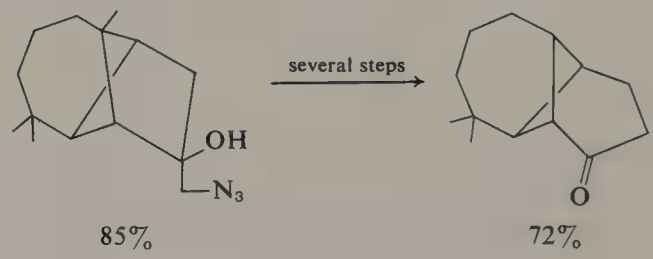
cleavage of the epoxides derived from methylene transfer to cyclic ketones offers an attractive route to the amino alcohol intermediates in the Tiffeneau–Demjanov expansion.[39] Nitrous acid deamination gives the ring-enlarged

ketone. In this way, cycloheptanone underwent ring enlargement to cyclooctanone in an overall 35% yield. This method has been extended to the synthesis of D-homosteroids[38] and serves as a key step in the synthesis of the longipinenes [Eq. (5.4)].[40] Opening of the epoxide with enolates of

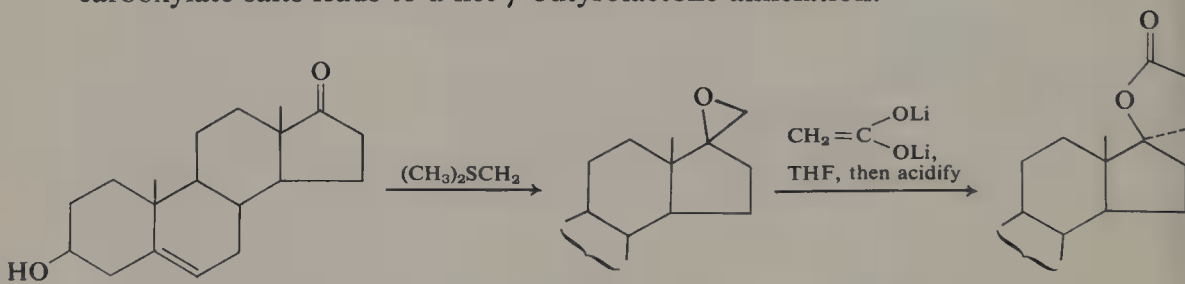




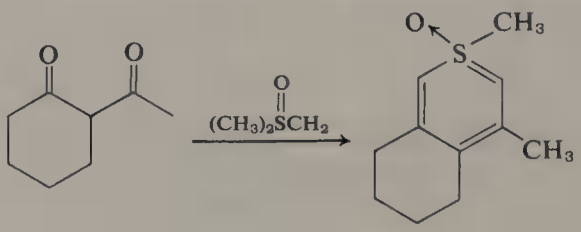
(5.4)



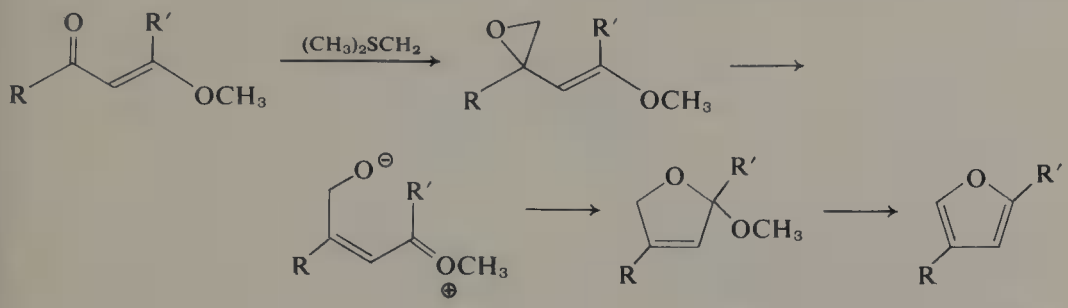
carboxylate salts leads to a net γ-butyrolactone annelation.[41]



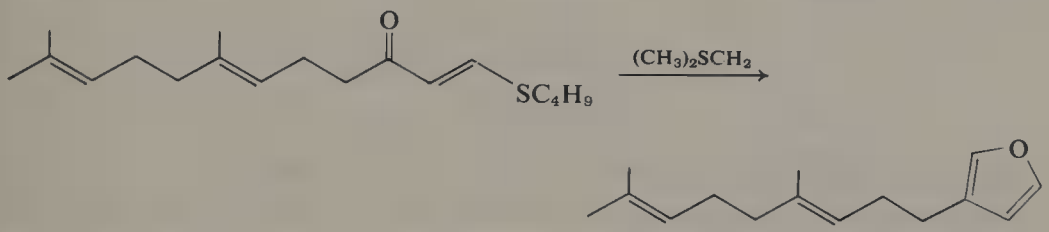
1,3-Diketones do not react normally with ylides. The oxosulfonium methylide produces *S*-methylthiabenzene *S*-oxides; whereas the sulfonium methylide yields only starting materials as a result of deprotonation to an



enolate.[30] On the other hand, enol ethers[42] and enol thioethers[43] of 1,3-diketones do condense normally, but the epoxides are not stable. Ring opening is facilitated by the enol ether or thioether which ultimately collapses to generate a furan after elimination. A facile conversion of geranylacetone to dendrolasin, a major constituent of the mandibular gland of ants, utilized this method.

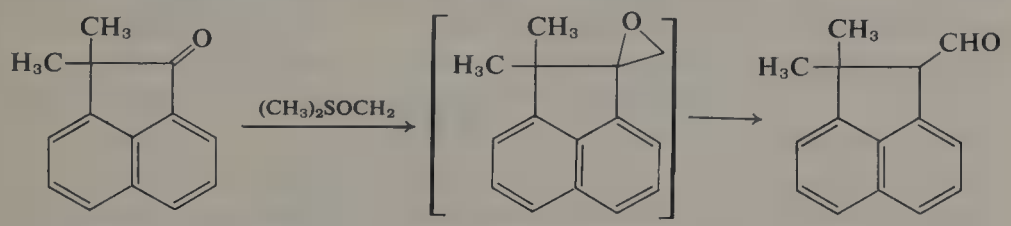


R = R′ = Ph	42%
R = CH_3, R′ = Ph	41%
R = Ph, R′ = H	8%



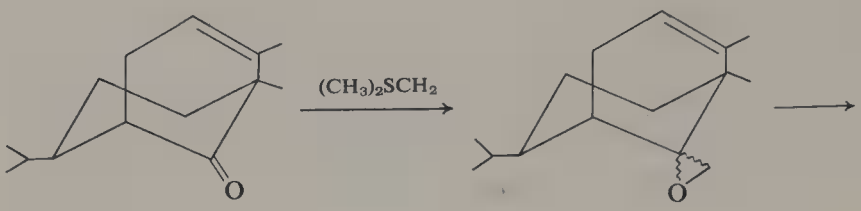
Dendrolasin
54%

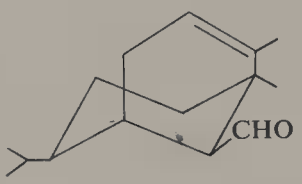
In some simple ketones, epoxide isolation proves difficult because of facility of rearrangement to the corresponding aldehyde. Thus, 2,2-dimethylacenaphthenone yielded only the aldehyde on work-up.[44] Such a side reaction may



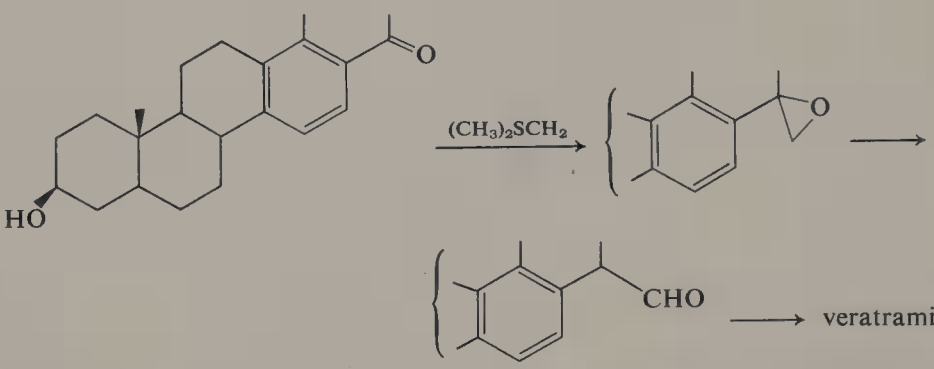
not be undesired. This one-carbon chain extension process served as a key step in the synthesis of helminthosporal [Eq. (5.5)][45] and veratramine [Eq. (5.6)][46]—these examples being just two of many. In these two, the epoxides are rearranged by treatment with Lewis acids, the more common technique.[47]

α-Haloketones form the only class of carbonyl compounds that have



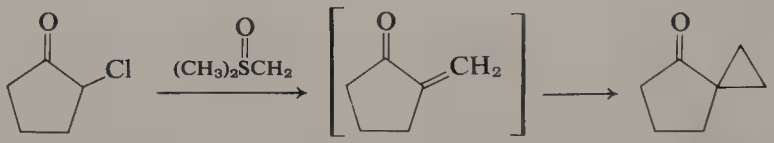


helminthosporal (5.5)



veratramine (5.6)

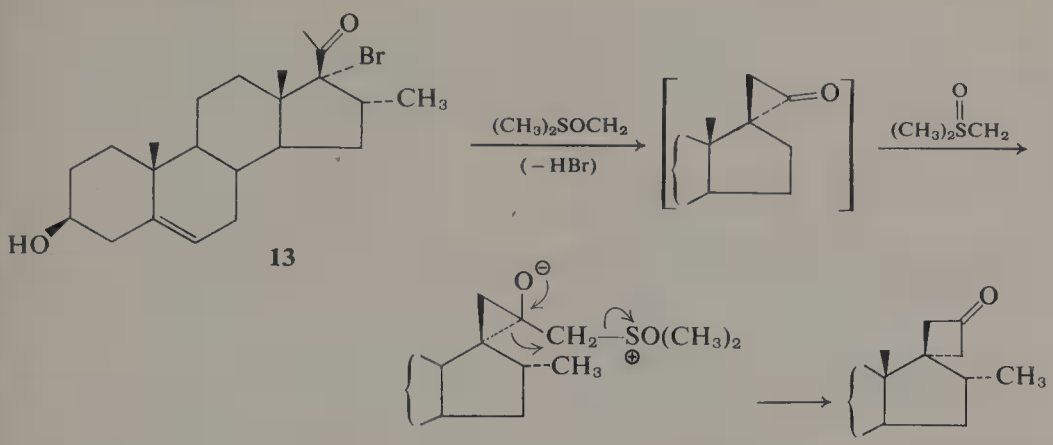
generally led to alternative reaction pathways. Thus, treatment of 2-chlorocyclopentanone with dimethyloxosulfonium methylide produces spiro[4.2]-heptan-2-one as the major product.[48] In this case, alkylation of the ylide takes



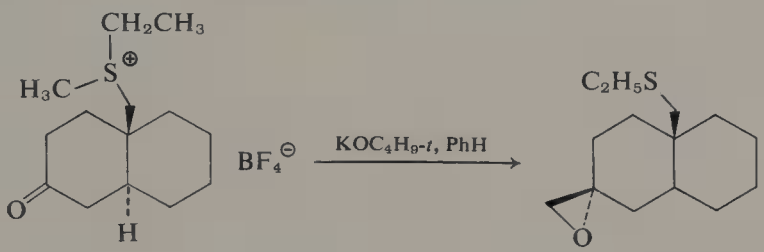
30%

precedence over carbonyl addition to generate 2-methylenecyclopentanone after base-catalyzed elimination of dimethyl sulfoxide. Such an α,β-unsaturated ketone would be expected to cyclopropanate quite readily with the oxosulfonium methylide. If alkylation is sterically hindered in the α-haloketone, a third pathway, proton abstraction, intervenes. Thus, the α-bromoketo steroid **13** produced the spirocyclobutanone presumably through the intermediacy of a cyclopropanone.[49]

Several novel sulfonium methylides have recently been prepared. Incorporating dimethylsulfonium or dimethyloxosulfonium groups onto a polystyrene backbone allows use of a heterogeneous reagent in which the sulfide by-product is simply removed by filtration.[50,51] Placing the ylide within the same molecule as the carbonyl allows intra-molecular transfer

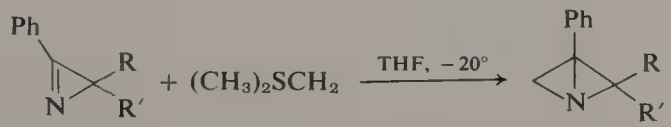


even though a seven-membered transition state is involved.[52] The ability to desulfurize the resultant product makes this technique a method to control stereochemistry. This alkylidene transfer also demonstrates the selectivity for methylide over ethylide generation.



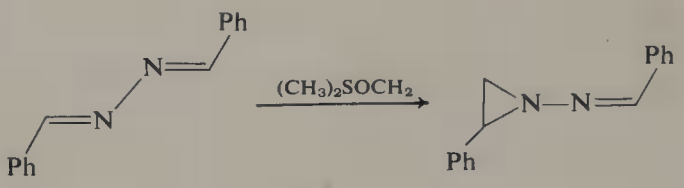
50%

Many other functional groups capable of additions similar to carbonyl groups have been examined using sulfur ylides. While these related reactions are outside the scope of this chapter, the reactions of imines must be mentioned. Aziridine synthesis by methylene transfer to imines utilizing sulfur ylides has had only limited success compared to carbonyl addition.[14a,53]



R = R′ = H	60–70%
R = CH_3, R′ = H	41%
R = R′ = CH_3	47%

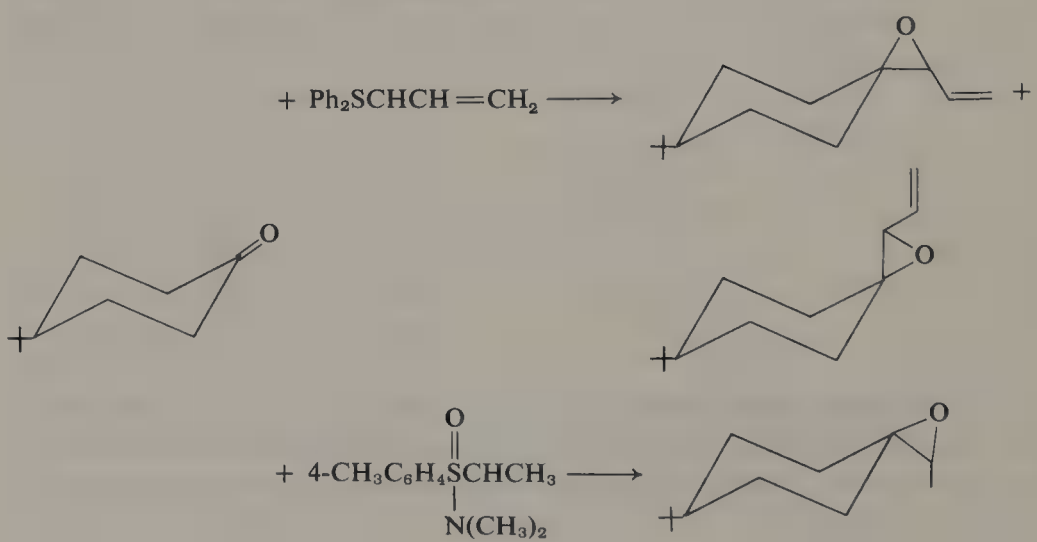
However, a spectacular illustration is the synthesis of 1-azabicyclobutanes by the direct condensation of azirines with dimethylsulfonium methylide.[54] Azines condense with the oxosulfonium ylides to give mainly *N*-iminoaziridine derivatives.[46,55]



5.3 EPOXIDATIONS WITH ALKYLIDES

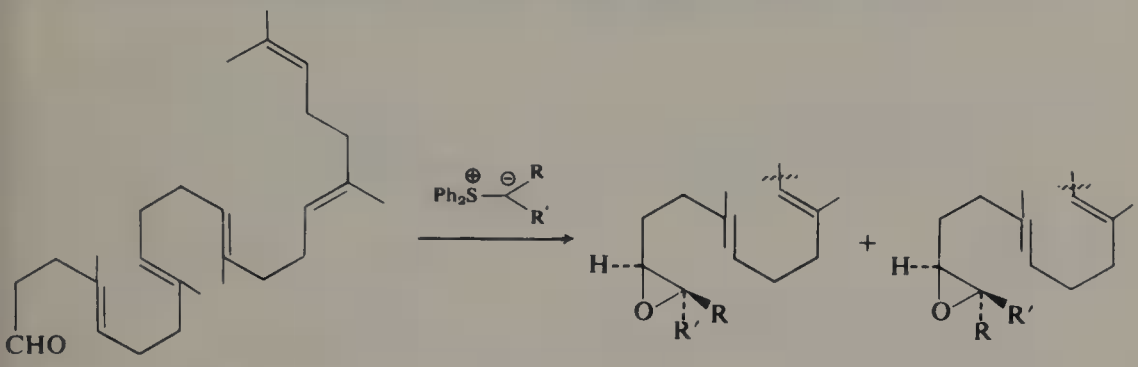
This category includes all substituted ylides which must be generated *in situ*. Thus, the cyclopropylide, allylide, and benzylide are treated here although some stabilization of the ylide must be present in each of them. Oxosulfonium alkylides are virtually unknown except for the sulfoxamine ylides becase of the difficulty in their preparations.[56]

Like the methylides, the alkylides normally condense with both aldehydes and ketones to generate substituted epoxides. Thus, diphenylsulfonium ethylide reacted equally readily with cyclohexanone and benzaldehyde to generate the corresponding epoxides in 74 and 85% yields, respectively.[57] (Dimethylamino)-*p*-tolyloxosulfonium ethylide with *p*-chlorobenzaldehyde and acetophenone produced the respective epoxides in 78 and 62% yields.[58] No systematic study of the effects of substituents on the carbonyl partner has been made. Insufficient examples exist to generalize about the stability of various functional groups to these ylides; however, the reactions of 4-nitrobenzaldehyde with diphenylsulfonium butylide and diphenylsulfonium benzylide demonstrate the stability of the nitro group, usually sensitive to basic media, under the normal condensation conditions.[59] It should be anticipated that the behavior of alkylides toward other functional groups will parallel dimethylsulfonium methylide.



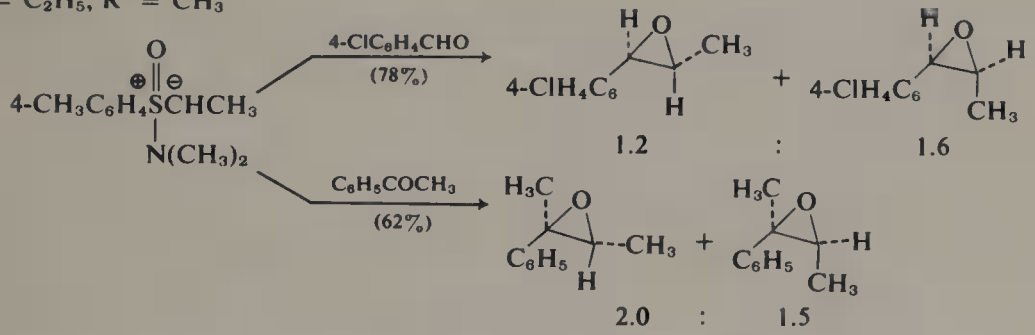
The stereochemistry of addition to an unsymmetrical ketone has not been widely studied. Diphenylsulfonium allylide reacted with 4-*t*-butylcyclohexanone to generate a 1:4 mixture of the *trans*- and *cis*-epoxides.[60] Only equatorial attack is claimed for the sulfoxamine ethylide with the same ketone.[58] Their attack appears to be end-on and generates products typical of carbanion additions.

Unsymmetrical alkylides react with aldehydes and ketones to give mostly equimolar mixtures of the two isomers. For example, reaction of the long-chain aldehyde **14** with diethylsulfonium or diphenylsulfonium ethylide,[61,62] propylide,[61] or 2-butylide[61,63] leads to an approximately 1:1 ratio of cis and

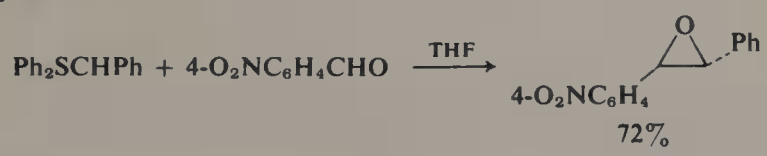


14

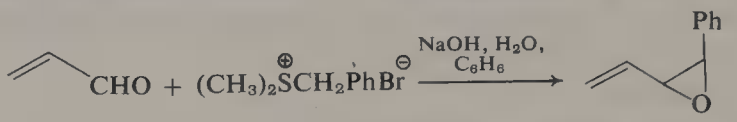
R = CH_3, R′ = H
R = C_2H_5, R′ = H
R = C_2H_5, R′ = CH_3



trans isomers in each case. The sulfoxamine ethylide reacted with *p*-chlorobenzaldehyde and acetophenone to give a mixture of both geometric isomers in a ratio of nearly one.[58] The low selectivity may be attributable to the high reactivity of the ylides. The somewhat more stabilized benzylide is reported to give only the thermodynamically more stable *trans*-epoxide with *p*-nitrobenzaldehyde.[59]

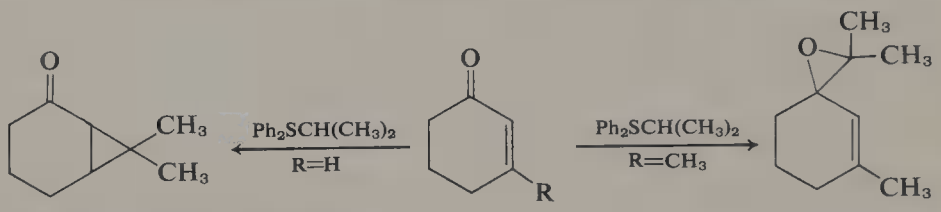


The use of α,β-unsaturated aldehydes normally leads to epoxides. Acrolein even combines with the somewhat stabilized dimethylsulfonium benzylide to produce epoxide in 16% yield.[64] No cyclopropanes are isolated. The low



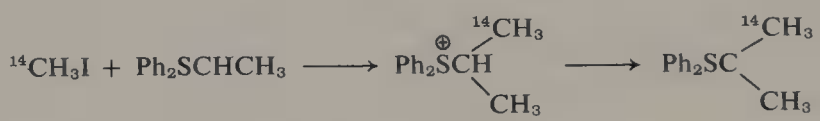
yield may be attributable to the instability of the acrolein to the hydroxide base.

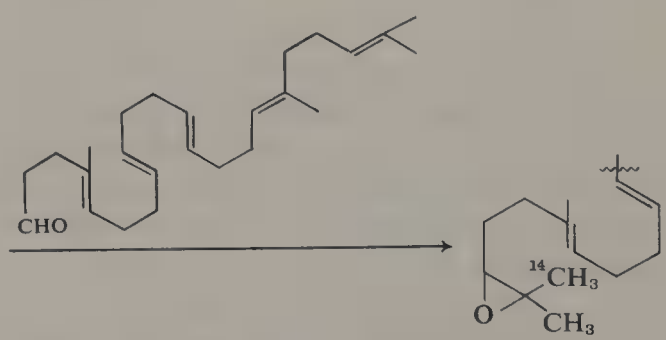
α,β-Unsaturated ketones are more difficult to classify in terms of their behavior toward alkylides. Thus, diphenylsulfonium isopropylide undergoes



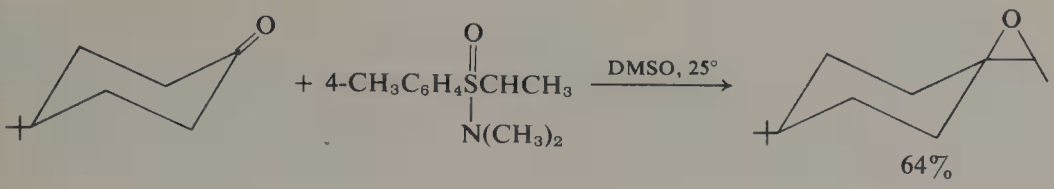
only cyclopropanation with cyclohexenone.[65] Only if Michael addition is hampered by the presence of a 3-alkyl substituent does the reaction lead to epoxides. The preference for cyclopropanation is quite surprising since the simple alkylides should have been anticipated to behave like dimethylsulfonium methylides. The various rationalizations for this observation are discussed in Chapter 4.

The use of isotopically labeled ylides serves as a convenient source of labeled compounds for bioorganic studies. Thus, starting with ^{14}C-labeled methyl iodide, labeled diphenylsulfonium isopropylide was available to generate ^{14}C-labeled epoxide precursors for squalene cyclase studies.[66]

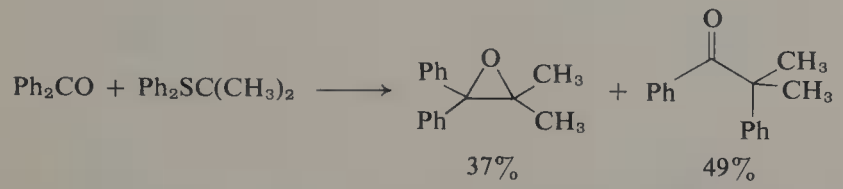




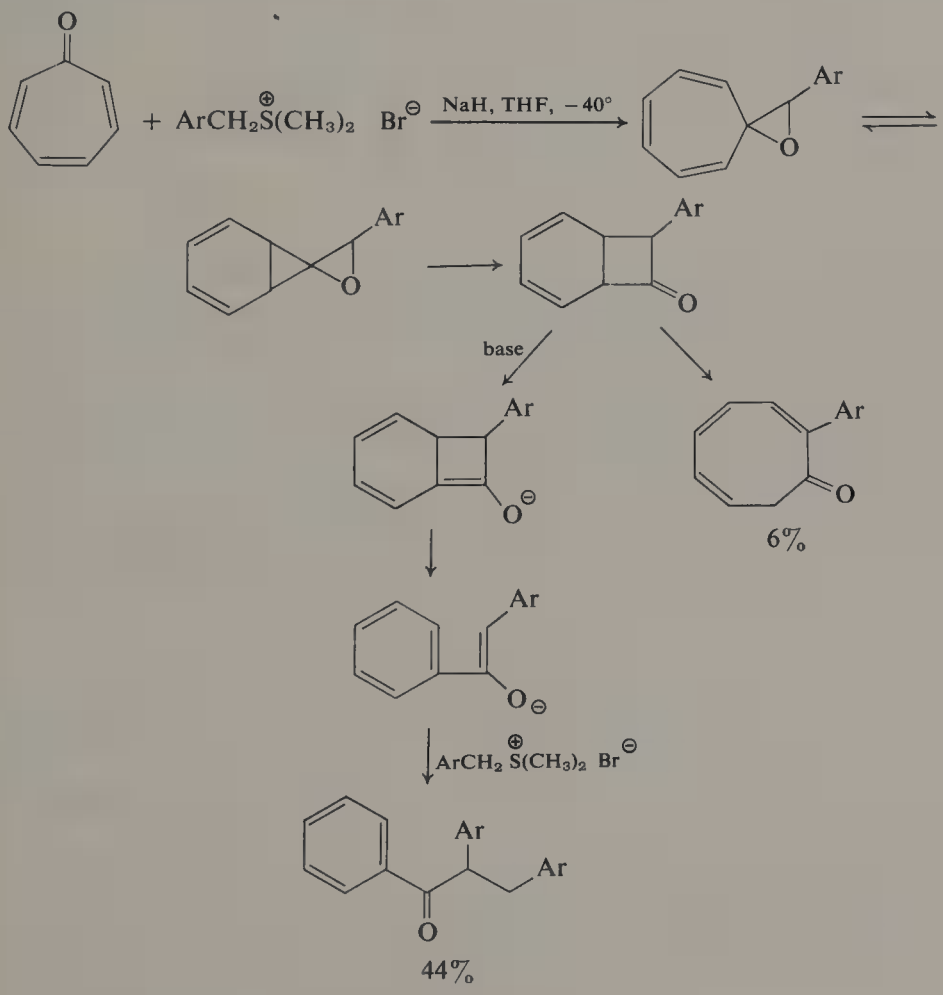
The sulfoxamine alkylides have the potential of effecting asymmetric syntheses.[26] Nevertheless, only one example exists and the optical yield is undetermined.



$[\alpha]_D^{25°} +3.24$

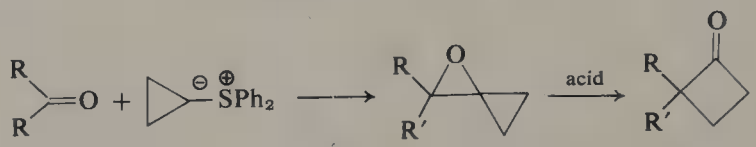


The more highly substituted epoxides that are the products of these reactions have a greater tendency to undergo rearrangement than the simpler substituted epoxides. The reaction of benzophenone and the isopropylide produced, in addition to the desired epoxide, the product of acid-catalyzed

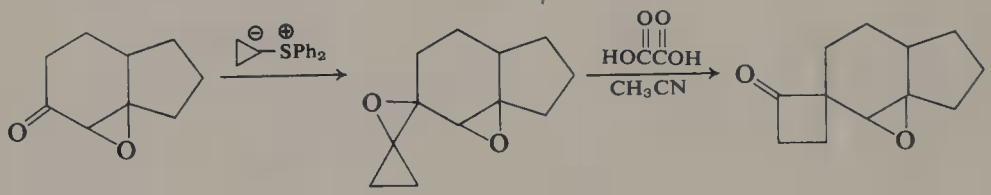


Scheme 5.2

rearrangement.[67] The products derived from combining dimethylsulfonium *p*-nitrobenzylide and tropone can be rationalized by decomposition of an initially produced epoxide.[68] (See Scheme 5.2.) Oxaspiropentanes, the products of condensation of aldehydes and ketones with diphenylsulfonium cyclopropylide[69] are difficult to isolate because of the propensity for acid-catalyzed

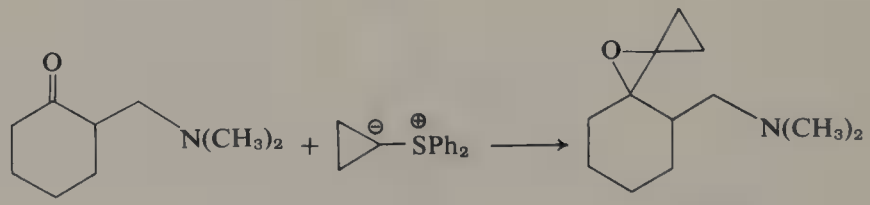


rearrangement to cyclobutanones.[70,71] If R and R′ are hydrogen or a simple alkyl, the oxaspiropentanes are isolable. If R and/or R′ is cyclopropyl or R and R′ are phenyl, only the cyclobutanones are isolable. The high reactivity of the oxaspiropentane is clearly demonstrated by the selected rearrangement of the diepoxide **15**.[72] The fact that the rearrangement is quantitative makes this

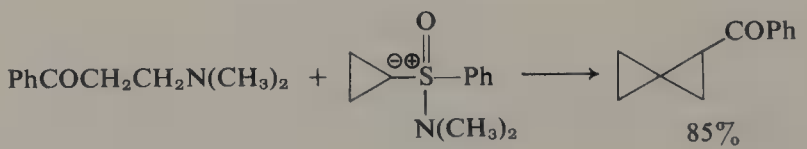


15

approach a very valuable one as a general cyclobutanone synthesis. Although (dimethylamino)phenyloxosulfonium cyclopropylide condensed with cyclohexanone to give products like the above, extension to other carbonyl partners failed.[58] One further difference between the two classes of cyclopropylides is their condensation with Mannich bases.[73] The sulfonium ylide undergoes normal carbonyl condensation,[74] whereas the oxosulfonium ylide initiates elimination and subsequently undergoes conjugate addition.[58] Generation of the sulfonium cyclopropylide under reversible conditions does



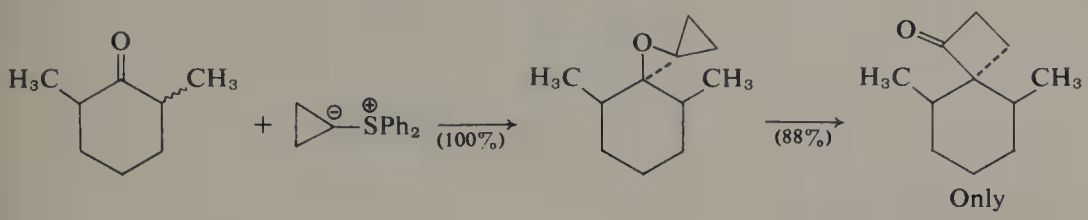
81%



85%

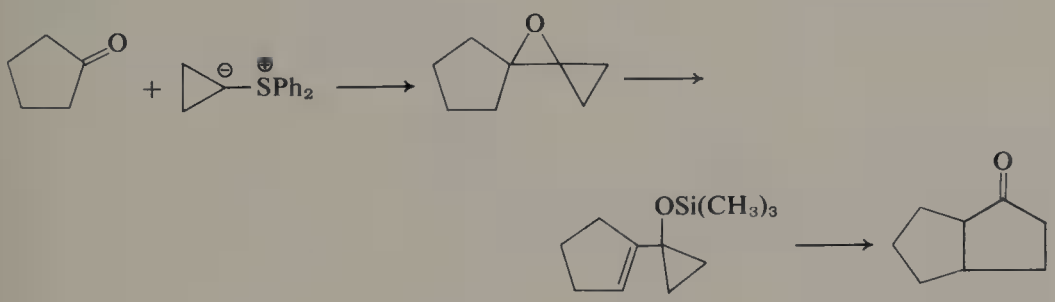
lead to epimerization of the carbonyl partner faster than condensation [Eq. (5.7)].

A mixture of *cis*- and *trans*-2,6-dimethylcyclohexanone produces the cyclobutanone (after rearrangement of the oxaspiropentane) possessing only *cis*-methyl substituents.[76] This example also demonstrates the high stereoselectivity of the ylide reaction.

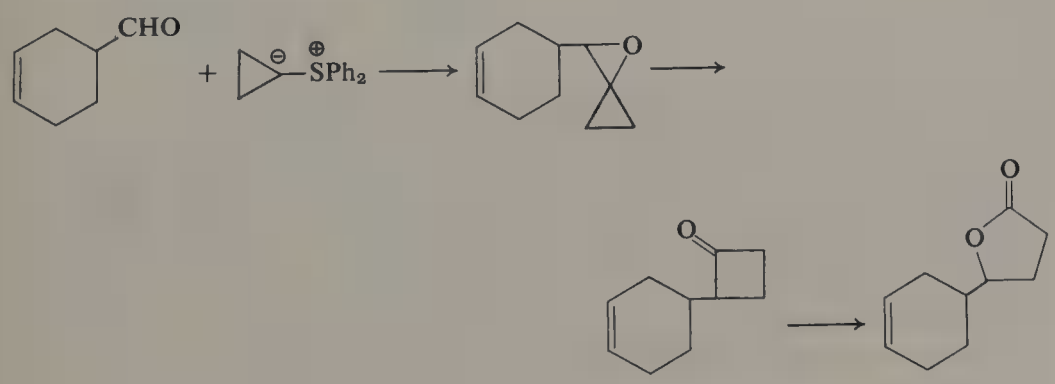


Based on the chemistry of the cyclopropylides, several fascinating new synthetic sequences have been developed. Their general utility, however, remains yet to be established.

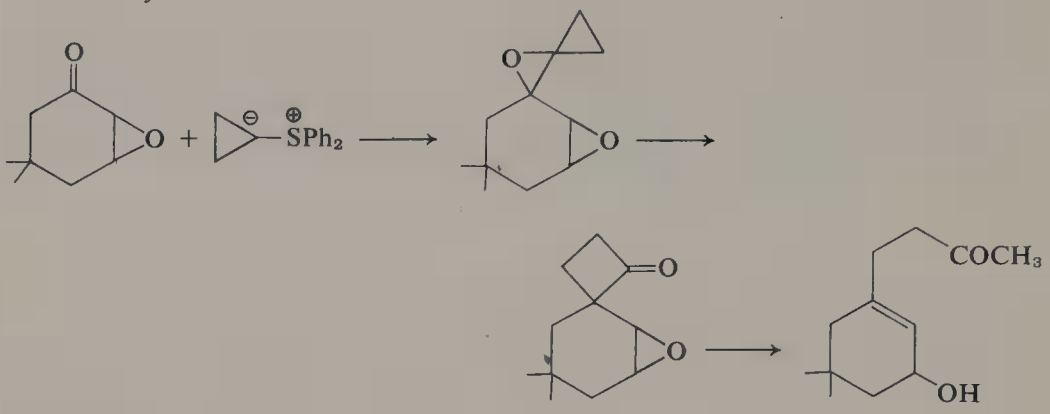
Cyclopentanone Annelation[70]



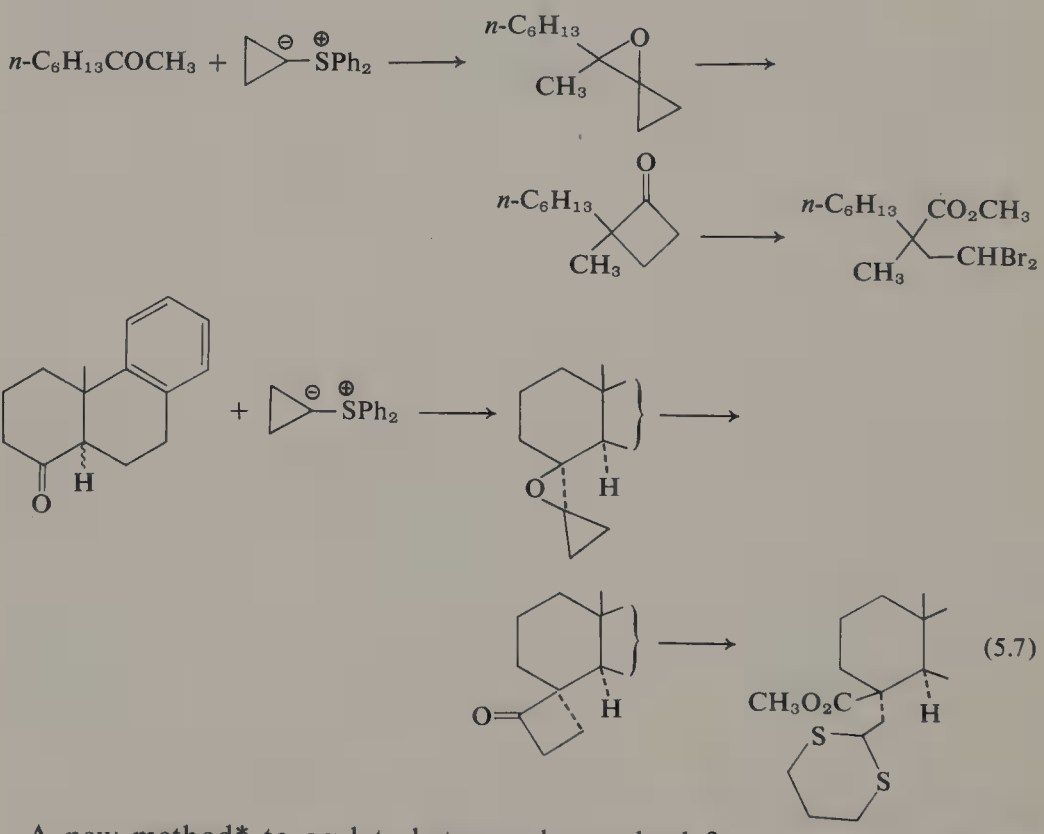
γ-Butyrolactone Annelation[71]



Secoalkylation[72]



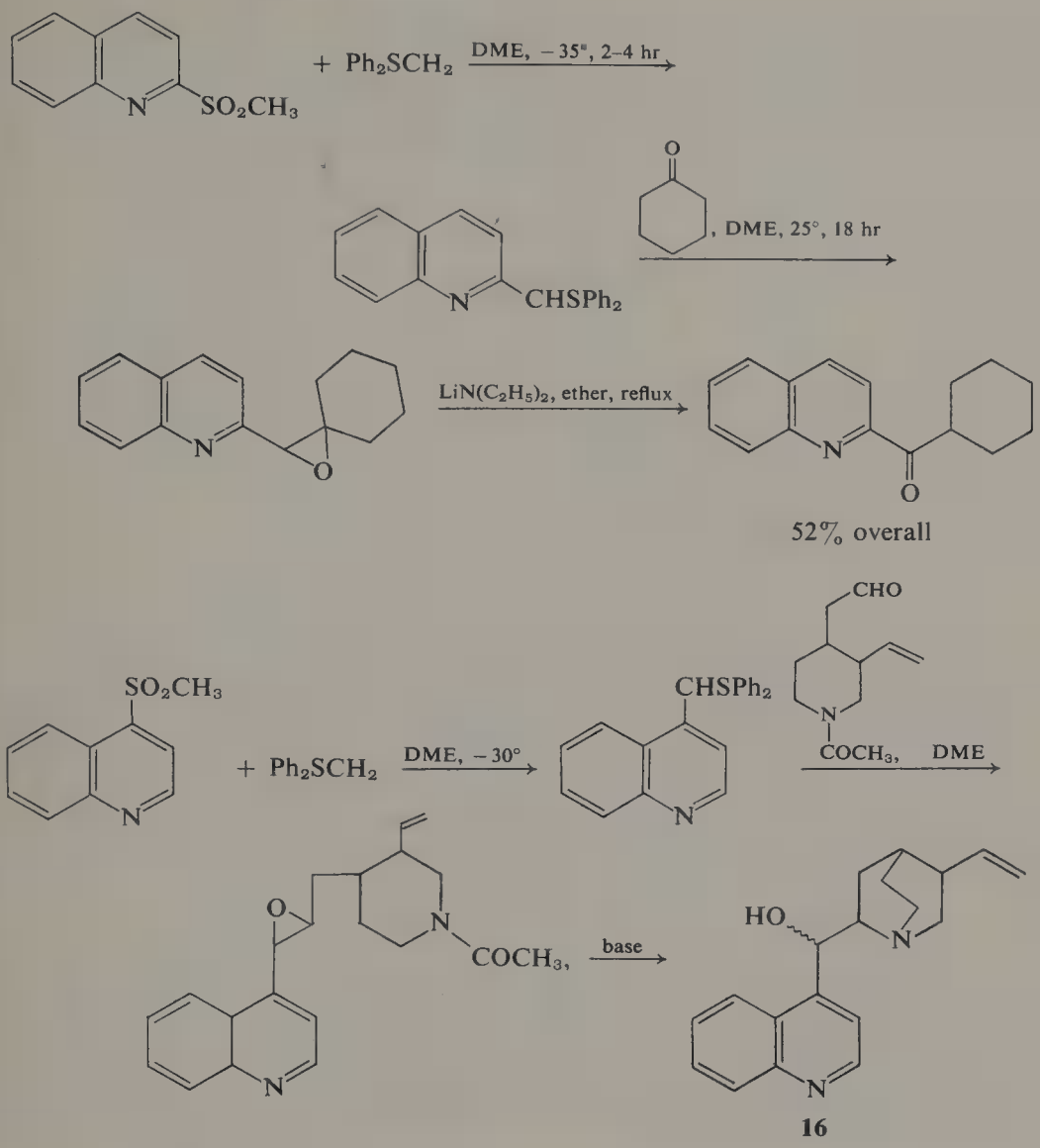
Geminal Alkylation[75,76]



(5.7)

A new method* to acylate heterocycles evolved from rearrangements of epoxides derived from sulfur ylides.[77] Intra-molecular nucleophilic ring opening of the epoxides derived from heterocyclic arylides culminated in a one-pot synthesis of the quinine relatives cinchonine and cinchonidine **16**.[78] The area of new sulfonium alkylides holds much promise for future developments.

* See reaction sequence, top of p. 71.

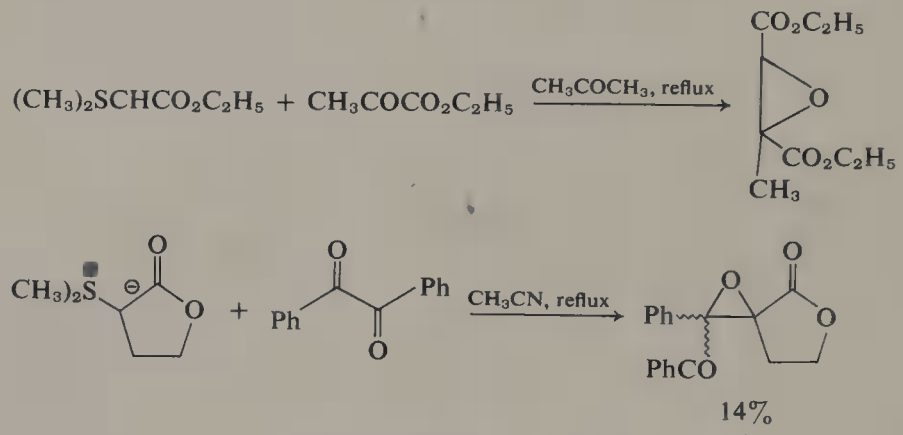


16

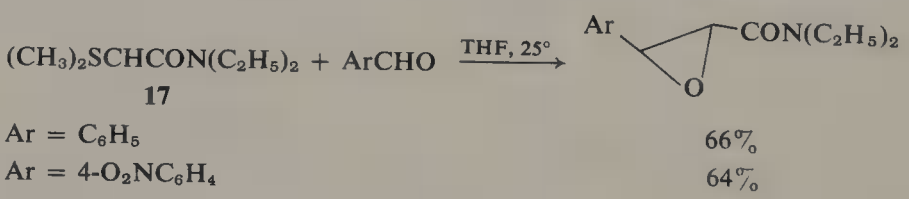
5.4 Epoxidations with Stabilized Ylides

This category includes all ylides stabilized by the presence of electron-withdrawing groups on the ylidic carbon generating, in most cases, an ylide stable enough to be isolated. Whereas the nonstabilized sulfonium ylides and the oxosulfonium methylides react with most carbonyl partners to produce high yields of epoxides, the stabilized ylides normally condense only with exceptionally reactive carbonyl partners. Dimethylsulfonium carbethoxymethylide does not condense with simple aldehydes or ketones, but does form epoxides with 1,2-dicarbonyl systems.[79] Its reaction with ethyl pyruvate is

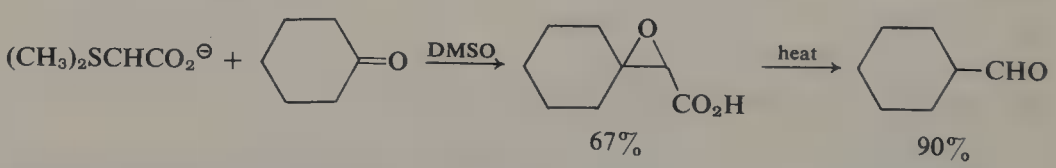
best accomplished in refluxing acetone solution. Dimethylsulfonium 2-oxotetrahydrofuryl-3-ylide adds only to the carbonyl group of 1,2-dicarbonyl compounds that cannot enolize, like benzil.[80] Decreasing the stabilizing effect of the ester increases the reactivity of the ylide. The amide-stabilized



ylide **17** reacts with benzaldehyde and 4-nitrobenzaldehyde in good yield.[81] However, no reactions with ketone partners have been reported. The dimethylthetin anion readily condenses with cyclohexanone to generate the glycidic



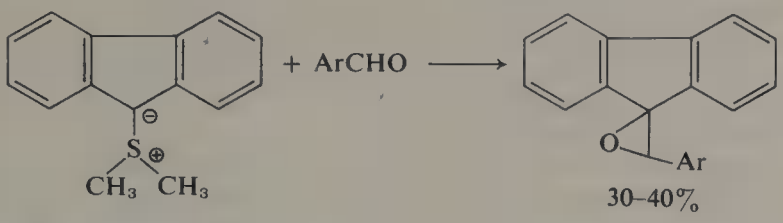
acid; however, hindered ketones like diisopropyl ketone still fail to react.[82] The ability to generate the glycidic acid directly makes this technique an attractive alternative to the Darzen's homologation procedure.[3] In the Darzen's sequence, hydrolysis of the glycidic ester to its corresponding acid



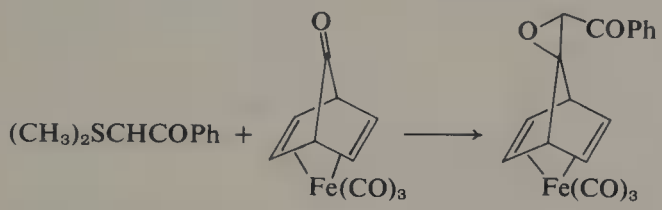
is frequently a low-yield process.[83] By the thetin anion technique, the crude product can be directly subjected to thermal decarboxylation. Thus, this reagent serves as either a one- or two-carbon chain extender. Such facile modification of reactivity cannot normally be achieved with the other non-reactive sulfur ylides.

Other types of reactive carbonyl partners include α-haloaldehydes like chloral[79] and aromatic aldehydes possessing strongly electron-withdrawing

substituents. Thus, dimethylsulfonium fluorenylide produces the corresponding epoxides with 2,4-dichloro-, 2,- 3,- or 4-nitro-, or 4-chlorobenzalde-

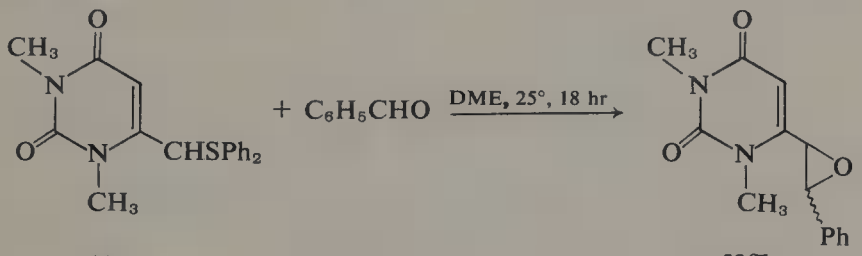


hyde although no reaction is reported with benzaldehyde.[3] Dimethylsulfonium phenacylide has been reported to form epoxides only with 4-nitrobenzaldehyde[84] and the iron tricarbonyl complex of norbornadienone.[85] The mildness



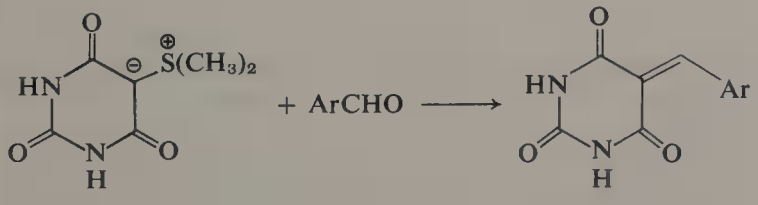
of these almost neutral ylides is clearly illustrated by this latter example as all stronger nucleophiles led only to decomposition of the complex.

A vinylog of an α-ketoylide, e.g., **18**, behaves similarly to the carbonyl-stabilized ylide.[77] There have been two reports of carbonyl-stabilized ylides



18

undergoing olefin formation with aldehydes.[86,87] This unprecedented behavior of sulfur ylides requires more study.



Ar = 4-$(CH_3)_2NC_6H_4$, 4-$(C_2H_5)_2NC_6H_4$, or 2-$O_2NC_6H_4$

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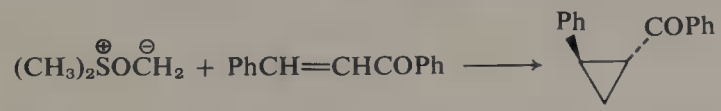
6

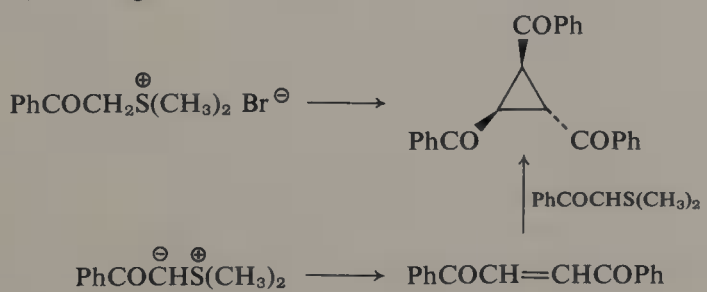
Conjugate Additions

6.1. INTRODUCTION

α,β-Unsaturated ketones are ambident in their behavior with anions. With highly reactive anions, they undergo 1,2-addition, whereas with stabilized anions they undergo 1,4-addition (Michael addition). Most sulfur ylides undergo the latter reaction preferentially. One of the first examples recognized as such involved the addition of dimethyloxosulfonium methylide with chalcone to produce *trans*-1-benzoyl-2-phenylcyclopropane; dimethylsulfonium methylide produced only the epoxide with the same substrate.[1]

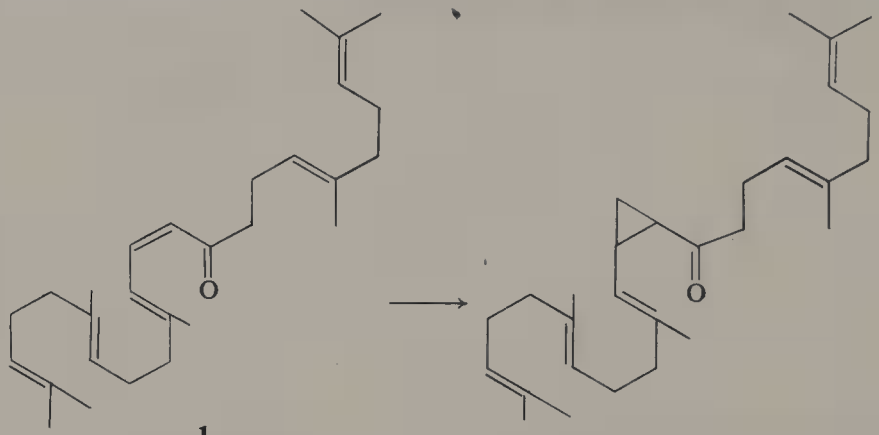


However, cyclopropanation reactions starting from sulfonium salts were known earlier, although the mechanism of the reactions was not understood.



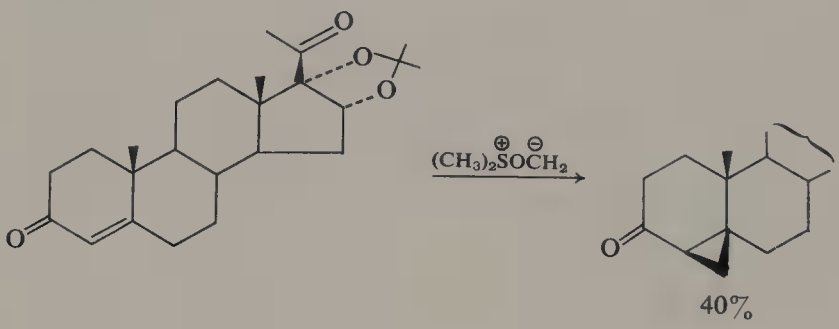
The decomposition of dimethylphenacylsulfonium bromide in base to *trans*-1,2,3-tribenzoylcyclopropane was discovered in 1950.[2] Only in 1966 was it demonstrated that the reaction proceeded by the addition of dimethylsulfonium phenacylide to dibenzoylethylene.[3,4]

Subsequent to these early investigations, this method of introducing cyclopropane rings has become one of the most widely utilized besides carbene (or carbenoid) additions and the Simmons–Smith method.[5] Thus, addition of dimethyloxosulfonium methylide to the hexaenone **1** effected nucleophilic methylene transfer exclusively to the α,β double bond to produce



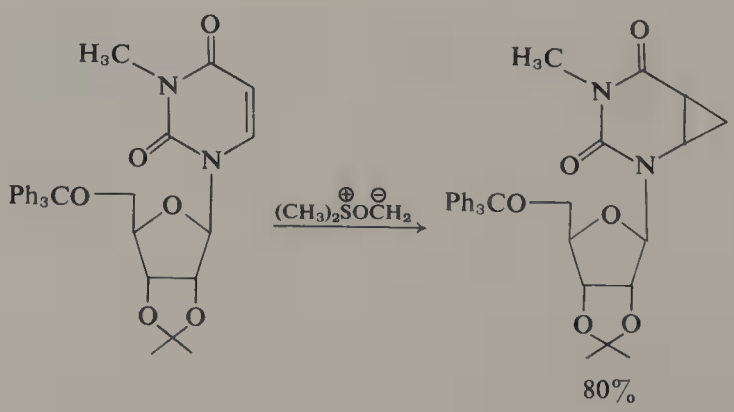
1

a proposed "presqualene."[6] In this fashion, cyclopropanated steroids [Eq. (6.1)] and nucleosides [Eq. (6.2)] are also readily prepared.



40%

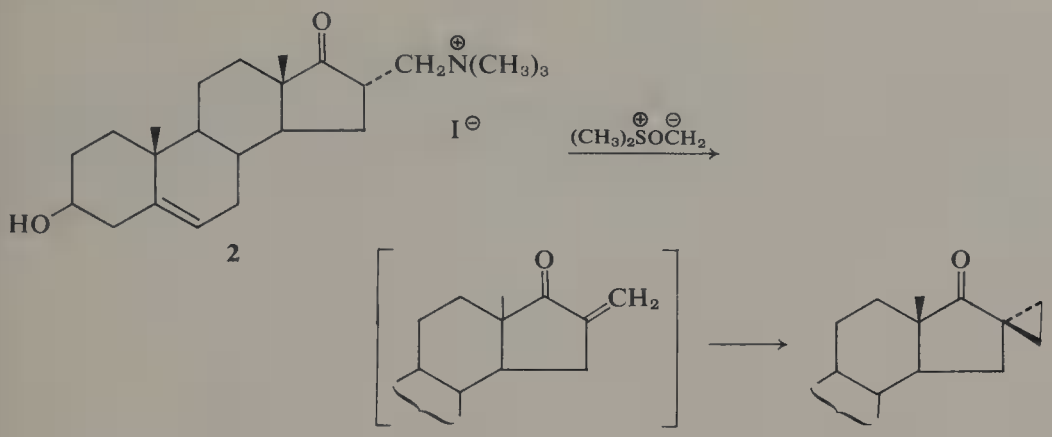
(Ref. 7) (6.1)



80%

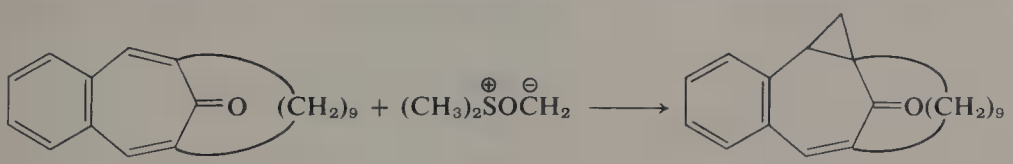
(Ref. 8) (6.2)

Much of the attractiveness of this approach lies in the ready availability of the Michael acceptor systems. The unmasking of such an acceptor system *in situ* expands the applicability of the method. Thus, Mannich bases such as **2** eliminate trimethylamine under the basic conditions to give the corresponding enone which then undergoes cyclopropanation.[9] The continuing growth of the use of this reaction firmly establishes this method as a major approach to cyclopropanes.

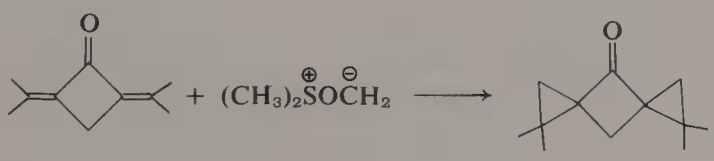


6.2. CYCLOPROPANATIONS WITH METHYLIDES

A wide variety of Michael acceptors has been explored with the oxosulfonium methylides. α,β-Unsaturated ketones,[1,10–17] nitriles,[17] isonitriles,[18] sulfones,[19,20] sulfonamides,[21] sulfonates,[21] and nitro[22] compounds give good to excellent yields of cyclopropanation (see tabular survey). Bis-Michael systems undergo mono- [e.g., Eq. (6.3)] or bis- [Eq. (6.4)] cyclopropanation depending on the ratio of ylide to substrate. The required acceptor system may be generated *in situ*. As indicated in the introduction, quaternarized

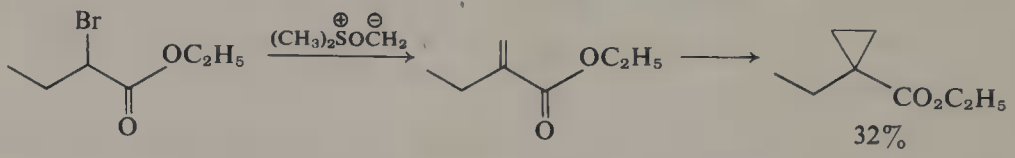


(Ref. 23) (6.3)

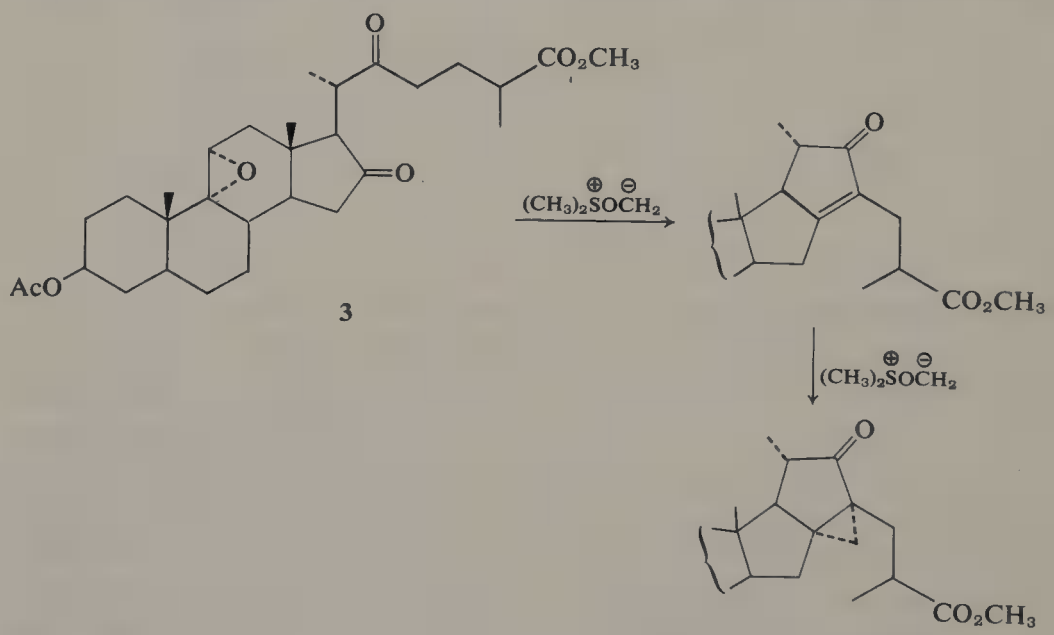


(Ref. 24) (6.4)

Mannich bases which suffer elimination to the α,β-unsaturated ketone under the basic reaction conditions may be employed directly in such reactions. It has also been found that α-bromoketones and esters combine with two equivalents of ylide to give cyclopropanes in 25–40% yields.[25,26] Such



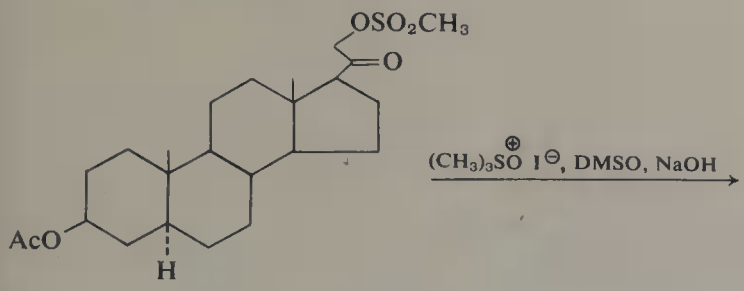
reactions presumably proceed by initial alkylation and then elimination to the α,β-unsaturated ketone or ester followed by the normal cyclopropanation. In a case of a 1,4-diketone in which the epoxidation was sterically hindered (e.g., **3**), an enone system was created by aldol condensation for which the ylide served as base. Subsequent reaction led to the observed cyclopropane.[27]



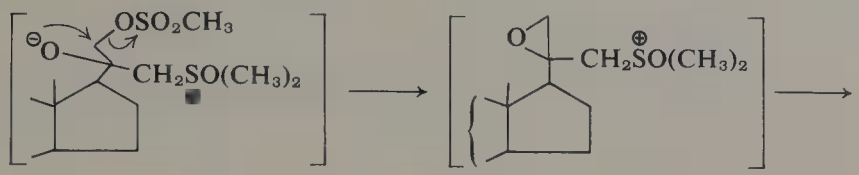
3

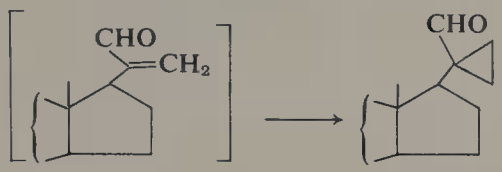
Independent generation of the supposed intermediate confirmed the interpretation. Attempted epoxide formation of steroidal ketone **4** also led to eventual cyclopropanation via the presumed α,β-unsaturated aldehyde **5** as outlined in the accompanying reaction (see p. 81).[28]

The many examples of cyclopropanation of α,β-unsaturated ketones offer the best opportunity to evaluate the substituent effects. Alkyl substitution on the double bond diminishes reactivity as illustrated by the series of methylated cyclopentenones.[29] Although substitution at either the α- or β-carbon atoms causes such a retardation, substituents on the α-carbon atom appear to have the greater effect. Inductive destabilization of the developing negative charge at the α-carbon atom rationalizes the result. Although steric

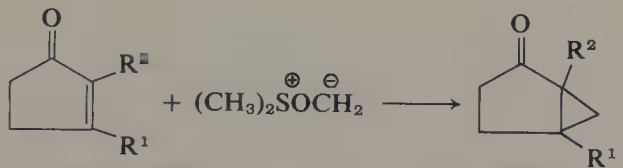


4



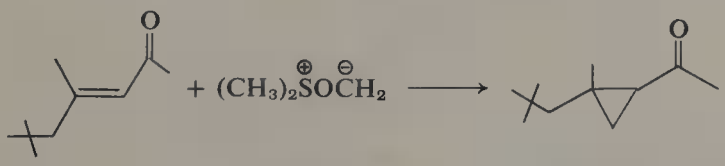


5 26%

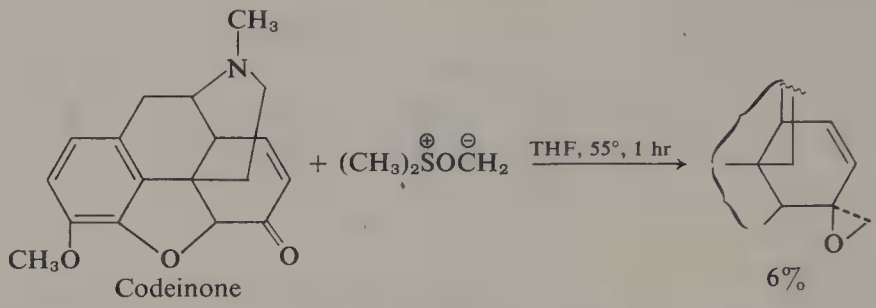


$R^1 = CH_3$, $R^2 = H$	82%
$R^1 = H$, $R^2 = CH_3$	60%
$R^1 = R^2 = CH_3$	40%

hindrance may decrease the rate of cyclopropanation, it need not preclude it. Dimethyloxosulfonium methylide cyclopropanates 4,6,6-trimethyl-3-hepten-2-one, an exceptionally hindered system, in 80% yield.[10] One notable



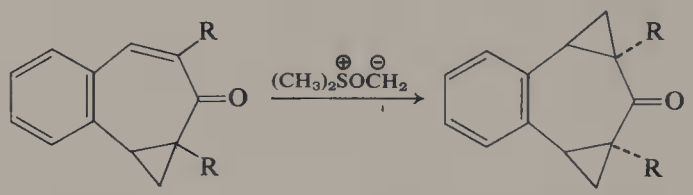
exception is codeinone in which only a low yield of nucleophilic epoxidation product was obtained.[30] The severe steric hindrance to conjugate addition completely inhibits cyclopropanation. Ring size also plays a role. Whereas, five-, six-, and seven-membered enones react smoothly (see Appendix, A.IV), 2-cyclooctenone undergoes cyclopropanation only in 12% yield.[31] In such medium-sized rings, conformational factors minimize the conjugation of the



Codeinone 6%

double bond and the carbonyl group and thereby reduce the susceptibility of the double bond toward nucleophilic attack.

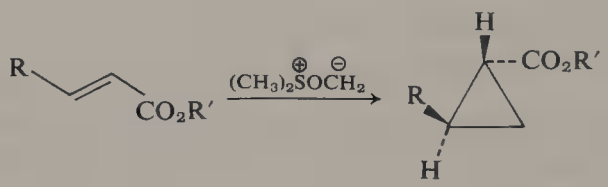
Substitution of the enone with electron-withdrawing substituents enhances the reactivity of the system. Whereas cyclopropanation of 3,4-benzotropone (**6**, R = H) with the oxosulfonium ylide proceeds poorly, if at all,[32,33]



6

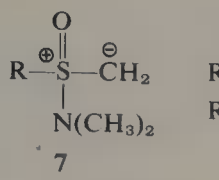
smooth cyclopropanation occurs with **6** (R = $CO_2C_2H_5$).[33]

Competition between carbonyl addition and cyclopropanation becomes more acute with α,β-unsaturated esters. Whereas ethyl acrylate or crotonate react with the oxosulfonium ylide to give the desired cyclopropanes in 60–65% yields,[34] the hindering of Michael addition by placement of a bulky phenyl



R = H, R′ = C_2H_5	65%
R = CH_3, R′ = C_2H_5	60%
R = Ph, R′ = C_2H_5	31%
R = Ph, R′ = $C(CH_3)_3$	65%
R = Ph, R′ = $CH(CH_3)_2CH_2CH_2CH_3$	69%

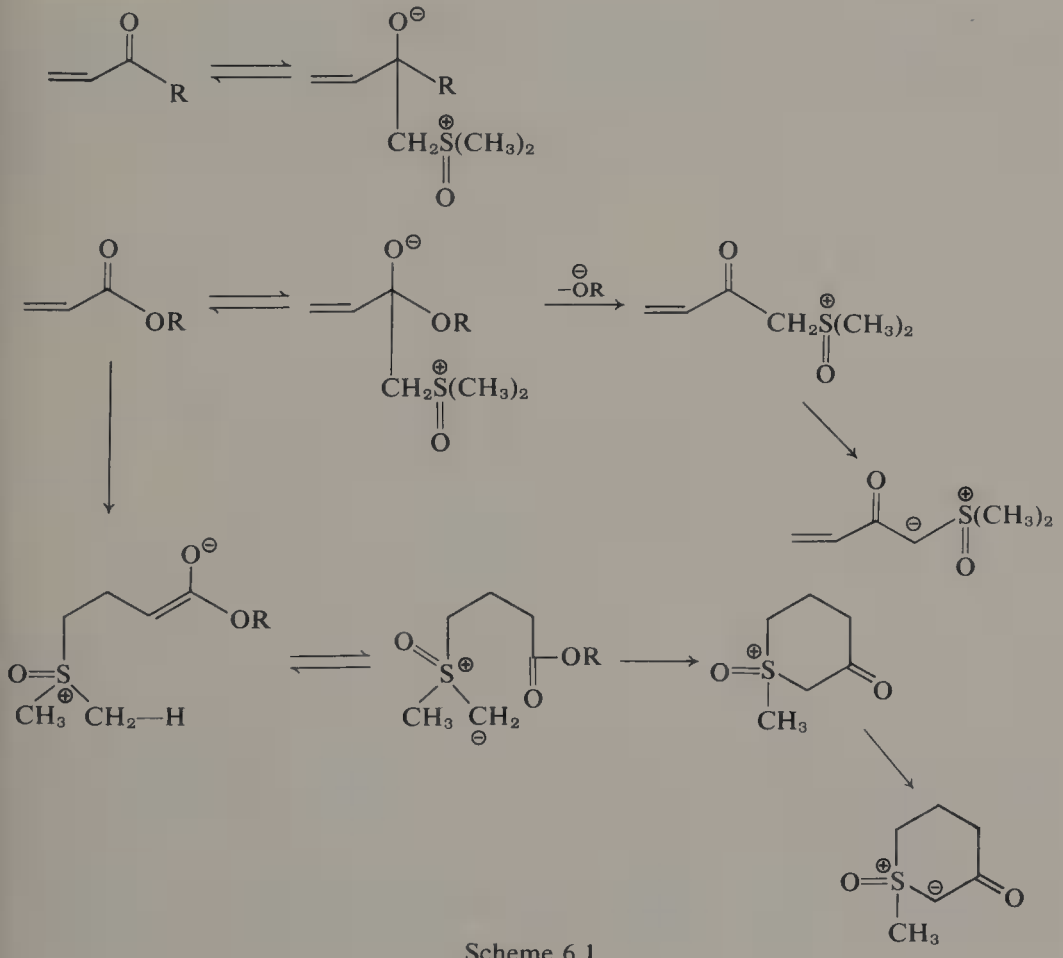
group on the β-carbon atom as in ethyl cinnamate reduces the yield to only 31% with the major product arising from acylation.[34,35] The ratio of cyclopropanation to acylation is a function of the acylating power of the ester. Thus, hindering carbonyl addition by utilizing sterically large R groups increases cyclopropanation dramatically.[35] A similar trend is observed with the sulfoxamine ylides **7** which led to 72–82% yields of methyl *trans*-2-phenylcyclopropane-1-carboxylate even with methyl cinnamate as the acceptor. It



7

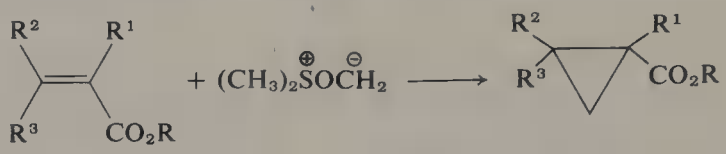
R = C_6H_5 (Ref. 36)
R = CH_3 (Ref. 37)

appears these ylides are to be preferred for cyclopropanations of α,β-unsaturated esters. At first glance, it seems somewhat surprising that the α,β-unsaturated ketones are not plagued by similar problems. The difference may merely reflect the reversibility of the oxosulfonium methylide addition to the carbonyl group of the ketone, whereas such reversibility is not as pronounced with the esters because of competition with alkoxide elimination in the tetrahedral intermediate. Alternatively, the intermediate Michael adduct may undergo prototropic shift faster than 1,3-elimination. The newly formed ylide can suffer intramolecular acylation to form a β-ketoylide[38] (Scheme 6.1).

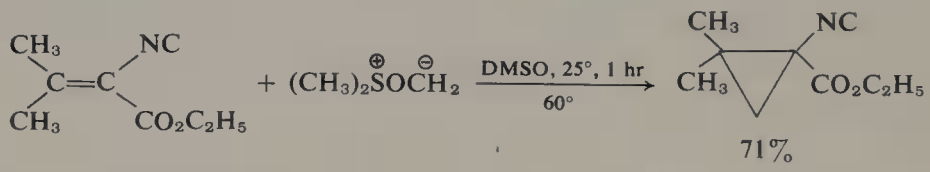


Scheme 6.1

In these cases too, alkyl substitution on the α- or β-carbon atom of the enone system hinders reaction. The yields of cyclopropane decrease from acrylate to crotonate to α- methacrylate to β,β-dimethylacrylate.[34] Hindrance for Michael attack enhances the formation of products derived from acylation.

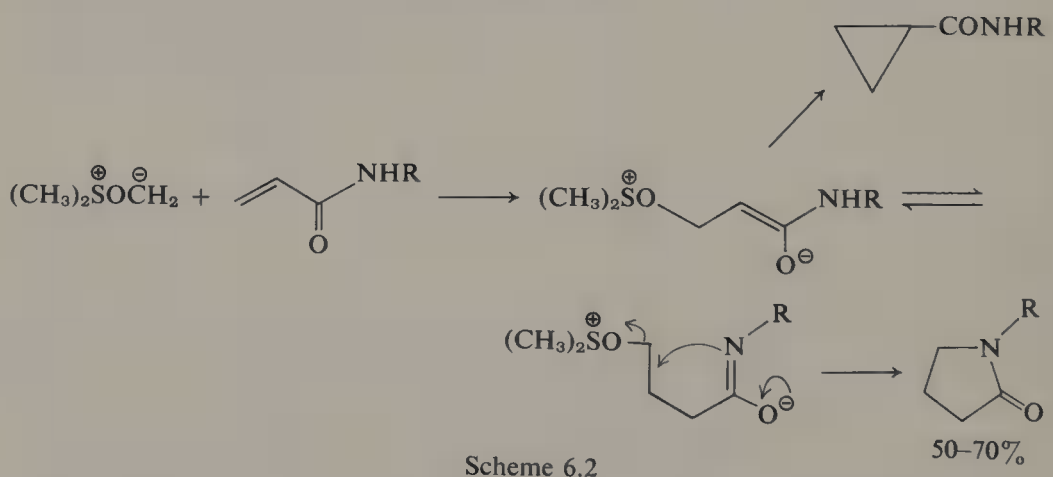


Introduction of additional electron-withdrawing substituents may overcome such problems. A fascinating illustration introduced an isonitrile group at the α-carbon.[18]



71%

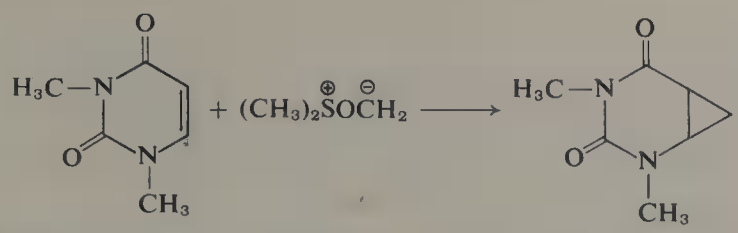
α,β-Unsaturated primary and secondary amides frequently yield γ-lactams instead of cyclopropanes[39] (see Scheme 6.2). *N*-methyl- or *N*-phenylacrylamide gives the corresponding lactams with no trace of cyclopropanes. The initial adduct suffers essentially irreversible prototropic rearrangement of the very acidic amide hydrogen faster than 1,3-elimination. Amides which



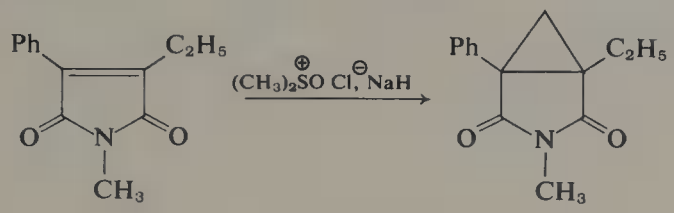
50–70%

Scheme 6.2

preclude such prototropy (e.g., tertiary amides) or cyclization of the resultant amide anion (e.g., lactam) do not suffer such complications and cyclopropanation becomes the major course of reaction. In such cases, even deactivating the Michael system by placing an amino group on the β-carbon does not inhibit reaction. Thus 1,3-dimethyluracil is cyclopropanated in 66% yield by the oxosulfonium ylide.[8] Products from carbonyl addition are unim-

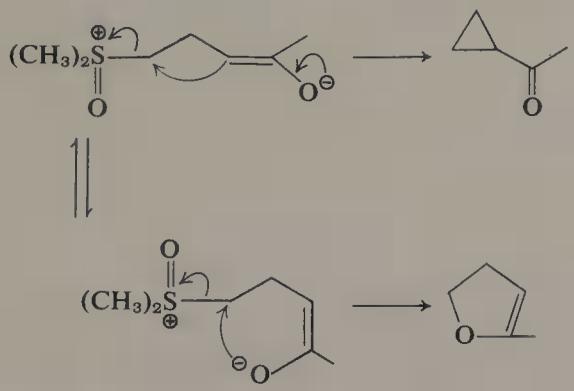


portant in amide reactions in contrast to the ester cases. Even the reactive carbonyl group of an imide function allows cyclopropanation to proceed unimpaired.[40]

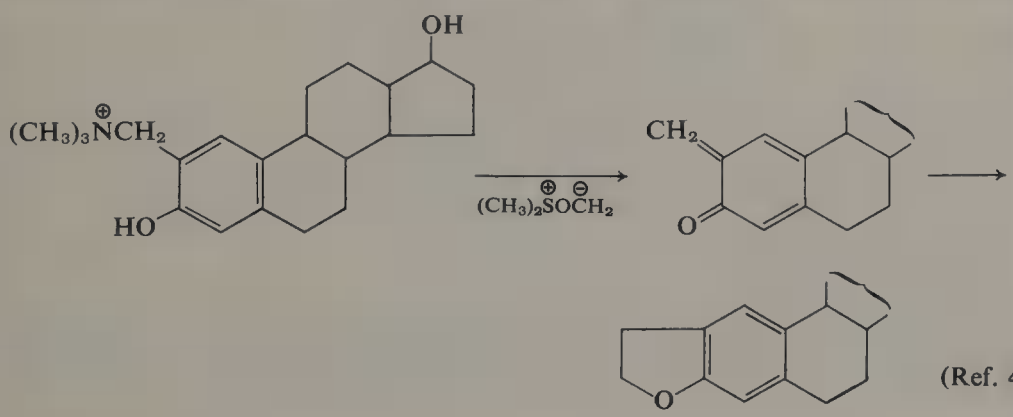


81%

A similar dichotomy may be envisioned in all cases since, in principle, the zwitterion intermediate can undergo collapse by either O- or C-alkylation.

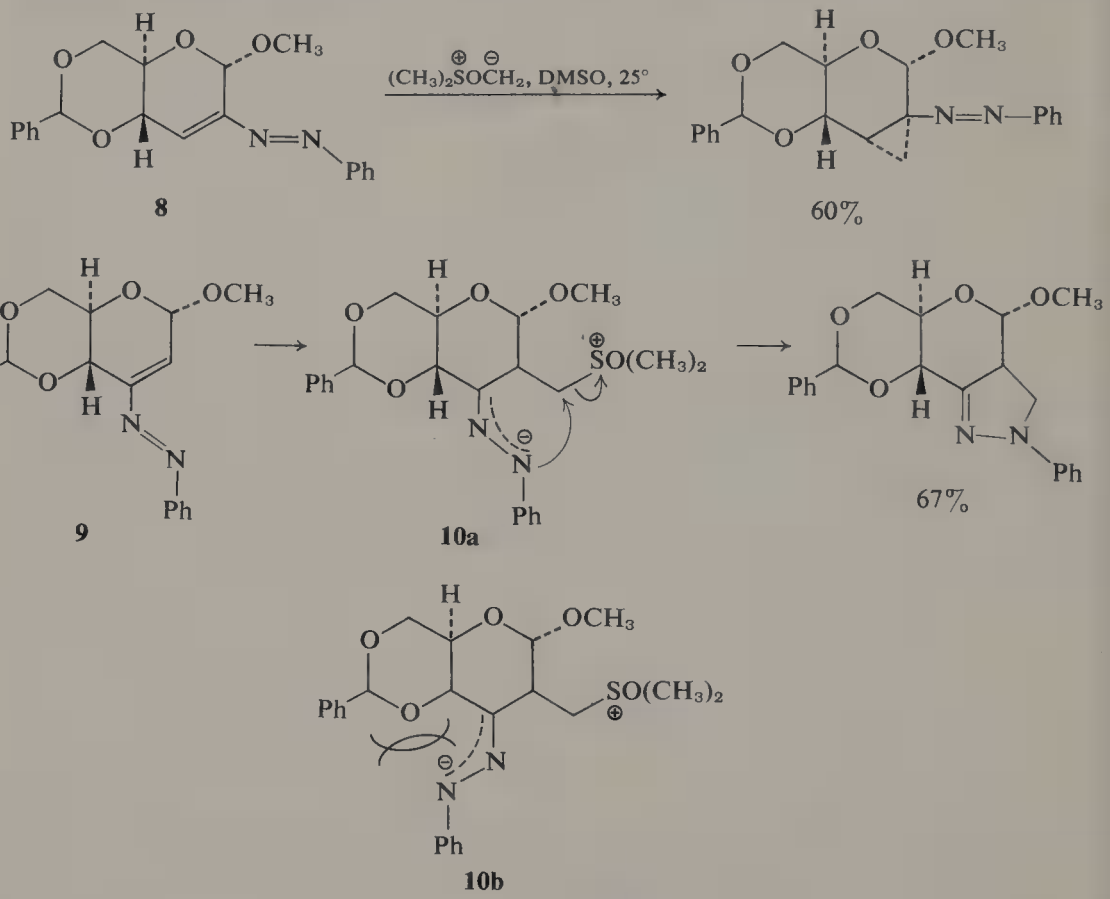


The general preference for three-membered ring formation over five, the preference for *trans*-enolate generation in the Michael addition, and the



(Ref. 42)

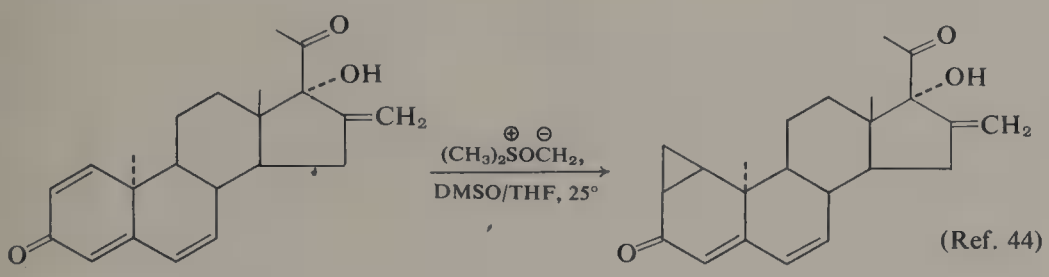
thermodynamic preference for C- versus O-alkylation of enolates, all dictate cyclopropanation as the usual course. Nevertheless, dihydrofuran formation can intervene in those instances in which an unusually stable enolate form held cisoid exists. Thus, condensation of the quaternized Mannich product of phenols with two equivalents of ylide produces the dihydrofuran exclusively in a perfectly general reaction.[41,42] The α,β-unsaturated azo compounds, rather unusual acceptor systems, exhibit both 1,3- and 1,5-eliminations.[43]



8 **9** **10a** **10b**

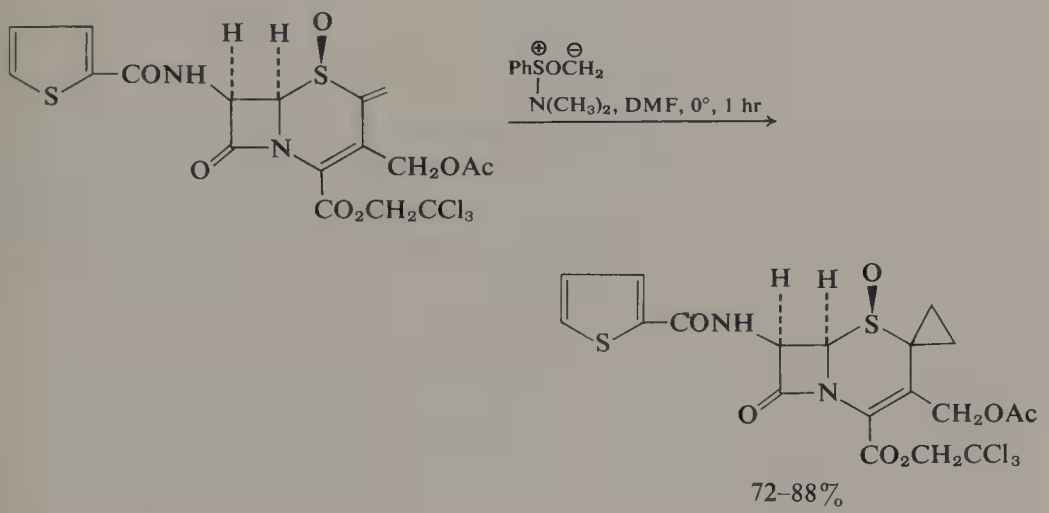
Whereas, the three-substituted azo compound **8** produces an excellent yield of cyclopropane, the four-substituted isomer **9** only yields the pyrazoline. Consideration of the conformations of the intermediate zwitterions provides a rationale for this difference. Of the two possible intermediates from **9**, **10a** is freer of unfavorable eclipsing interactions than **10b**. Thermodynamic and charge distribution factors suggest that five-membered ring formation should predominate from **10a.**

Most functional groups, among them hydroxyl, sulfhydryl, amino, imino, nitro, nitrile, isonitrile, carbonyl, sulfonyl, and sulfoxide as well as isolated double and triple bonds (cf. **11**) do not interfere with the cyclopropanation



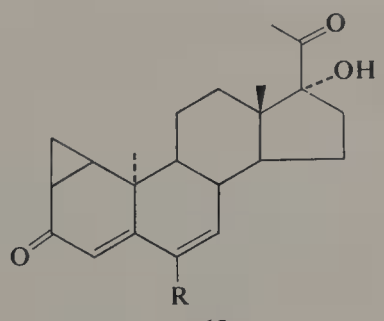
11 52% (Ref. 44)

reaction. An outstanding example of the chemospecificity of the oxosulfonium ylides is the successful reaction of these reagents with cephalosporin derivatives without affecting the sensitive β-lactam.[45] To some extent, the reactivity of the acceptor system determines the possibility of interference.



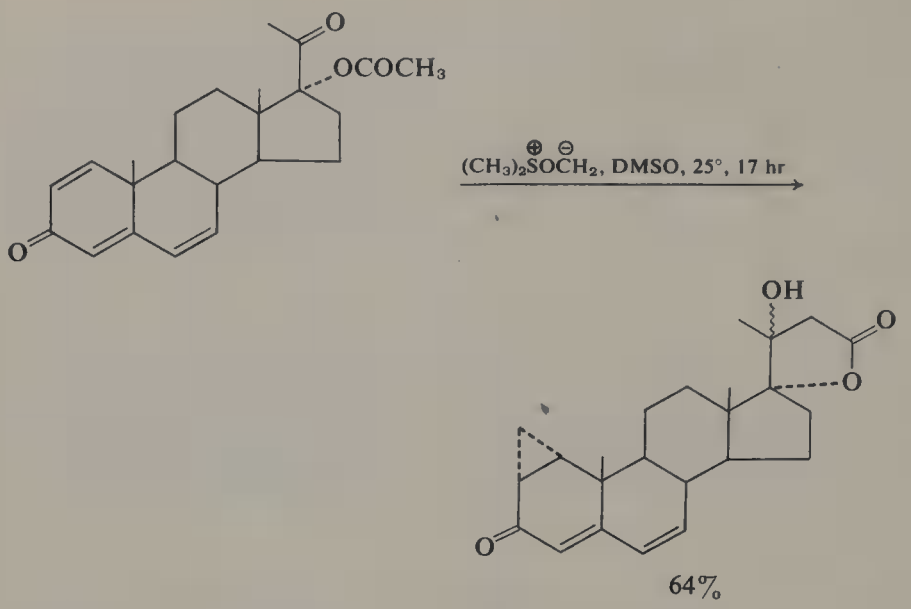
72–88%

Substrate **12** (R = H) required protection of the C-17 hydroxyl group, whereas **12** (R = Cl) does not. Although acetates have normally been



12

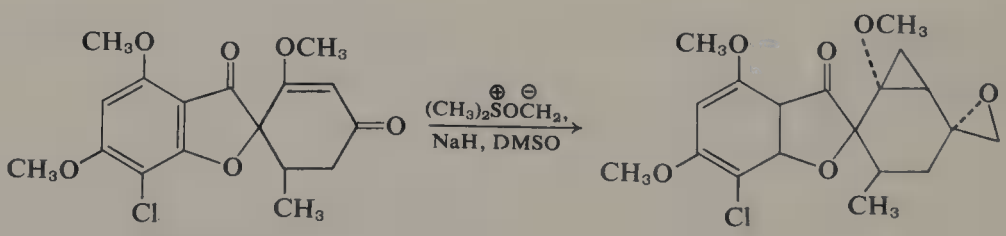
present without complications, prolonged reactions can lead to base-catalyzed processes.[46,47]



(Ref. 47)

64%

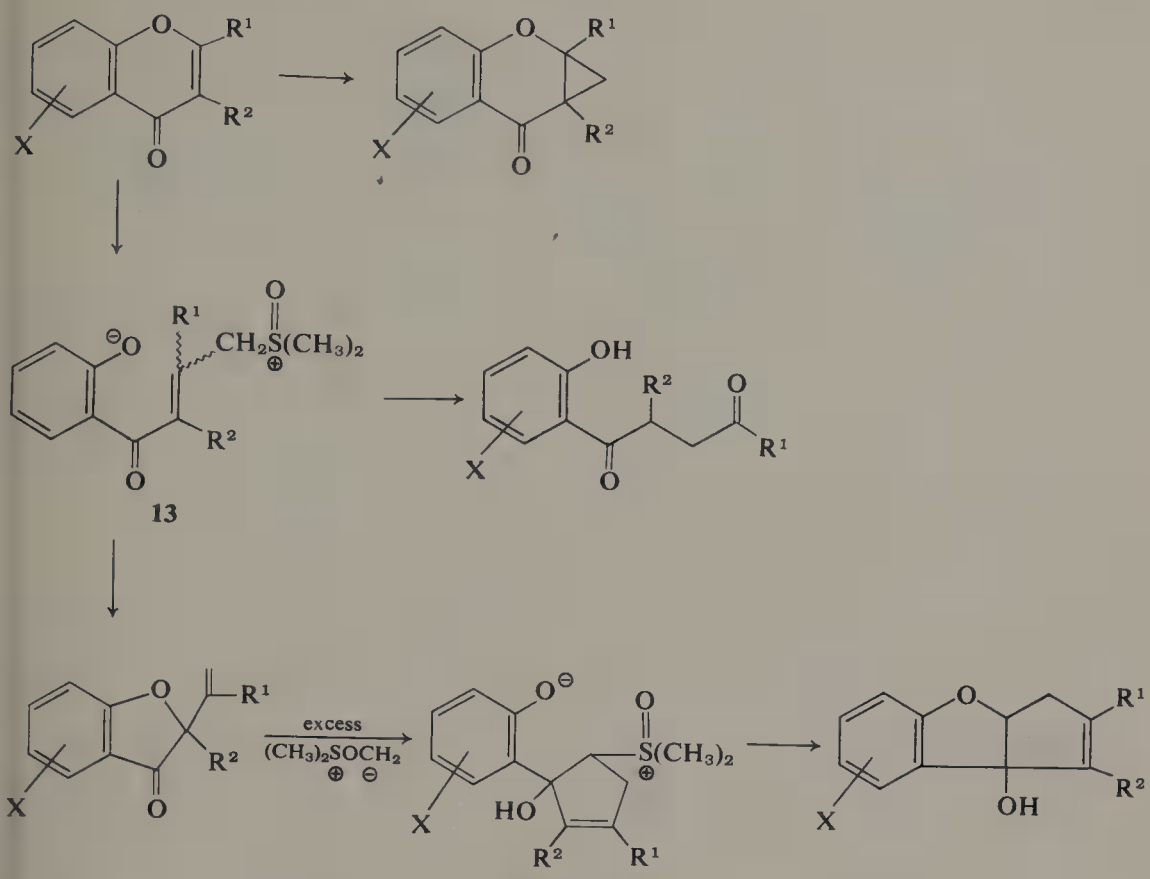
On the other hand, α,β-unsaturated systems substituted in the β position with a good leaving group may lead to anomalous products. For example, Ollis and his co-workers determined that flavones may react in one or all of three modes depending on the substituents when treated with dimethyloxosulfonium methylide.[48] Two of the three products are derived from vicinal elimination of the intermediate enolate to generate **13** in preference to 1,3-elimination (see Scheme 6.3). Like alkyl substitution, heteroatom substitution of the enone retards cyclopropanation. Thus, griseofulvin undergoes cyclopropanation followed by epoxidation so that only the cyclopropane epoxide can be isolated cleanly.[49]



Griseofulvin

The stereochemistry of attack generally follows the principle of steric approach control.* Steroidal enones differing only in the stereochemistry of the AB ring fusion illustrate this principle. Conformational drawings clearly indicate the topside (β face) of the cis- and bottomside (α face) of the trans-fused systems to be the least hindered. Enone **14** demonstrates the importance

* See p. 90.



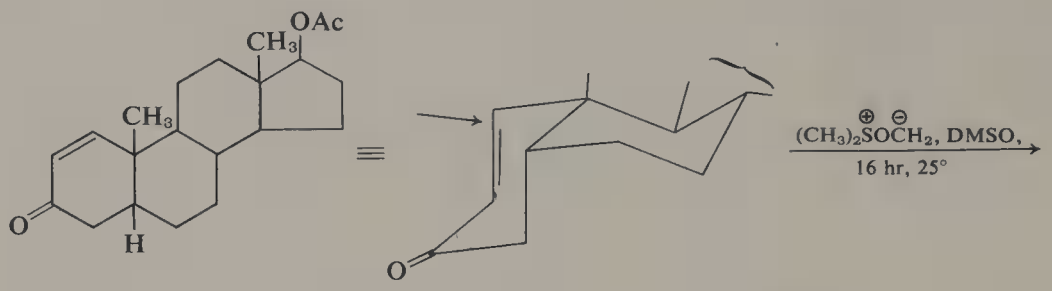
13

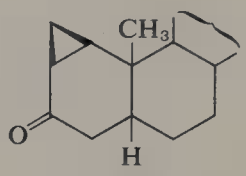
Scheme 6.3

of this factor since such stereochemical considerations force the bulky pivaloyl group to the more hindered face of the molecule.[52] In the absence of overwhelming steric factors, the addition to cyclohexenones favors formation of an axial carbon–carbon bond at the site of initial attack. Carvone condenses with the oxosulfonium ylide to generate the cyclopropyl ketone **15**.[53] Preference for axial attack may be attributed to stereoelectronic control. Topside or axiallike attack (mode a) generates the half-chair cyclohexane enolate directly, whereas bottomside or equatoriallike attack (mode b) generates a boat conformation for the enolate. The greater stability of the former conformer dictates preferred axial attack in the absence of other steric considerations. A similar analysis explains the formation of the syn isomer from cyclopropanation of **16**.*[54]

In addition to selectivity with respect to relative configurations, sulfur ylides offer an approach to generate specific absolute configurations. By the use of optically active ylides with asymmetry at sulfur, optically active cyclopropanes can be obtained directly in delightfully high optical yields with

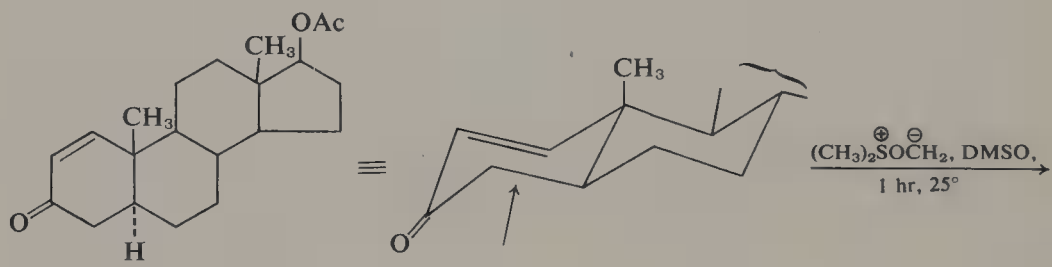
* See p. 91.

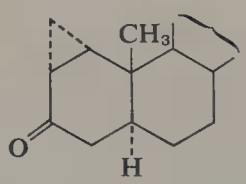




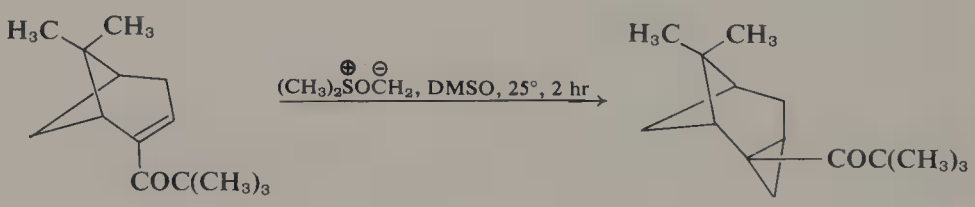
(Ref. 50)

40%



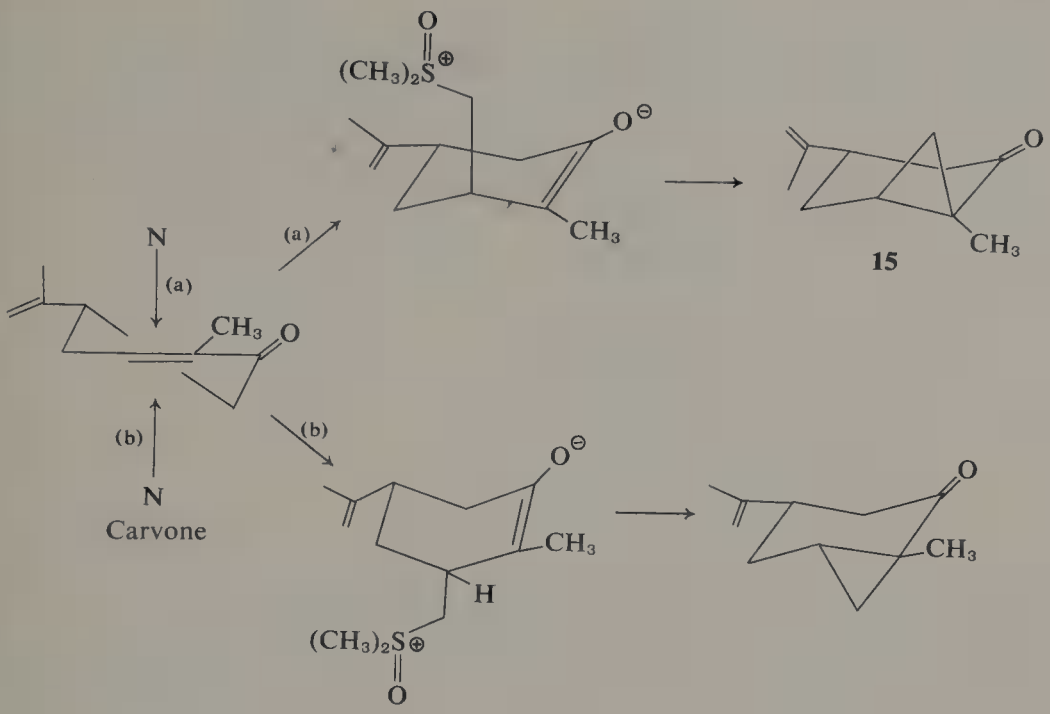


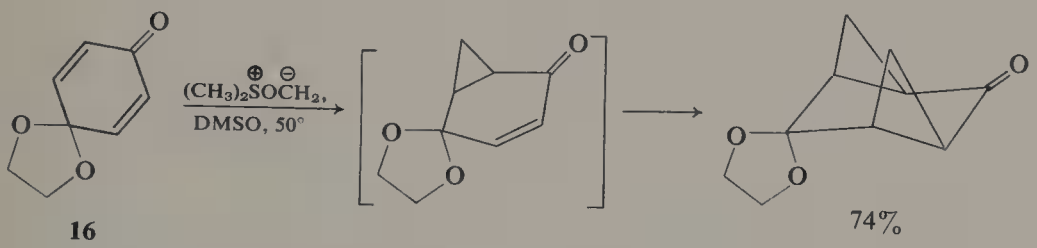
(Ref. 51)

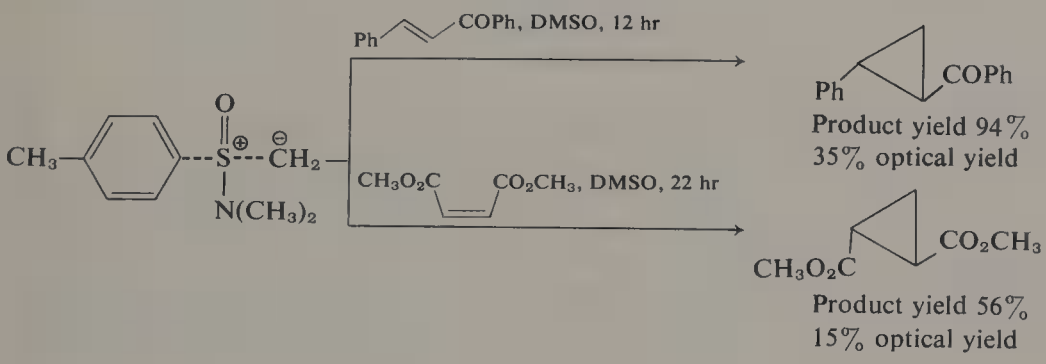


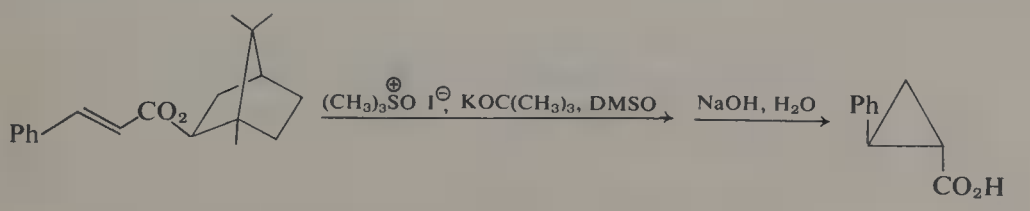
14

oxosulfonium ylides[55] but not sulfonium ylides.[56] For example, *R*-dimethylamino-*p*-tolyloxosulfonium methylide transfers methylene to a variety of acceptors with optical yields ranging from 15–37%.[55] Optically active cyclopropanes also arise from reactions of achiral ylides with α,β-unsaturated esters whose alcohol unit is optically active. Thus, (+)-bornylcinnamate undergoes cyclopropanation with the oxosulfonium ylide with an optical induction of 3–4%.[57]

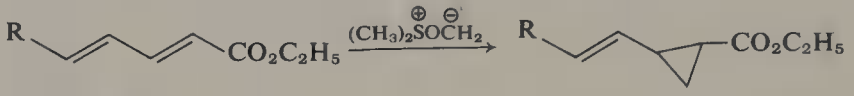

(a)
(b)
N
Carvone
CH3
O
(CH3)2S⊕
O⊖
H
15


(CH3)2SOCH2,
DMSO, 50°
16
74%

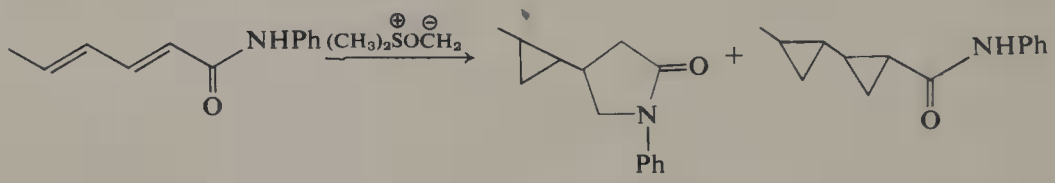

Ph
COPh, DMSO, 12 hr
CH3
N(CH3)2
CH3O2C
CO2CH3, DMSO, 22 hr
Product yield 94%
35% optical yield
Product yield 56%
15% optical yield


Ph
CO2
(CH3)3SO I⊖, KOC(CH3)3, DMSO
NaOH, H2O
CO2H

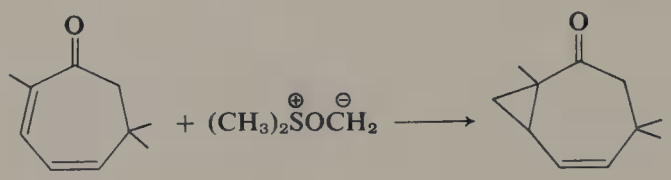
The position of cyclopropanation of polyenones might be expected to follow normal Michael condensations. However, this point has not been sufficiently studied to allow this conclusion. In fact, the few examples that exist lead to much confusion. Thus $\alpha,\beta,\gamma,\delta$-dienoates generally show preference for reaction at the α,β double bond,[34] but $\alpha,\beta,\gamma,\delta$-dienamides react

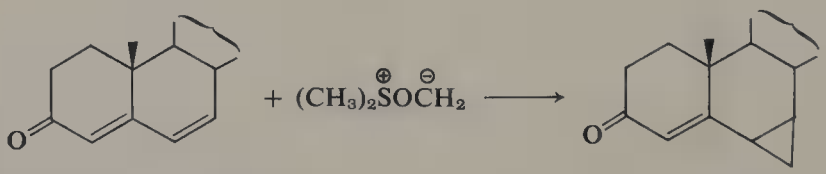


R = H, CH_3



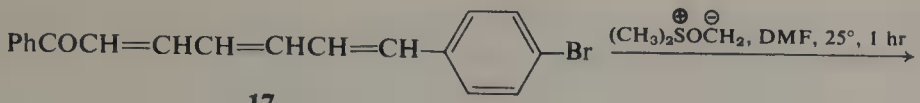
initially at the γ,δ site of unsaturation.[17,39] With $\alpha,\beta,\gamma,\delta$-dienones, steric factors determine the position of cyclopropanation. Eucarvone with geminal methyl substitution hindering δ attack cyclopropanates at the α,β double bond,[1] but the steroidal 4,6-dienones where the β-carbon atom is a



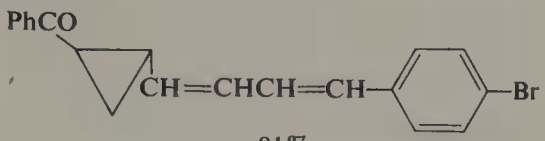


bridgehead cyclopropanate only at the γ,δ double bond.[58,59] The stereochemistry in the latter case depends on the orientation of the C-10 methyl group following normal steric hindrance rules. When the 19-methyl group is beta, the 6,7-cyclopropane ring is a mixture, but with the α-configuration predominating.[58,60] When the 19-methyl group is alpha, the 6,7-cyclopropane ring possesses the β-configuration.[59] In the one case where steric factors would appear to play no role, i.e., **17**, only cyclopropanation at the most electron-deficient α,β site of unsaturation is reported.[61]

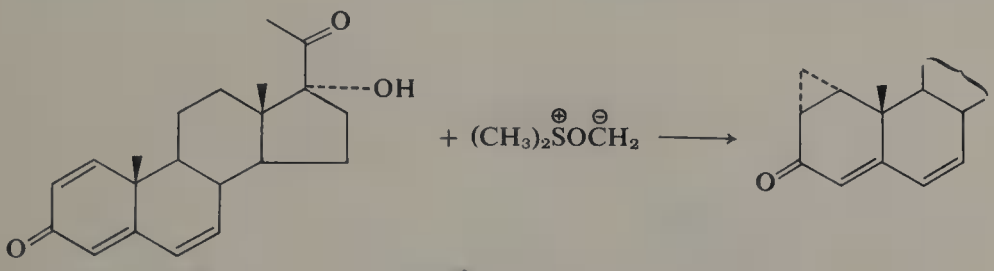
In competition between enones and dienones the former are more reactive as cyclopropanation of **18** illustrates.[47] However, enhancement of the reactivity of the dienone by substitution with additional electron-withdrawing groups, as in **19**, may alter the orientation.[59]



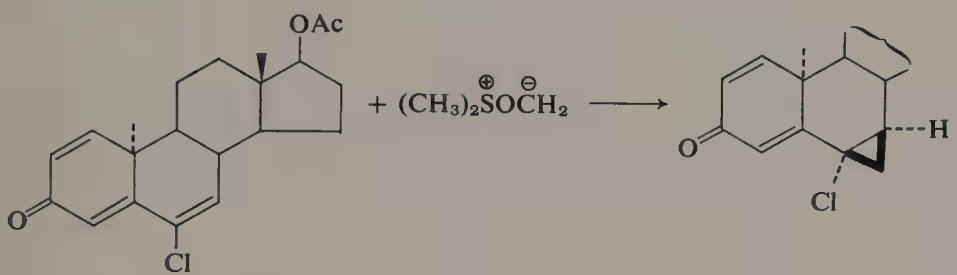
17



81%

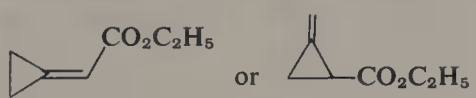


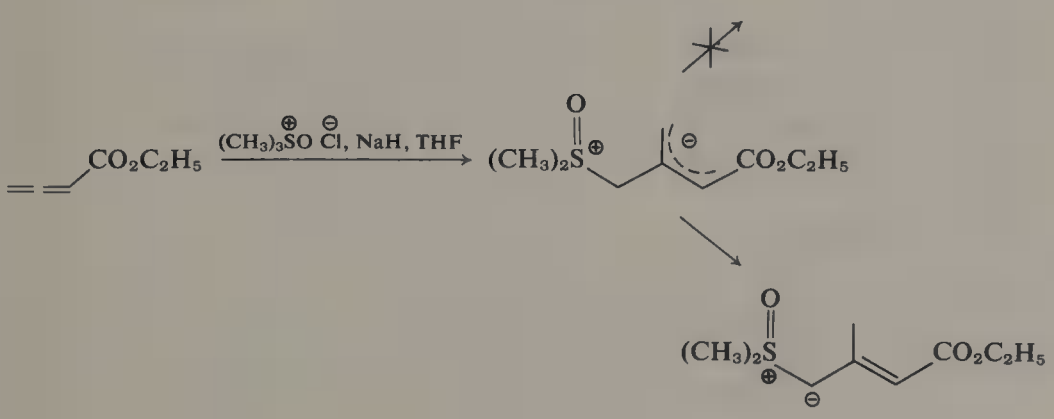
18



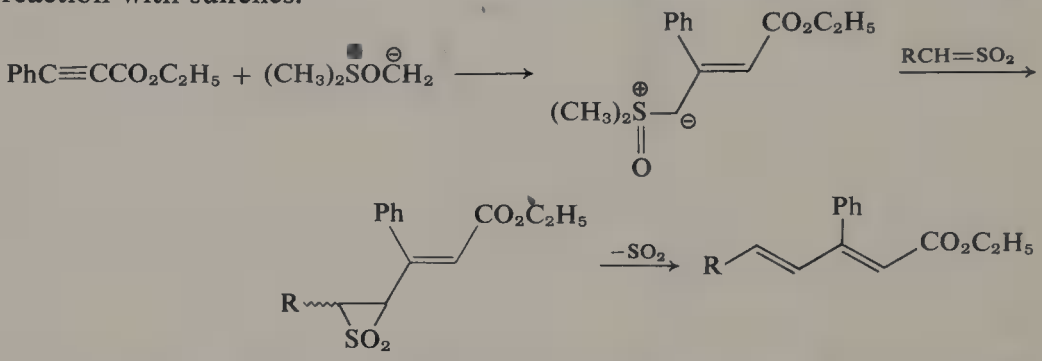
19

There exists only one report of an allenic ester reacting with the oxosulfonium ylide. Proton transfer to form the stabilized ylide takes precedence over collapse of the zwitterion by 1,3-elimination because of the large strain energy in producing a methylenecyclopropane.[34]

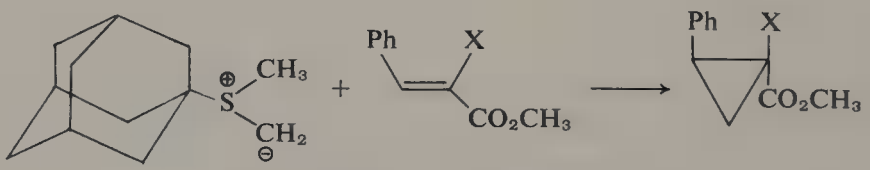




Like allenes, acetylenic Michael systems do not lead to cyclopropanation because of the high strain energy of the product. Instead, stabilized ylides result from prototropic shift in the intermediate zwitterion.[35] The stabilized ylides have found application in the synthesis of dienes by subsequent reaction with sulfenes.[62]

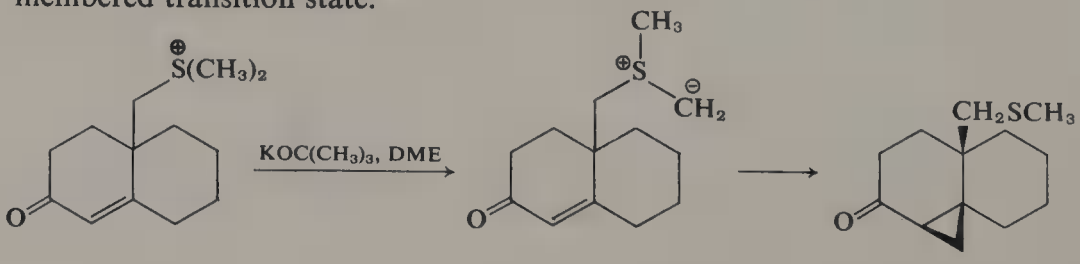


Whereas, all oxosulfonium methylides behave similarly, the more reactive sulfonium methylides deviate from the above behavior. Thus, dimethylsulfonium methylide is not, in general, a useful cyclopropanating agent owing to competition with direct addition to the electronegative group. Benzalacetophenone undergoes exclusive epoxide formation with dimethylsulfonium methylide in contrast to the oxosulfonium methylide (Chapter 5).[1] With exceptionally reactive Michael systems, cyclopropanation has been observed, e.g., with methyl 2-cyanocinnamate or dimethyl benzylidenemalonate.[63]

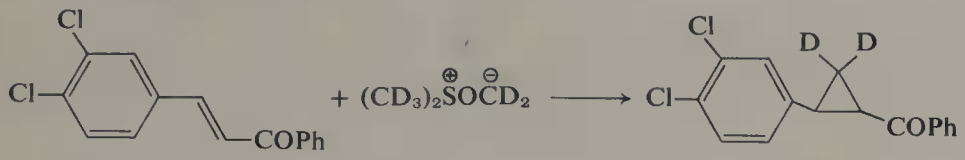


X = H	< 5%
X = CN	49.3%
X = CO_2CH_3	94.3%

Only one enone has been successfully cyclopropanated with a dialkylsulfonium methylide.[64] In this instance, the intramolecular delivery of the methylide directs it via the preferred five-membered transition state to the β-carbon atom of the enone rather than the remote carbonyl carbon, a seven-membered transition state.

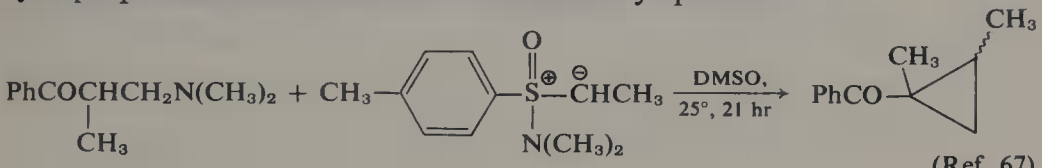


The facile H–D exchange of the sulfonium and oxosulfonium salts makes this route exceedingly attractive for preparing deuterated cyclopropanes. A series of gem-deuterated cyclopropanes have been prepared by the deuteromethylide transfer to chalcones.[65]



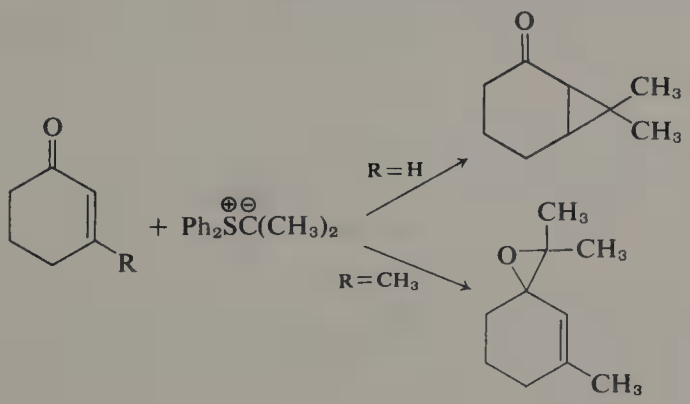
6.3. CYCLOPROPANATIONS WITH ALKYLIDES

Because of the general inaccessibility of substituted oxosulfonium ylides, cyclopropanations involving substituted ylides normally utilize the sulfonium series. For simple saturated alkylides, this fact limited their general application in forming cyclopropanes. For example, diphenylsulfonium ethylide has not been successfully utilized in such reactions with enones presumably because of preferential epoxidation. The aryldimethylaminooxosulfonium ylides appear to remove this limitation.[66,67] In principle, the precursor salts are available from the corresponding sulfoxides. The ethylide of this series cyclopropanates enones without interference by epoxidation.

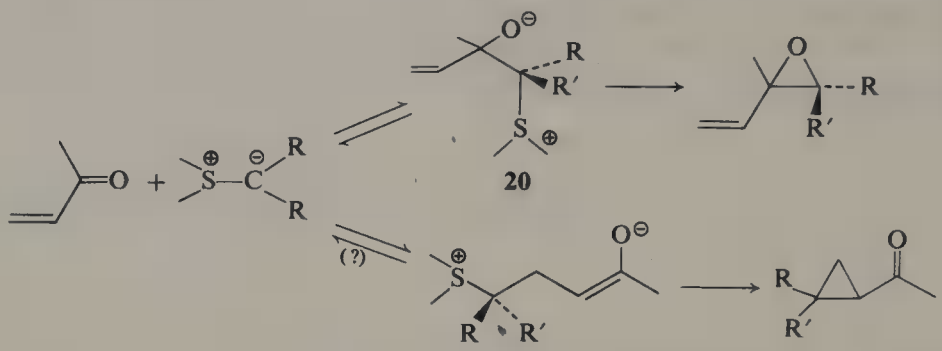


(Ref. 67)

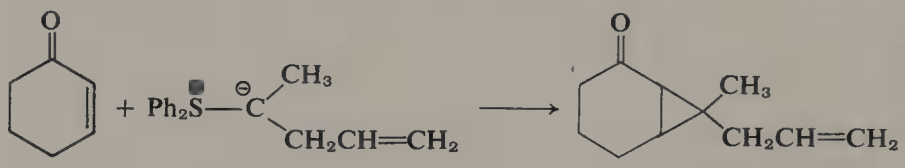
Sulfonium dialkylides do cyclopropanate α,β-unsaturated enones. The structure of the enone as well as the ylide determines the course of reaction. As for methylides, β-alkyl substitution of the enone hinders conjugate addition relative to 1,2-addition. Thus, diphenylsulfonium isopropylide cyclopropanates cyclohexenone, but epoxidizes 3-methylcyclohexenone.[68]



Ylide substituents (R and R′) that affect the collapse of the betaine **20** alter



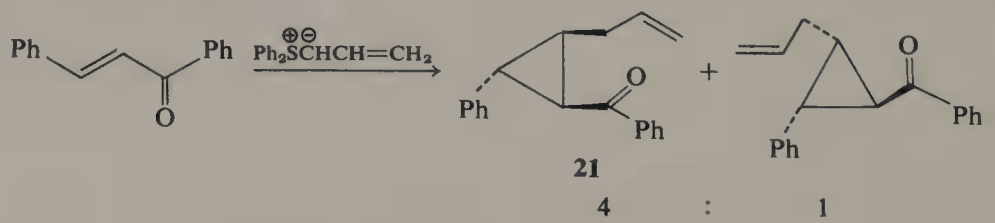
the ratio of products derived from carbonyl addition versus conjugate addition. The surprising finding of facile cyclopropanation rather than epoxidation with the isopropylide and the 1-pentene-4-ylide may result from



(Ref. 69)

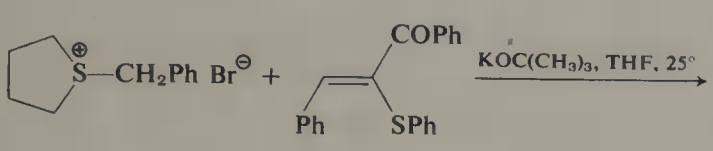
the severe retardation of the 1,3-elimination in the betaine for epoxidation because it requires an S_N2 displacement at a quaternary carbon. Thus, the formation of the betaine then becomes reversible and ultimately the thermodynamic product results. No test of this concept, for example by the independent generation of such a betaine, has yet been reported.

If the substituent in the ylide is moderately stabilizing, enhancement of cyclopropanation occurs most likely as a result of making betaine formation reversible. It is also conceivable in such instances that decreasing the reactivity of the ylide makes thermodynamic stabilities of intermediates more important in the transition state for reaction and thus leads preferentially to cyclopropane. Thus, although diphenylsulfonium allylide undergoes facile epoxidation with saturated aldehydes and ketones, it undergoes only cyclopropanation with unsaturated aldehydes and ketones.[70] Consideration of the



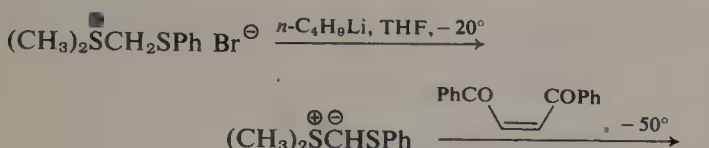
nonbonded interactions in the zwitterion intermediate formed by addition of the ylide to the enone allows prediction of stereochemistry. In the reaction

of the allylide with benzalacetophenone, such considerations lead to the expectation that cyclopropane **21** should be the major product, as is observed. Other substituents that lead to a reactivity paralleling that of the allylides include alkynyl,[71] phenyl,[72] and phenylthio.[73]



91%

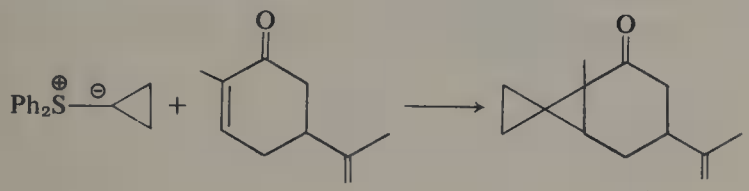
(Ref. 72)



53%

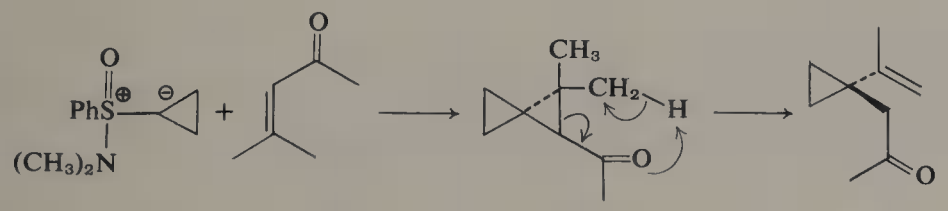
(Ref. 73)

An interesting application of cyclic sulfur ylides is the synthesis of spiro[2.*n*] systems—a reaction termed spiroannelation.[74] In the case where $n = 2$,



75%

(Ref. 75)



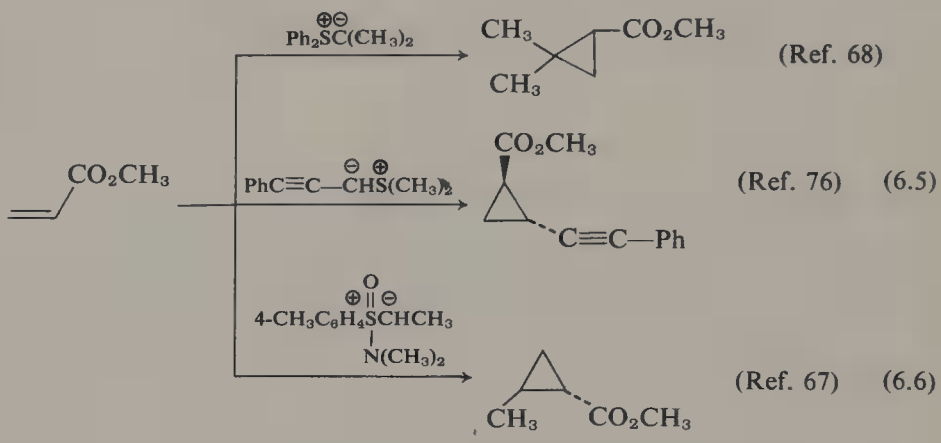
61% 100%

(Ref. 67)

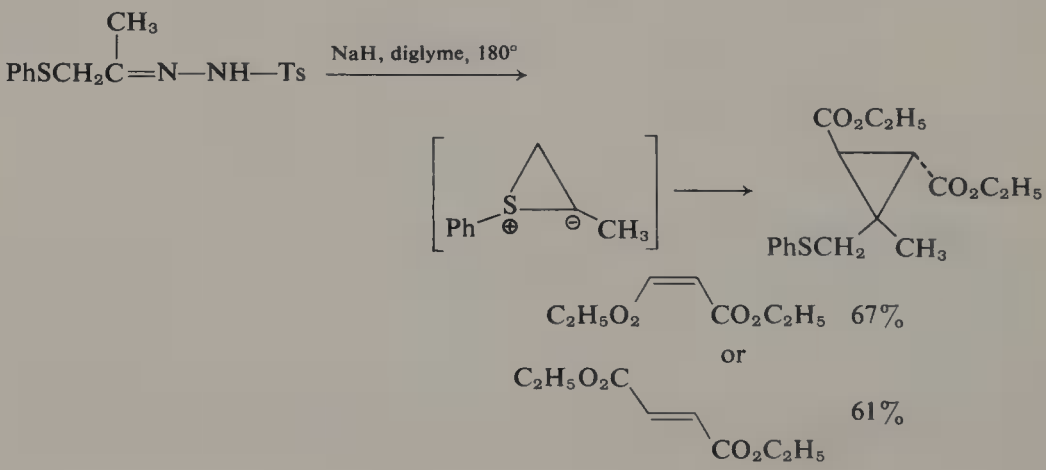
spiropentanes result in excellent yields. The easy thermal rearrangement of some of the spiro products expands the usefulness of the process to the synthesis of gem-alkylated cyclopropanes.

Cyclopropanation of enoates by the sulfonium or oxosulfonium alkylides also appears to be a good reaction with no appreciable complications arising from acylation. Diphenylsulfonium isopropylide,[68] dimethylsulfonium phenylpropargylide,[76] and *p*-tolyldimethylaminooxosulfonium ethylide[67] react with methyl acrylate to give the corresponding cyclopropanes in 71, 36, and 74% yields, respectively. In considering the eclipsing interactions in the intermediate zwitterion one can predict the observed trans geometry [Eqs.

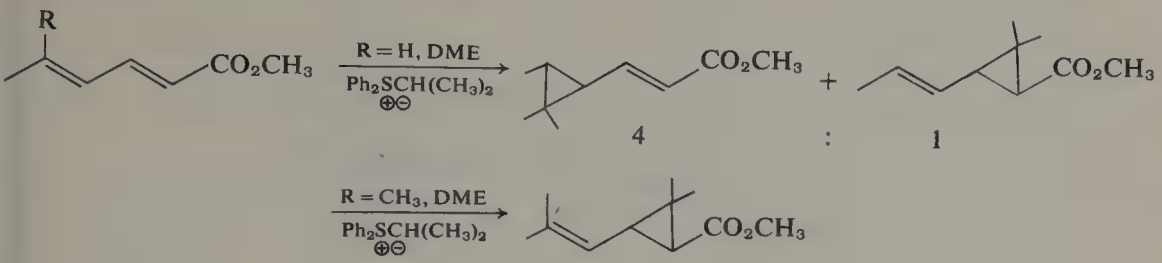
(6.5) and (6.6)]. Use of the optically active sulfoxamine ylide (*R* configuration) produces the cyclopropane [Eq. (6.6)] with a 43% optical purity. The existence of the first simple cyclic sulfonium ylide (in which both sulfur and the ylidic carbon are members of a ring) was demonstrated by trapping with

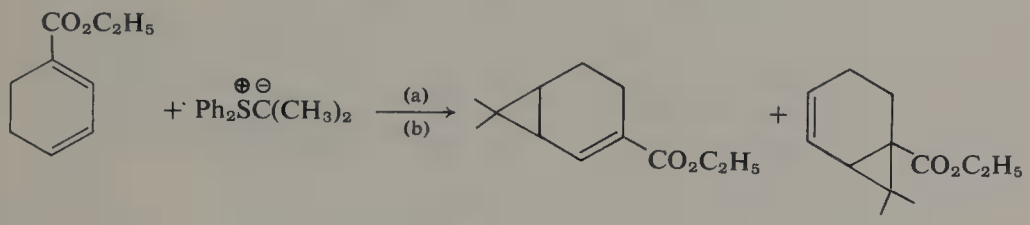


diethyl maleate or fumarate.[77] Note that in this as in all the cyclopropanations, the stereochemistry of the acceptor does not determine the stereochemistry of the product. Both fumarate and maleate produced the thermodynamically more stable isomer possessing the *trans*-ester groups.

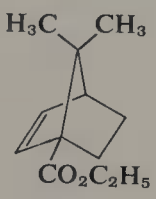


The site of reaction in polyenoates depends in part on steric considerations. With diphenylsulfonium isopropylide, methyl sorbate reacts preferentially at the γ,δ double bond,[78] but methyl 5-methylsorbate reacts exclusively at the α,β double bond.[68] The latter example constitutes a facile synthesis of methyl chrysanthemate. With ethyl 1,3-cyclohexadien-1-carboxylate, solvent plays an undetermined role in controlling the regiospecificity.[78] Most interestingly, no 1,5-elimination to the bicycloheptene **22** occurs even though the required cisoid conformation of the conjugate adduct is rigidly maintained.



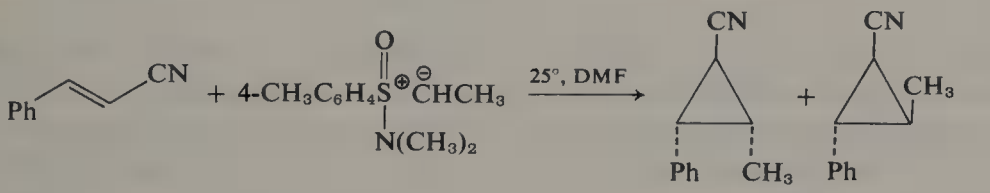


(a) = DME 4 : 1
(b) = THF 1 : 2



22

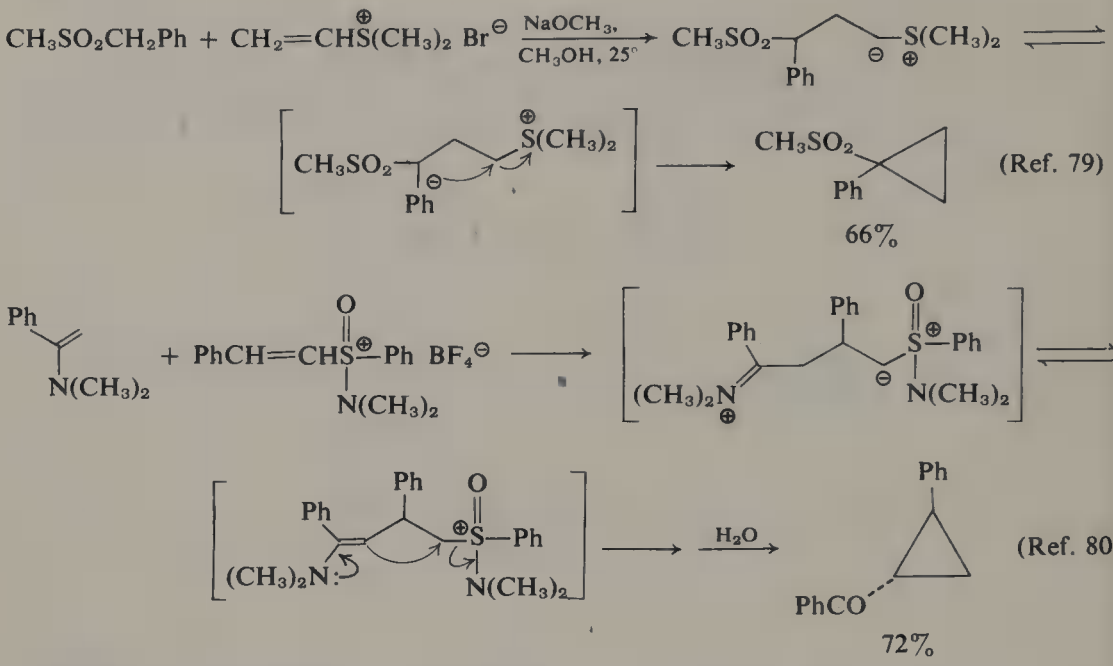
Cinnamonitrile represents the only other type of acceptor that has been reacted with alkylides. An alternative approach that has led to cyclopropanes



73% (Ref. 67)

involves *in situ* generation of alkylides by conjugate addition of stabilized anions or enolate equivalents to vinyl sulfonium and oxosulfonium salts. In these cases, the alkylides merely undergo prototropic shift to give the 1,3-zwitterionic precursor of the cyclopropanes which usually arose from conjugate addition of the methylide to a suitable acceptor.

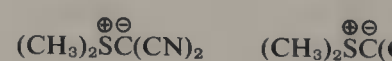
In principle, the same Michael acceptors that react with the methylides should react with the alkylides at least as well. In one instance, cyclopropanation was superior with the alkylides compared to the methylides; the addition of diphenylsulfonium isopropylide to dimethyl acetylenedicarboxylate produced dimethyl 2,2,4,4-tetramethylbicyclo[1.1.0]butane-1,3-dicarboxylate.[68] Unfortunately, the list of alkylides in such reactions remains limited



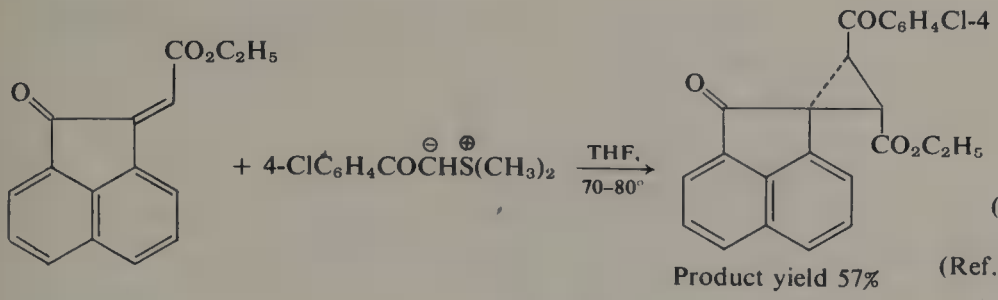
to those presented above. The discovery of additional alkylides remains a fruitful field of research. Certainly, as this method of cyclopropanation continues to grow, the list of useful cyclopropanating alkylides will grow.

6.4. CYCLOPROPANATIONS WITH STABILIZED YLIDES

The stabilized ylides generally only undergo cyclopropanation. The success of this reaction contrasted to the failure to form epoxides even with saturated ketones suggests that the addition of stabilized ylides to an enone requires the additional delocalization of charge over the conjugated system in the transition state for reaction to occur. In fact, the major problem appears to be the lack of reactivity of the stabilized ylides. Ylides stabilized by only one group normally cyclopropanate typical Michael acceptors. Ketone [Eq. (6.7)], ester [Eq. (6.8)], and cyano [Eq. (6.9)] groupings have served as the stabilizing function. On the other hand, ylides stabilized by two such functions such as dimethylsulfonium dicyanomethylide[84,85] or dimethylsulfonium dibenzoylmethylide[86] fail to react with even the relatively reactive Michael system of chalcone.

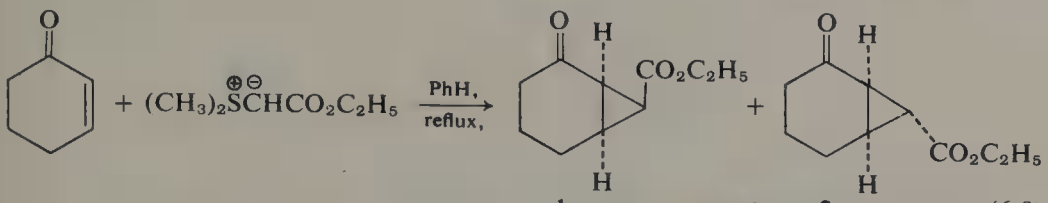


Only a limited number of Michael acceptors has been examined. Conjugated aldehydes and ketones react with most stabilized ylides to give in good yields the cyclopropane in which the ylide stabilizing group is trans to the



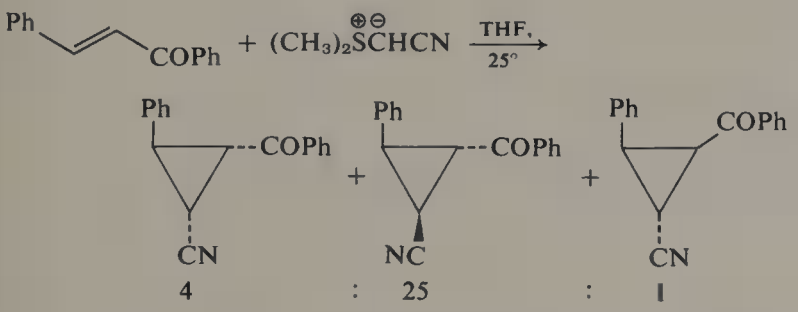
(6.7)

Product yield 57% (Ref. 81)



(6.8)

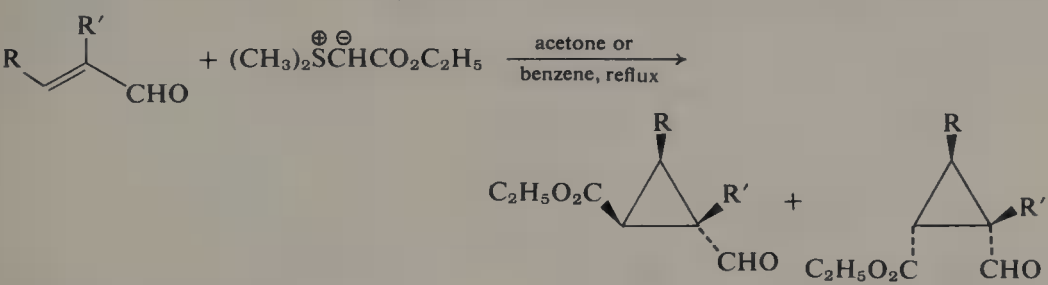
Product yield 71% (Ref. 82)



(Ref. 83) (6.9)

Product yield 91%

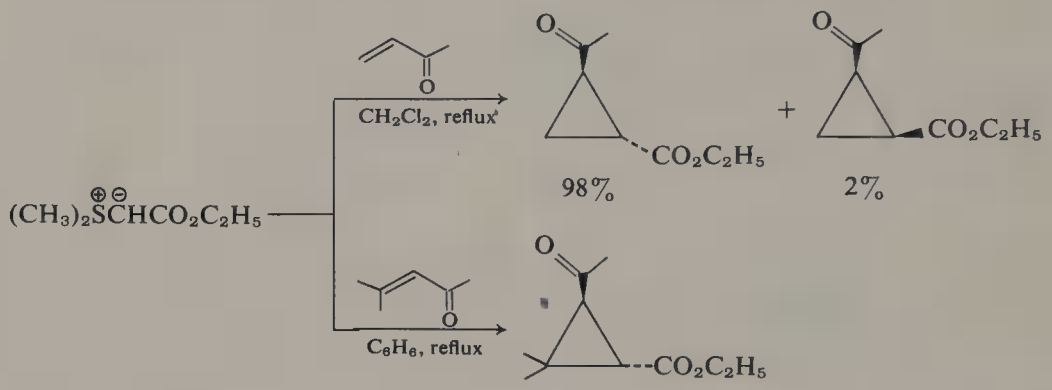
electron-withdrawing substituent of the Michael acceptor. Thus, 2-methylpropenal or 2-butenal reacts with dimethylsulfonium carboethoxymethylide



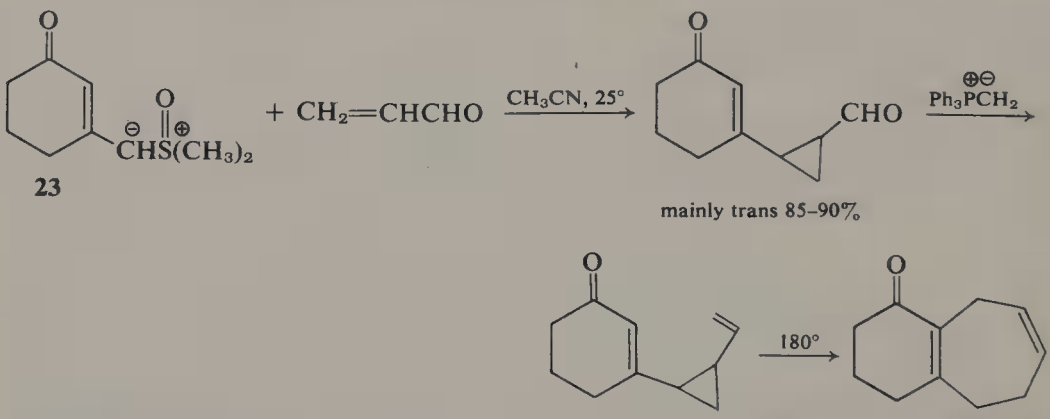
R = H, R′ = CH_3	68	32
R = CH_3, R′ = H	82	18

to produce the trans products predominantly.[82] Again, analyses of conformational stabilities of the intermediate zwitterions provide a rationale for the observed stereochemistry. Alkyl substitution hinders cyclopropanation. Thus, the above ylide cyclopropanates methyl vinyl ketone in 87% yield after only

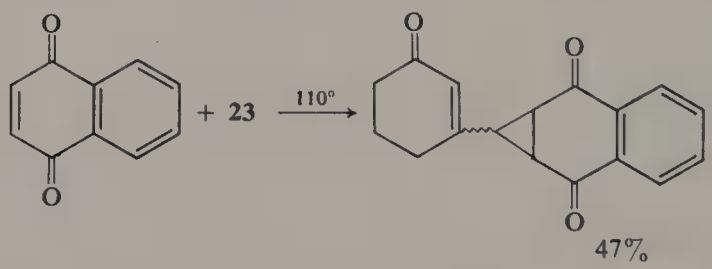
2.5 hr in refluxing methylene chloride, but requires refluxing in benzene for 18 hr to cyclopropanate 2-methyl-2-penten-4-one in 75% yield.[82]



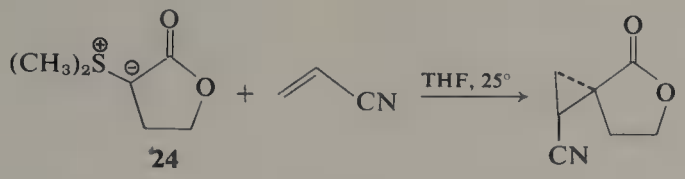
The vinylogously α-keto oxosulfonium ylide **23**[87] adds successfully to reactive Michael acceptors such as acrolein.[88] The cyclopropane has served



as an intermediate in a novel cycloheptane annelation.[89] A quinone, which may be considered to be a cross-conjugated enedione, has been cyclopropanated by this ylide.[87]

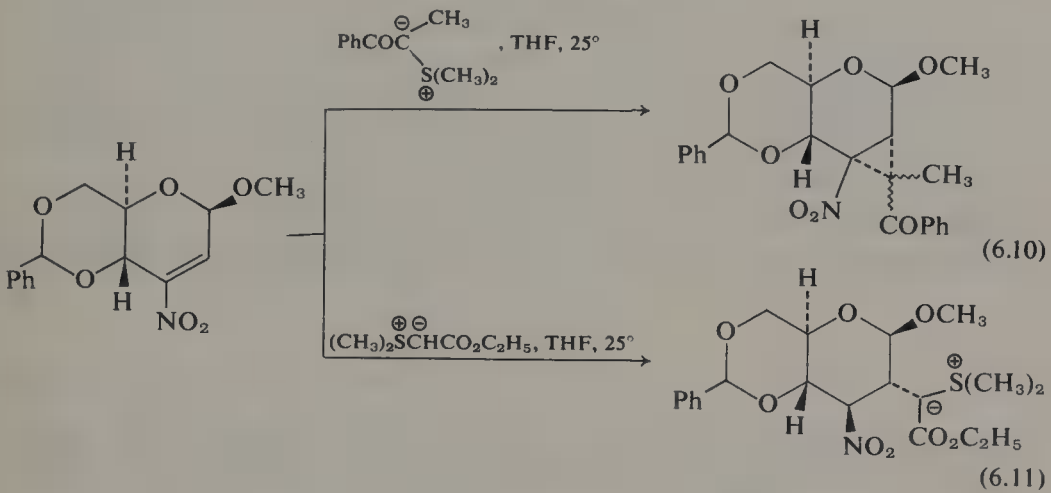


With selected stabilized ylides, other acceptors have been examined. The lactone ylide **24** condensed with acrylonitrile in yields as high as 90%.[90] The exclusive formation of the trans isomer may be accounted for by consideration of steric and dipole-dipole interactions in the intermediate zwitterion. The greater activating influence of the nitrile compared to the



24

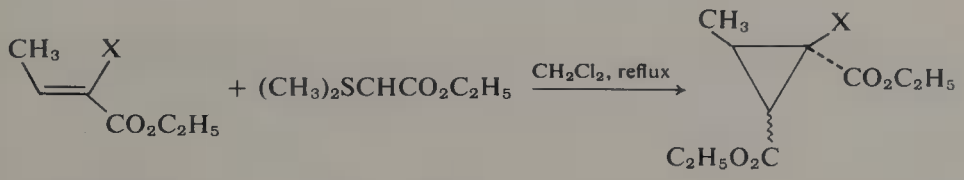
ester on the acceptor is suggested by the failure of simple enoates to react with **24**. The use of α,β-unsaturated nitro compounds has had mixed results. Whereas the oxosulfonium ylide **23**[88] and diethylsulfonium α-methyl phenacylide [Eq. (6.10)][91] react normally to give the cyclopropane, the carboethoxymethylide led to a new stabilized ylide via prototropic rearrangement in the zwitterion intermediate [Eq. (6.11)].[91]



(6.10)

(6.11)

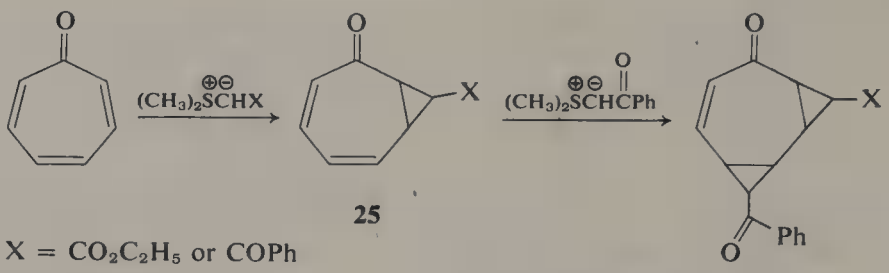
Enoates react with the stabilized ylides without complications. The rates of cyclopropanation are highly dependent on the structure of the enoates. Alkyl substitution hinders reaction, but addition of another electron-withdrawing group can overcome the retardation. For example, ethyl crotonate reacts in 71% yield with dimethysulfonium carboethoxymethylide, but diethyl ethylidenemalonate generates the corresponding cyclopropane with this ylide in 90% yield under identical conditions.[82]



X = H

X = $CO_2C_2H_5$

The use of polyenones has not been explored except for the unusual case of the tropones.[92] Reaction of tropone with the carboethoxymethylide and phenacylide generated cyclopropanes involving attack only at the α,β double

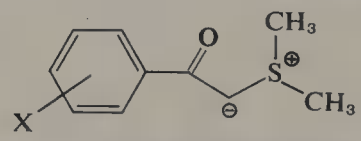


25

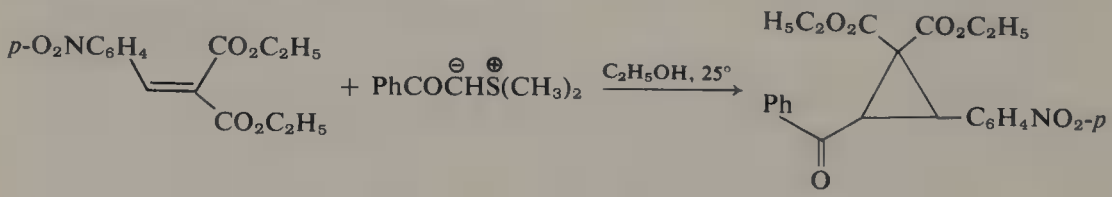
X = $CO_2C_2H_5$ or COPh

bond. The remaining dienone does condense further; however, reaction proceeds at the γ,δ-position. Considering that the transition state for condensation should be far along the reaction coordinate, delocalization of the negative charge in the developing enolate should be the major factor. Such a consideration leads to the expectation that reaction will occur at the more remote double bond in polyenones as was observed with **25**. The rationale for initial reaction of tropone at the α,β double bond may relate to the conformation of the molecule since the γ,δ double bond is considerably twisted out of the plane (and therefore out of conjugation) of the enone system.

The compatibility of various functional groups in both the ylide and the acceptor has not been studied. In the phenacylides, bromo, chloro, and nitro

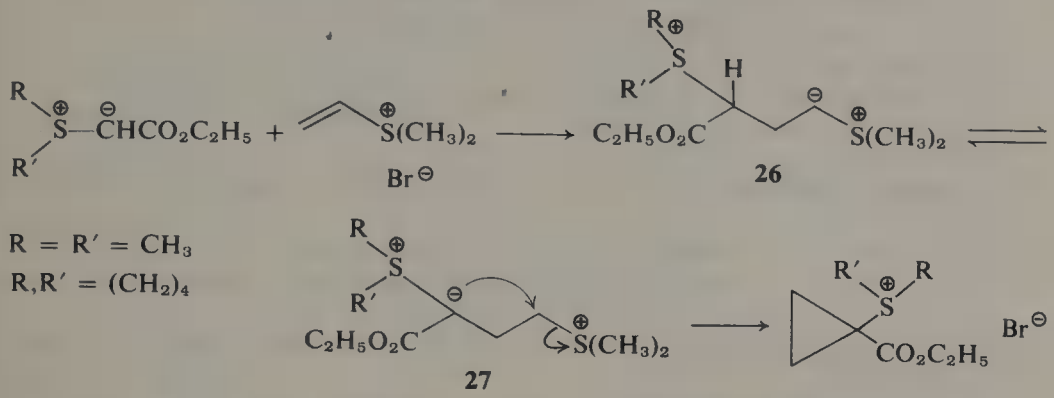


groups on the phenyl ring do not decrease the stability of the ylide nor inhibit its ability to cyclopropanate.[81,93] Similarly, such functional groups on the acceptor do not interfere in the cyclopropanation reaction. Thus, dimethylsulfonium phenacylide reacts with diethyl *p*-nitrobenzylidenemalonate to give the expected product in 35% yield.[94]



In all the reactions discussed so far, not much consideration has been given to the role of the remaining substituents on sulfur. These substituents have traditionally been phenyl, in the alkylides, and methyl, in the others. The effect of these groups on ylide reactivity deserves more study. Greater flexibility in the choice of the sulfur substituents exists in the stabilized ylides because the problem of isomeric ylides does not arise. However, here too only scant reports of varying sulfur substituents have appeared. A steric effect has been noted in the reactions of dimethylsulfonium carboethoxymethylide and tetrahydrothiophenium carboethoxymethylide. The former

reacts with dimethylvinylsulfonium bromide, a fascinating Michael acceptor, to give a cyclopropane in 77% yield, whereas the latter gives the corresponding cyclopropane in only 52% yield.[93] Michael addition to this



acceptor has the interesting feature of generating a sulfur ylide which, in principle, can undergo normal ylide reactions. In this particular case, the ylide **26** suffers prototropic shift to generate the more stable ylide **27**. This new ylide collapses by expulsion of dimethyl sulfide to the observed products. Apparently the steric bulk of the tetrahydrothiophene ring compared to the methyl groups accounts for the lower yields.

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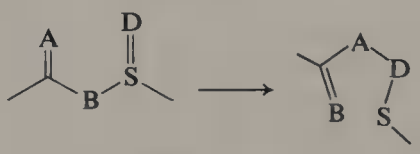
7

Rearrangements

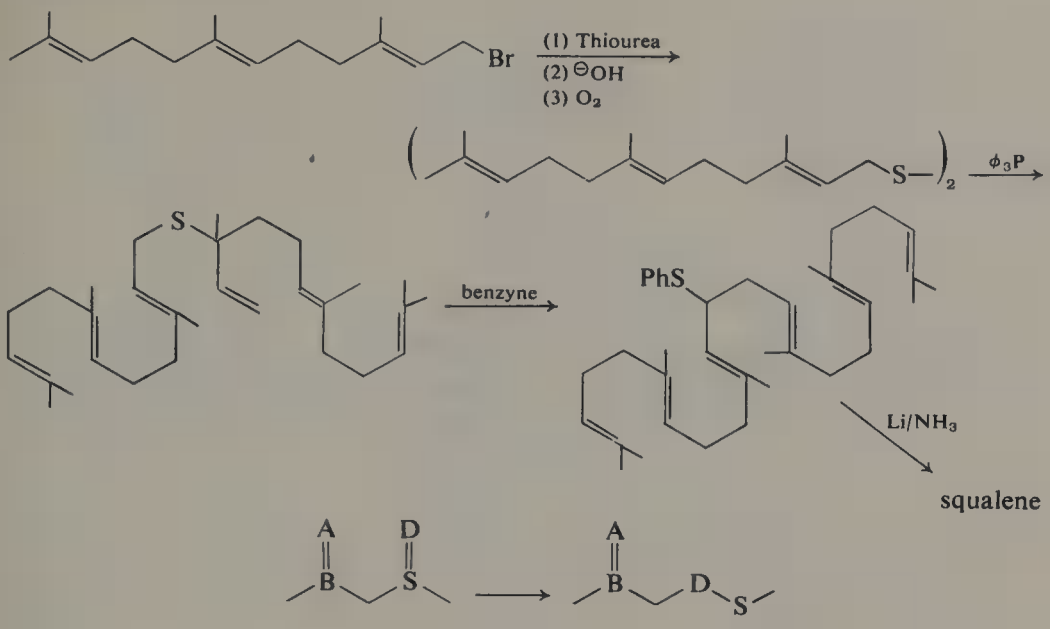
7.1. INTRODUCTION

Allylsulfonium alkylides undergo a thermal orbital symmetry-allowed [2.3]sigmatropic rearrangement to generate homoallylic sulfides. The rearrangement is represented for the general case in which A, B, and/or



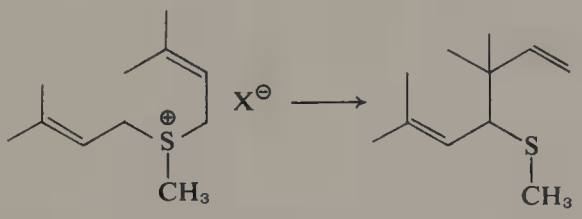
D need not be carbon.[1] However, for this chapter, only the case of A = B = D = carbon is exemplified. Random allylic coupling does not occur and reductive cleavage of the rearranged sulfides occurs with complete orientational specificity making this process attractive for stereospecific 1,5-diene syntheses. The synthetic utility of this process has been demonstrated by its use in a synthesis of squalene.[2]

Certain allylsulfonium ylides undergo an alternative mode of reaction equivalent to the 1,2-shift of the Stevens rearrangement. This reaction has also been observed for A=C or O and B=D=C. This reaction becomes synthetically useful when the allyl unit is incorporated in an aromatic ring (i.e., a benzyl system). These two reactions form the subject of this chapter.

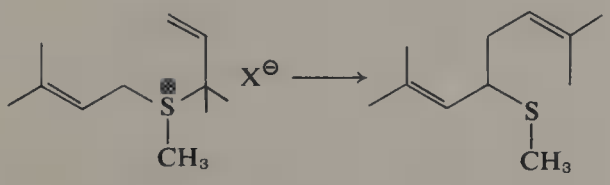


7.2. MECHANISM

The sigmatropic ylide rearrangement proceeds with complete allylic inversion as demanded by orbital symmetry control. Thus, starting with the sulfonium salt **1** only homoallylic sulfide **2** is obtained, whereas the isomeric sulfonium salt **3** produces the isomeric homoallylic sulfide **4**.[3,4]



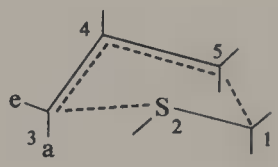
1 **2**



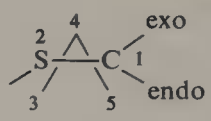
3 **4**

Theory suggests a suprafacial–suprafacial array (i.e., **5a–c**) for the [2.3]-sigmatropic rearrangement (structure **5a** illustrates the HOMO-LUMO interactions).[5] By analogy to the close parallelism between the conformations of the [3.3]sigmatropic rearrangement and the cyclohexane ring,[6] the preferred conformation of the [2.3]process should resemble the "folded

5a

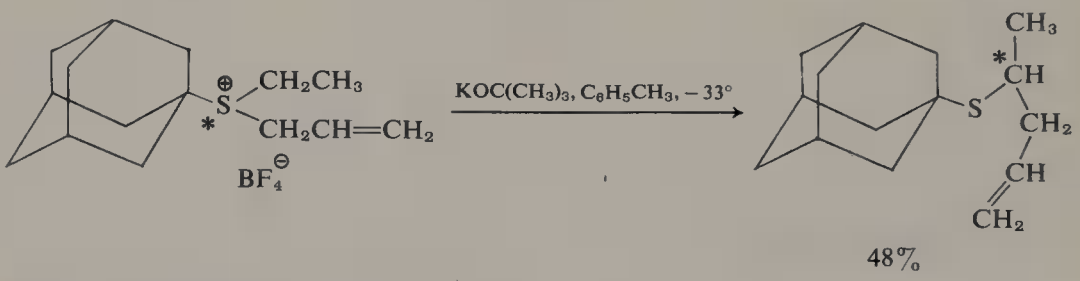


5b



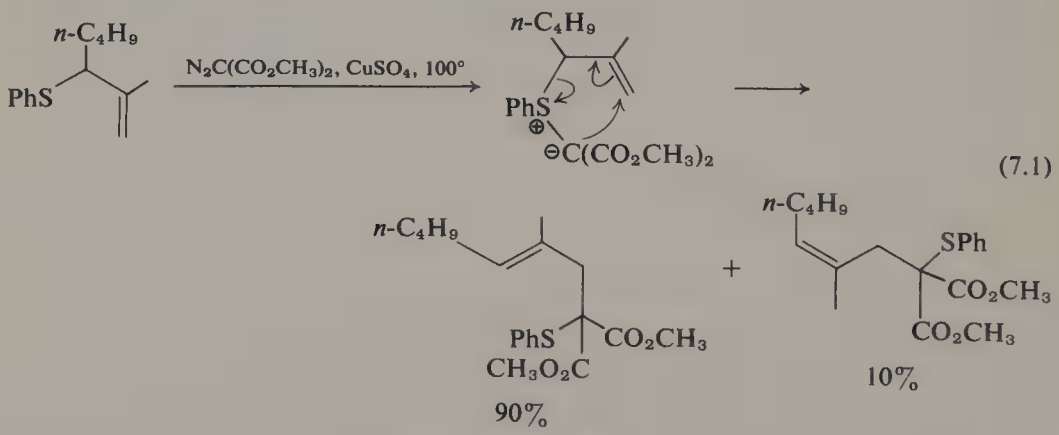
5c

envelope" conformation of a cyclopentane ring (i.e., **5b**). The fact that optically active (+)-adamantylallylethylsulfonium fluoroborate rearranges to *R*-4-adamantylthio-1-pentene possessing 94% optical purity indicates



48%

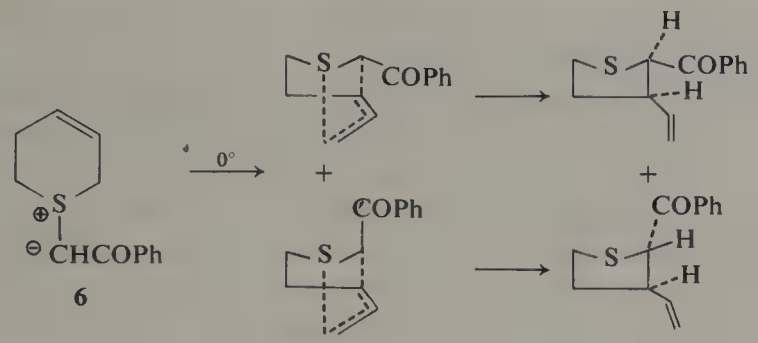
strong conformational requirements.[7] Introduction of a bulky group at C-3 (numbering from structure **5b**) leads to preferential formation of the *trans* isomer at the newly created double bond [see Eq. (7.1)].[8,9] Conformation **5b**



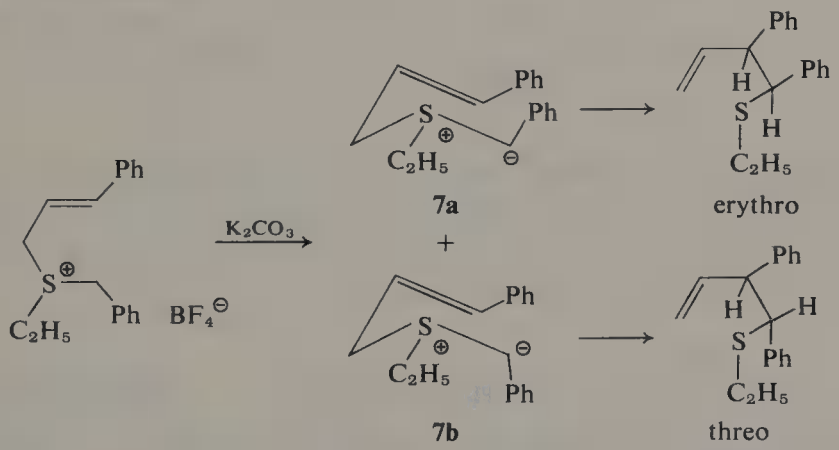
90% 10%

(7.1)

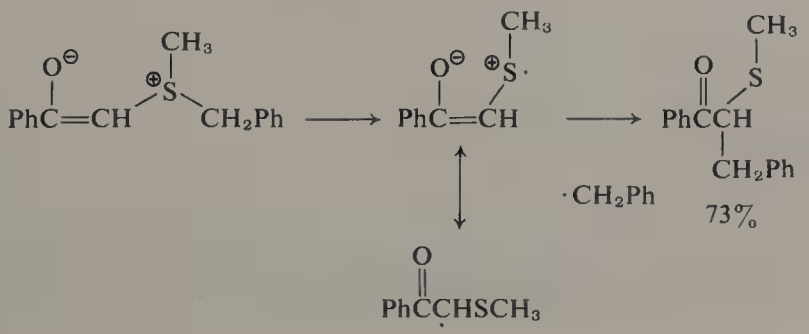
nicely accommodates this result. Of the two orientations at C-3, the larger C-3 substituent should preferentially occupy the pseudoequatorial orientation. Thus, the bulkier group at C-3 will eventually end up trans to the substituent bearing the thioether unit on the olefin of the product. Substituents at C-1 may be viewed as occupying the endo or exo orientation as depicted in the planar projection **5c**. A clear preference for the exo orientation (25:1) was seen in the rearrangement of **6**.[10] However, the bias shown in this case may not be



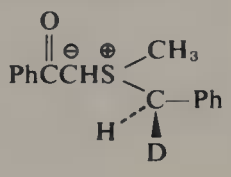
general because of the strong steric interactions with the CH_2–CH_2– unit of the six-membered ring. Substitution at C-1 and C-5 can lead to a mixture of diastereomers. Of the two conformations **7a** and **7b**, eclipsing interactions between the substituents indicate the latter to be the more stable. On the other hand, this conformation places the phenyl ring at C-1 in the less favorable endo orientation during rearrangement. The net result is a slight preference (60:40) for one isomer; unfortunately, its relative stereochemistry has not been assigned.[11]



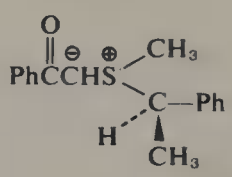
Although allylic sulfonium ylides invariably react by the [2.3]sigmatropic pathway, inclusion of the allylic portion in an aromatic ring may dramatically alter the course of the reaction. *S*-Phenyl-*S*-methylsulfonium phenacylide rearranges in aprotic solvents by a net 1,2-shift (Stevens type rearrangement)



to yield 1,3-diphenyl-2-methylthiopropan-1-one.[12] Such 1,2-shifts are forbidden in a concerted reaction mechanism. In fact, the accumulated evidence points to a diradical pathway. Thus, both products from symmetrical coupling (i.e., bibenzyl and 1,2-dimethylthio-1,2-dibenzoylethane) are produced. A CIDNP enhancement of the nmr signal for the benzylic methylene group of the unsymmetrical product is observed if the reaction is carried out in a nmr spectrometer.[12,13] The radicals react in a caged fashion as indicated by the relatively high retention of configuration (36 ± 15%) observed when optically active benzylic ylides rearrange (e.g., **8** and **9**) and the low amounts (18 ± 6%) of crossover observed when the two labeled ylides **10** and **11** are rearranged together.[14]

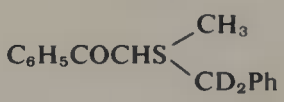


8



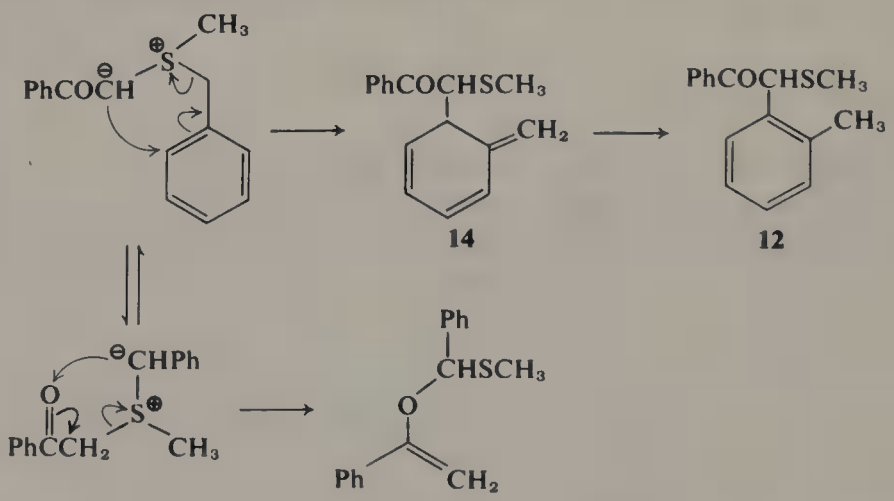
9

10



11

In protic solvents the orbital symmetry-allowed products do predominate.[15] The ratio of the two products **12** and **13** can be controlled by base concentration.[16] This effect can be attributed to the rate of establishment of the equilibrium between the two ylide precursors.

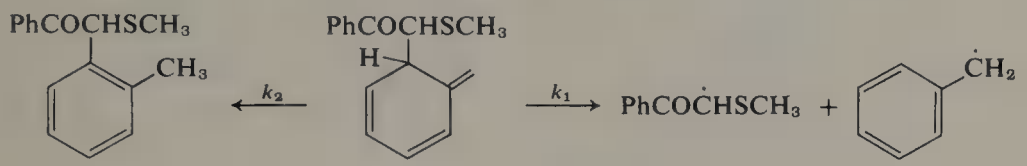


14 **12**

13

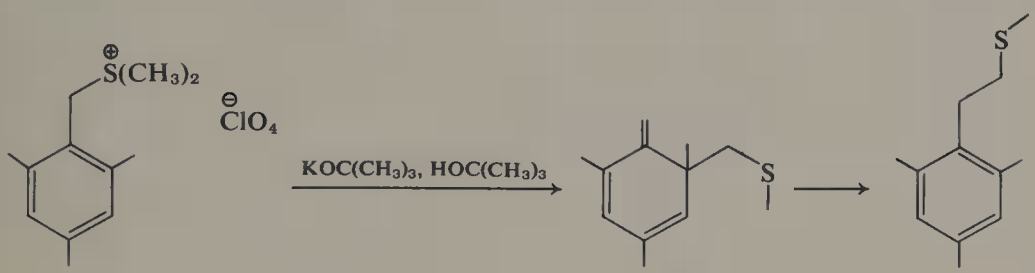
The striking result is the formation of a normal Sommelet–Hauser type product (orbital symmetry-allowed process) in basic protic conditions,

whereas in aprotic conditions only a Stevens type product (orbital symmetry-forbidden process) is formed. A possible explanation relates to the fate of the Sommelet–Hauser rearranged intermediate **14**. Aromatization requires proton abstraction followed by reprotonation—hence, the necessity for a base and an acid. In aprotic conditions this requirement is not met. Homolytic cleavage successfully competes with prototropic rearrangement (i.e., $k_1 > k_2$) and the ultimate product is that derived from the net orbital symmetry-



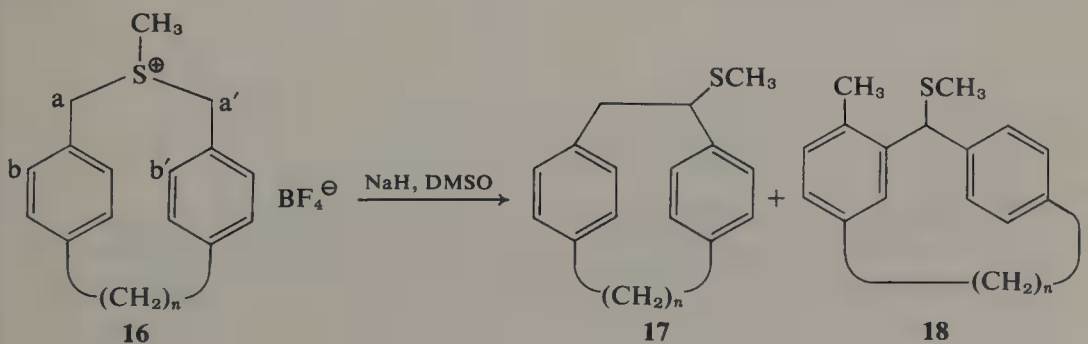
14

forbidden 1,2-shift. Intermediates of the type **14** (e.g., **15**) have been isolated and shown to yield the 1,2-shift product upon thermolysis.[16] A similar competition between the [1.2]- and [2.3]rearrangements was observed in the



15

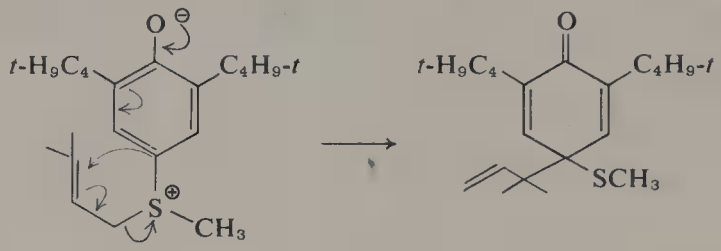
cyclophanes **16**. With $n < 8$, only **17** forms; with increasing n, the amount of **18** increases ($n = 8$, 8%; $n = 9$, 55%).[17] Although the trend is explicable as above, an alternative explanation recognizes that the short bridges preclude close approach of positions a′ and b (see **16** for assignments) required in the [2.3]process.



16 **17** **18**

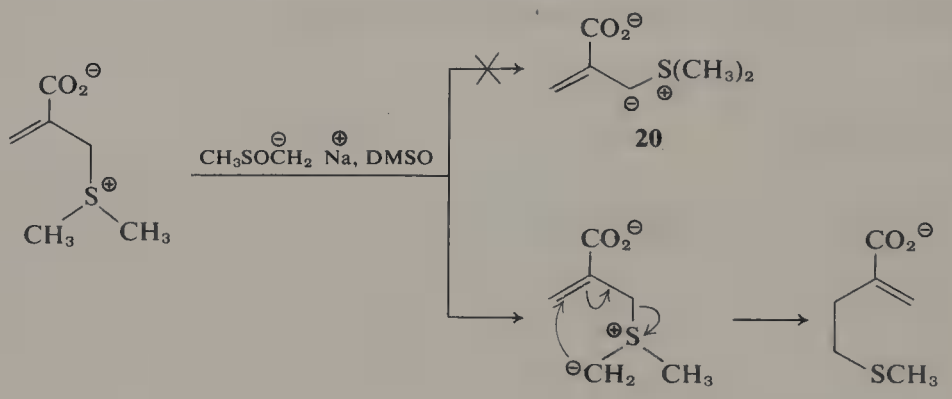
7.3. SCOPE AND LIMITATIONS

These sigmatropic rearrangements proceed with an unusual degree of facility. Even as stabilized an ylide as **19** rearranges at $-40°$.[18] In fact, the utilization of allylides in which sulfur bears an alkyl substituent with a



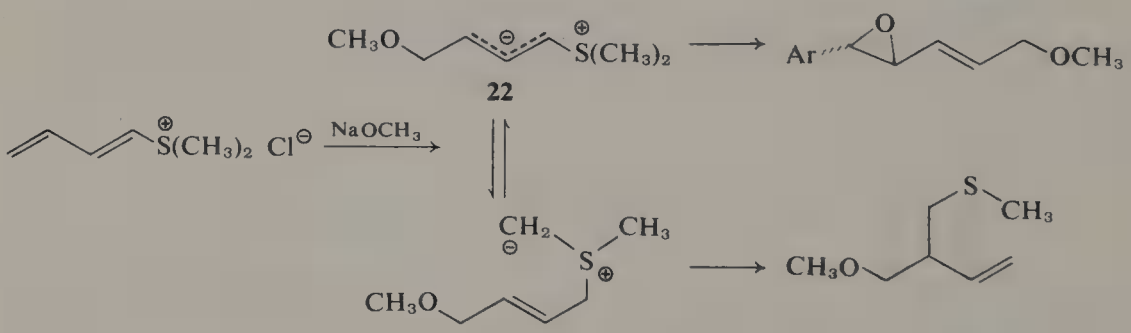
19

hydrogen on the α-carbon in alkylidene transfer reactions becomes very difficult. Attempts to generate allylide **20** only yield the homoallylic sulfide



20

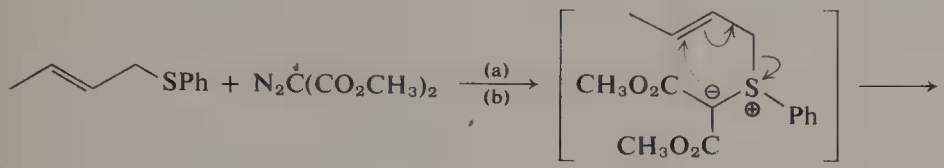
21
50%

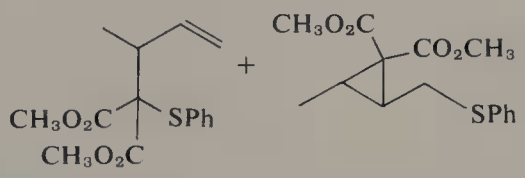


22

21.[19] Michael addition of methoxide to 1-buta-1,3-dienyldimethylsulfonium chloride provides the allylide **22** which undergoes protropic shift followed by sigmatropic rearrangement.[20] In this case, the allylide was trappable by reactive carbonyl partners.[21]

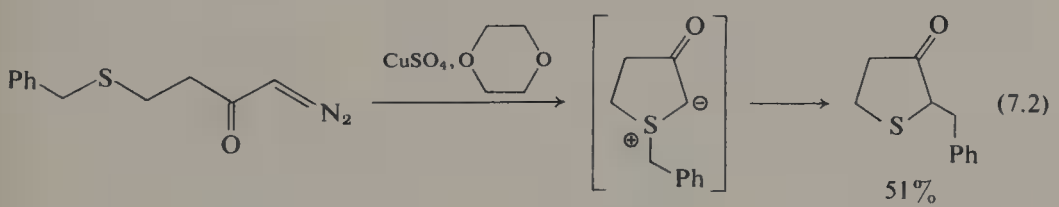
Direct methods of ylide formation appear most suitable (also see Chapter 3). Attack of a singlet carbene on an allyl sulfide gives the homoallylic sulfide





(a) = $h\nu$	47%	10%
(b) = $CuSO_4$	90%	—

with very little or no cyclopropane depending on the mode of carbene generation.[22,23] The intramolecular version [see Eq. (7.2)] is best accomplished by the copper salt-catalyzed thermal decomposition of the diazo compound.[22]



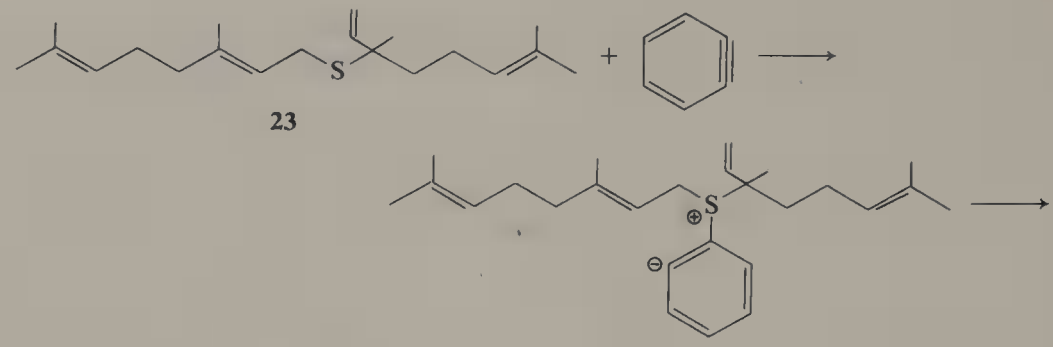
(7.2)

24

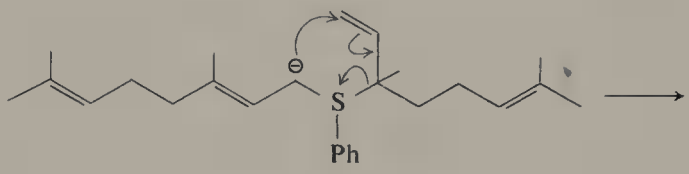
As Eq. (7.2) illustrates, this method applies to the Stevens type rearrangement too.[24] Reaction of dihalocarbenes with allyl sulfides produces similar results.[25]

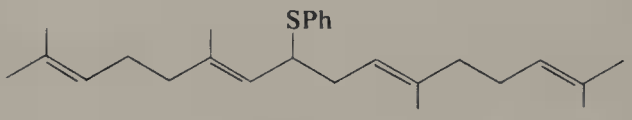
Benzyne (generated from *o*-bromofluorobenzene with magnesium) addition to a bisallyl sulfide also creates the requisite intermediate after proton shift. This method generally leads to greater competition between [2.3]- and [1.2]sigmatropic rearrangements because of the higher temperatures normally employed (see **23** → **24**).

The most common approach involves alkylation of a suitable sulfide to form a sulfonium salt followed by base treatment to effect rearrangement. The requisite sulfide is available either by alkylation of a mercaptide with an allylic halide[4,27] or phosphine-induced desulfurization of a disulfide [Eq. (7.3)].[28,29] Mercaptans which are not available may be obtained by alkylation of thiourea with an alkyl halide or by rearrangement of the xanthate of an allylic alcohol [Eq. (7.4)][30] followed by hydrolysis.



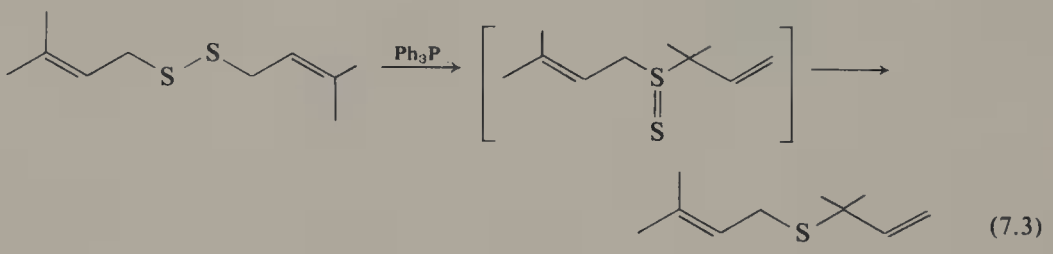
23



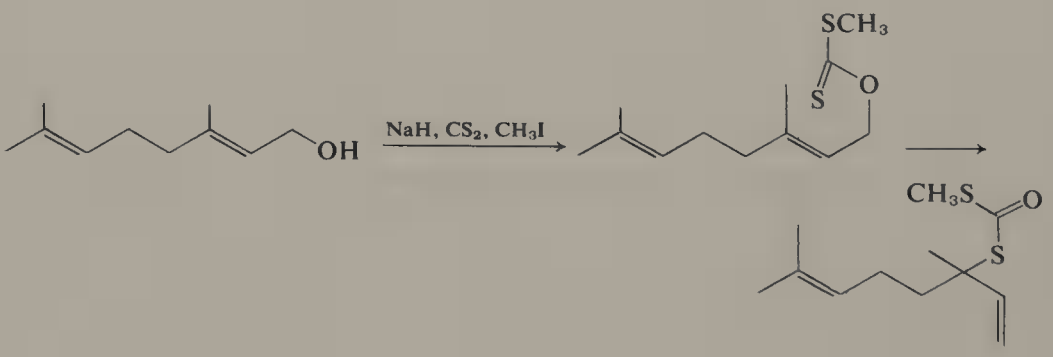


24

(Ref. 26)

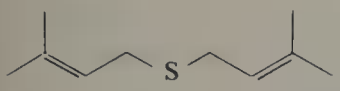


(7.3)

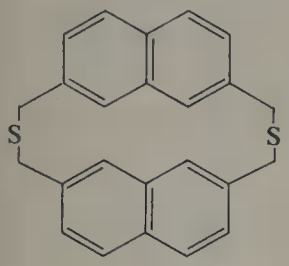


(7.4)

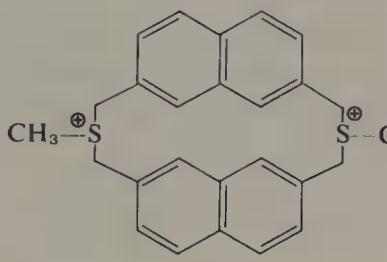
The preparation of sulfonium salts from the sulfides requires reactive alkylating agents. For the simplest alkyl groups, methyl and ethyl, the oxonium [Eq. (7.5)] or acyloxonium [Eq. (7.6)] fluoroborates are the most successful reagents. Sulfonium salt formation may also be achieved by the alkyl halide-silver fluoroborate procedure (see Chapter 2) as well as by the



(7.5)
(Ref. 31)



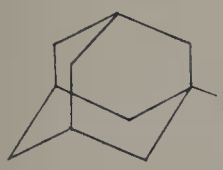
$(CH_3O)_2CH^{\oplus}\ BF_4^{\ominus}$, CH_2Cl_2



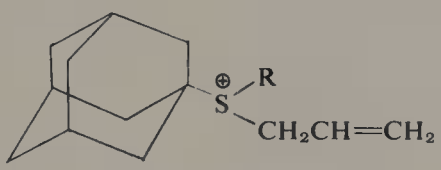
(7.6)
(Ref. 32)

>90%

use of carbonium ions. The preparation of sulfonium salts **25a** and **25b** illustrates this method.[7] Chapter 3 provides further coverage.

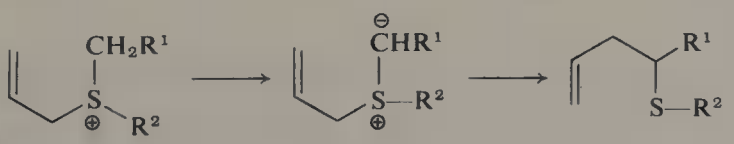


+ CH_2=$CHCH_2SR$ $\xrightarrow{AgBF_4,\ CH_2Cl_2}$



25a, R = C_2H_5, 76%
25b, R = CH_2Ph, 88%

The choice of the groups on sulfur and the base depend on the nature of the coupling process [Eq. (7.7)]. If R^1 is an anion-stabilizing group (e.g.,

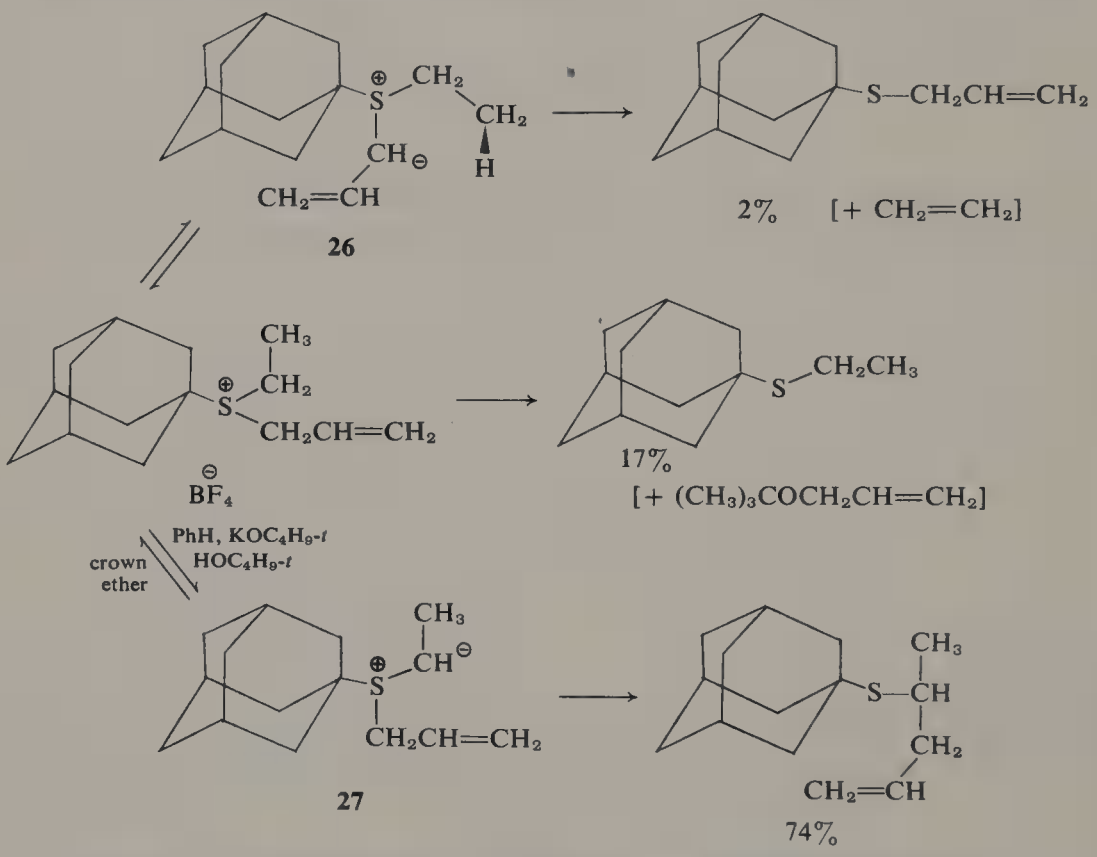


(7.7)

vinyl, phenyl, carbonyl, etc.), R^2 may be methyl or ethyl. Alternatively, if R^1 is simply alkyl, R^2 should not possess hydrogens on the carbon atom linked to sulfur. The most common choice of R^2 in this latter situation is phenyl, although adamantyl may be preferred owing to the ease of "adamantylating" sulfides.[7]

n-Butyllithium serves as the base for most salts;[11,31,33,34] however, alkoxides[1,4,11,35] (including hydroxide) and carbonates[11] have also been employed. The major problem with organolithiums as bases is dealkylation

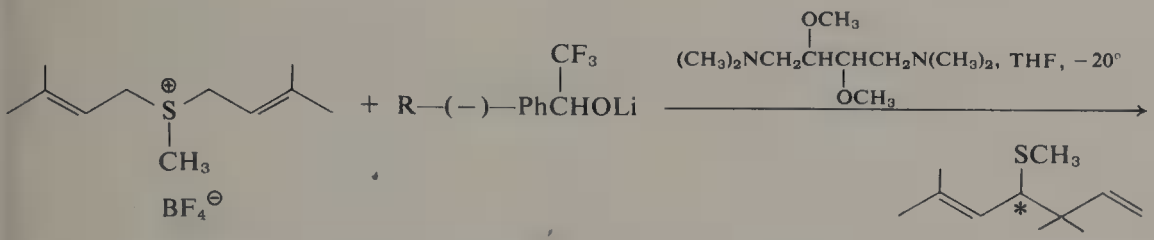
of the sulfonium salt which can be avoided with an alkoxide such as potassium *t*-butoxide. When R^1 = ethyl and R^2 = adamantyl, *n*-butyllithium cannot be employed (Scheme 7.1). Ylide generation by this base is irreversible and the ylide generated is exclusively the allylide **26**.[7] It decomposes by internal proton abstraction and formation of adamantylallyl sulfide. Use of potassium *t*-butoxide provides reversible ylide generation. Collapse of the ylide **26** is very much slower than sigmatropic rearrangement of **27** so that the major product is the desired homoallylic sulfide.[7] The rate of the reaction can be



Scheme 7.1. Rearrangement of adamantylallylethyl sulfonium fluoroborate.

greatly increased by use of dicyclohexyl-18-crown-6 ether.[36] Use of chiral bases induces net asymmetry in the rearrangement product [see Eq. (7.8)].[37] Since the rearrangement of optically pure sulfonium salt occurs with complete transfer of chirality from sulfur to carbon,[7] the optical induction observed here represents the chiral recognition by the base of the prochiral substituents on sulfur. This rearrangement is suggested as a model for the biosynthesis of nonisoprenoid monoterpenes such as artemisia alcohol and chrysanthemol.

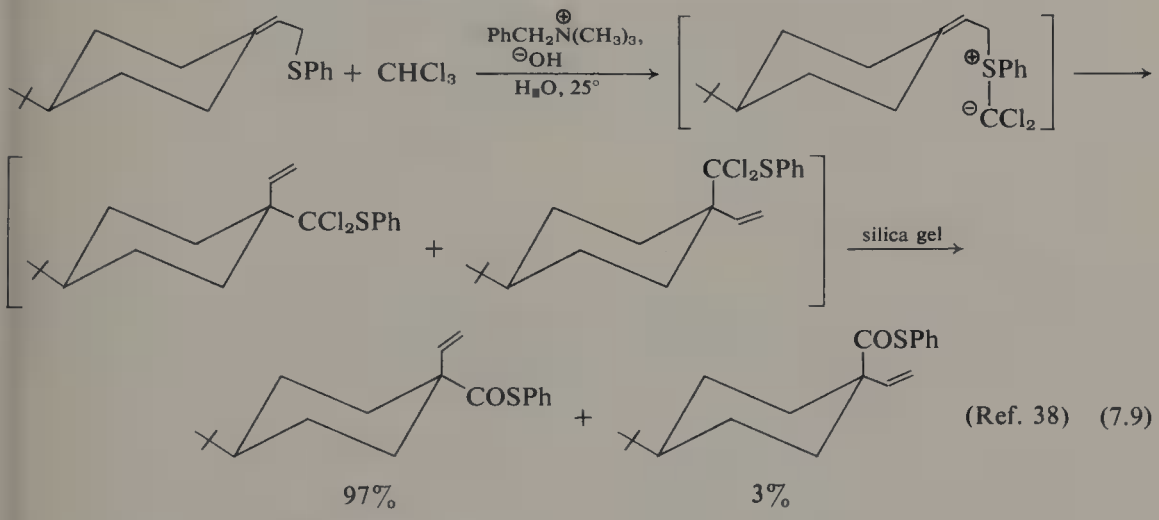
The applications of the method remain limited but highly promising. As pointed out in Section 7.2, trisubstituted double bonds form with a high



12 ± 2% optically pure

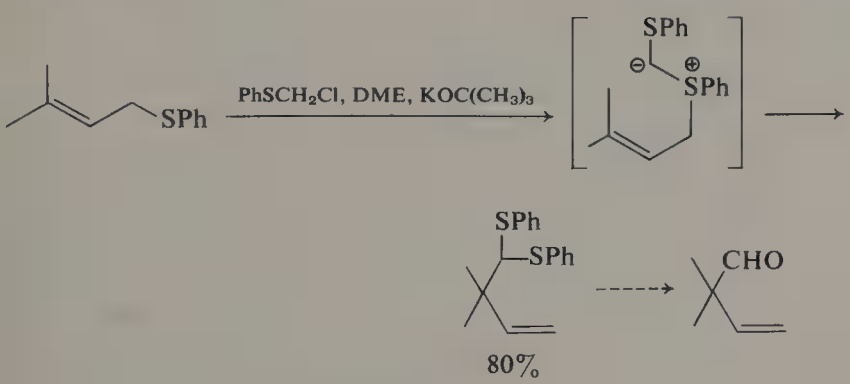
(7.8)

degree of geometrical specificity.[9] Furthermore [2.3]sigmatropic rearrangement in which a cyclohexyl ring carbon is the migration terminus occurs



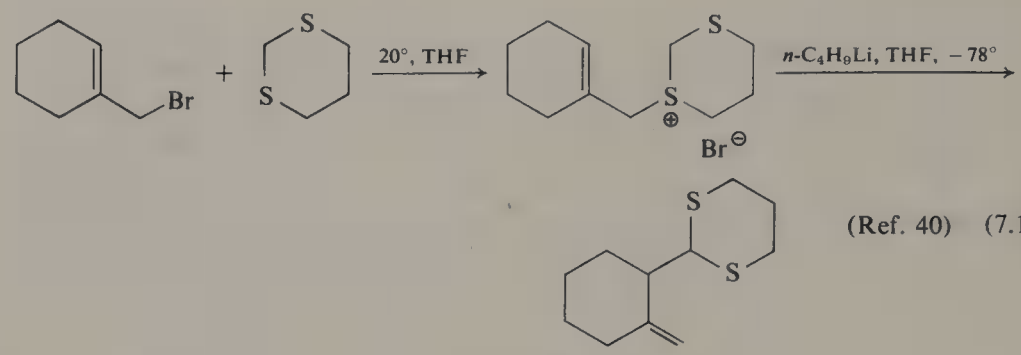
(Ref. 38) (7.9)

highly regiospecifically [Eq. (7.9)]. A novel and potentially very useful introduction of a carboxaldehyde equivalent at an allylic position has been

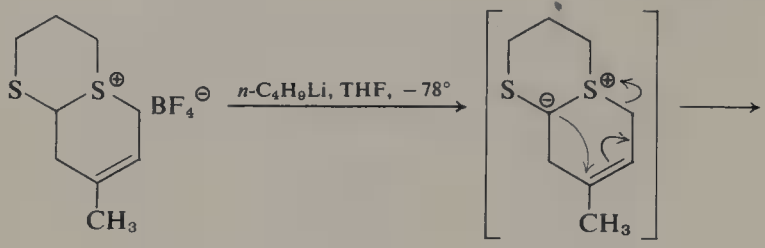


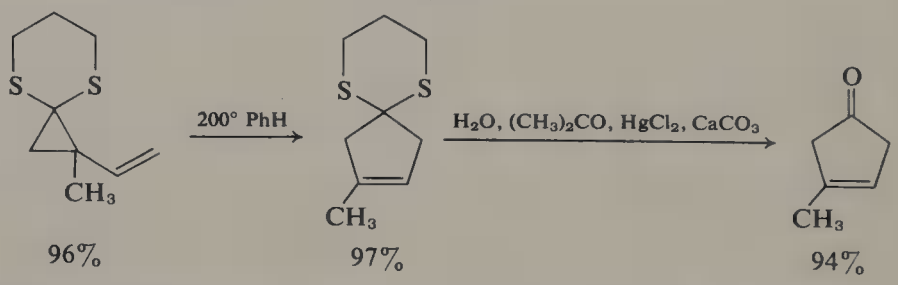
(Ref. 39) (7.10)

developed [Eq. (7.10) and (7.11)]. A Δ^3-cyclopentenone synthesis embodies a version of the [2.3]rearrangement as one of the key steps.[41]

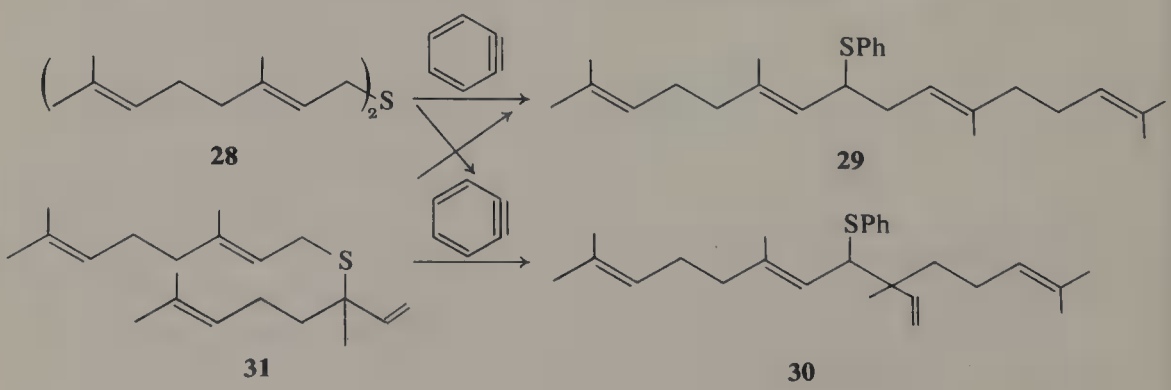


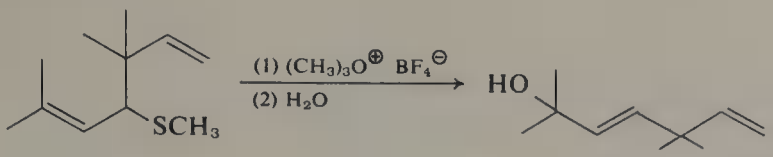
(Ref. 40) (7.11)





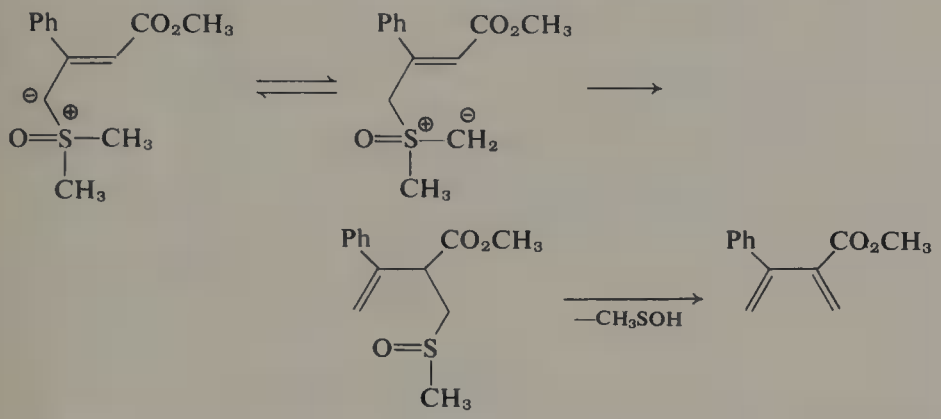
This coupling technique has been useful for the synthesis of nonisoprenoid as well as isoprenoid terpenes. Digeranyl sulfide **28** when treated with benzyne rearranges to form **29** and **30** in a ratio of 3:7. Likewise geranyllinalyl sulfide **31** rearranges to **29** and **30** in a ratio of 19:1, respectively. Reduction of **29** and **30** with lithium in liquid ammonia produces the isoprenoid and nonisoprenoid diterpenes, respectively.[26] Alkylation of the sulfide **2** followed by aqueous solvolysis produces Yomogi alcohol almost exclusively.[31]





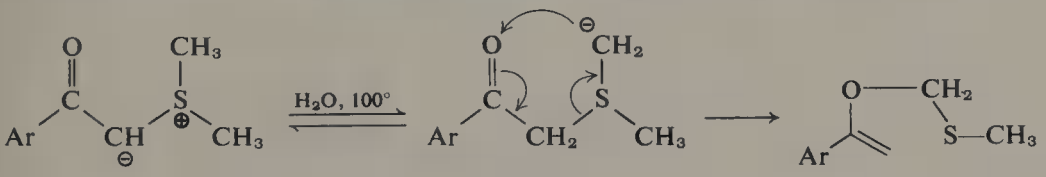
2 Yomogi alcohol

In one case, thermolysis of a stabilized oxosulfonium ylide has led to a product derived from a [2.3]sigmatropic rearrangement [Eq. (7.12)].[42-44]



(7.12)

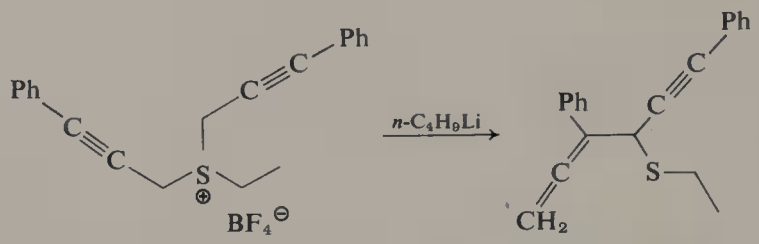
This reaction may be a useful approach to the synthesis of 2,3-disubstituted butadienes. The carbonyl functionality is also able to participate in the sigmatropic rearrangement yielding enol ethers [Eq. (7.13)].[15] The potential of this technique for generating enol ethers is as yet undefined.



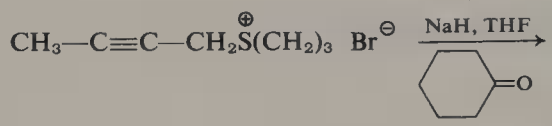
50–84% (7.13)

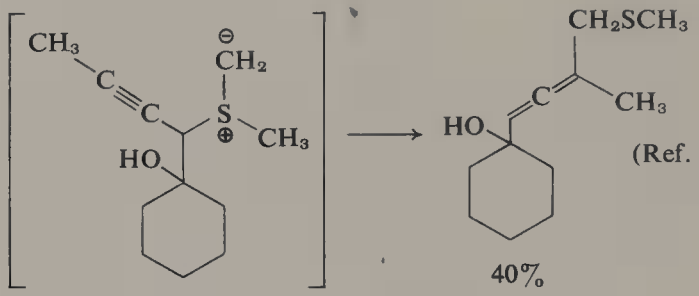
Just as in the Claisen rearrangement in which the replacement of a double bond by a triple bond does not prohibit reaction,[45] a similar change in substrate structure for the [2.3]sigmatropic rearrangement has no deleterious effect as exemplified by Eqs. (7.14) and (7.15). Apparently the amount of energy necessary to bend the linear acetylene group to achieve the geometry of the transition state is not great. Replacement of the double bond by an allene [Eq. (7.16)] also leads to a successful reaction. An interesting variant [Eq. (7.17)] utilized in a synthesis of artemisia ketone incorporated the ylidic carbon into an allene unit.

Functional group compatibility mainly remains unknown since virtually all the examples thus far involve hydrocarbons. The success of the reaction

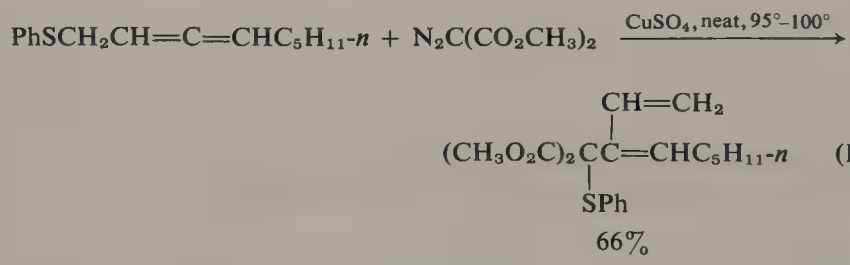


(Ref. 46) (7.14)

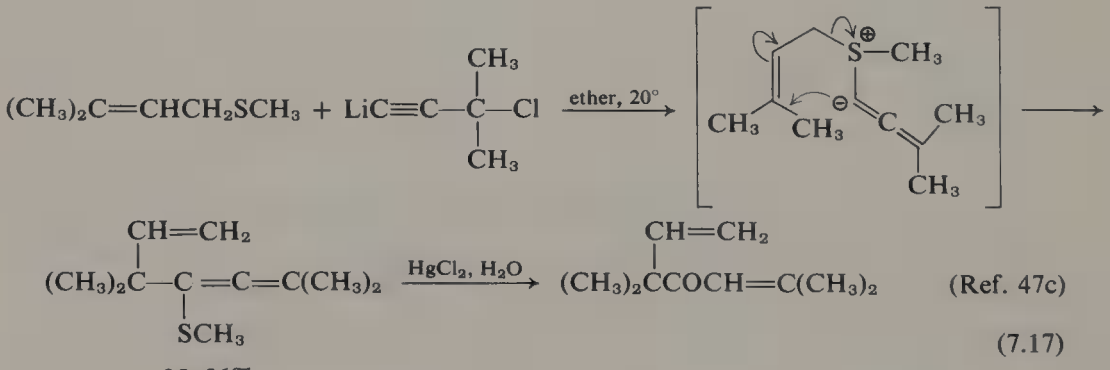




(Ref. 47a) (7.15)



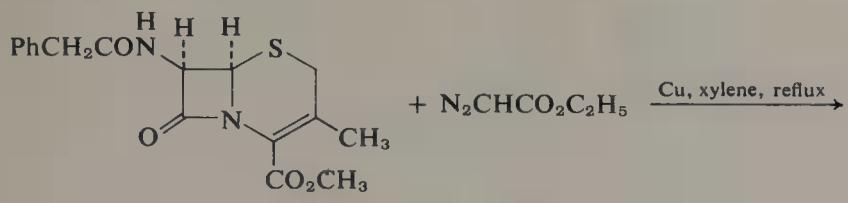
(Ref. 47b) (7.16)



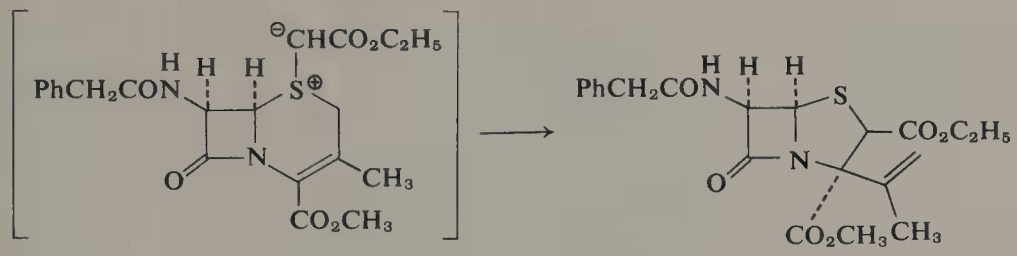
(Ref. 47c) (7.17)

with the cephalosporin **32** is an exciting sign that such factors will be of minor consequence.[48] Note that the cis stereochemistry of the product reaffirms the preferred exo-type transition state.

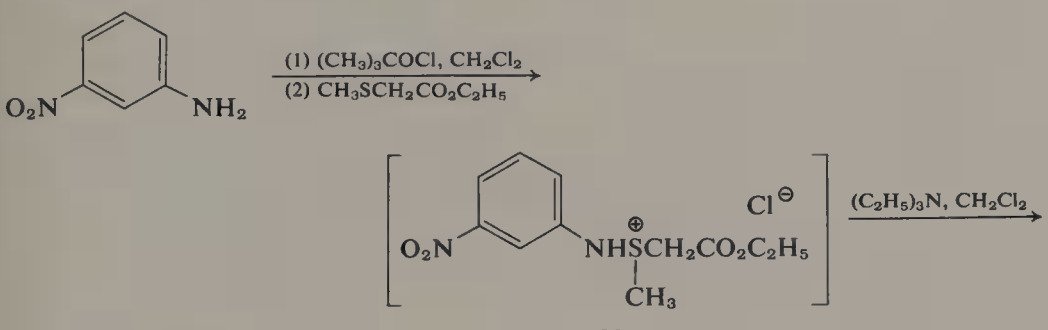
Although many related [2.3]shifts of synthetic usefulness exist, they are outside the scope of this volume. However, the rearrangement of the azasulfonium salt **33** merits special consideration because of the obvious relation-



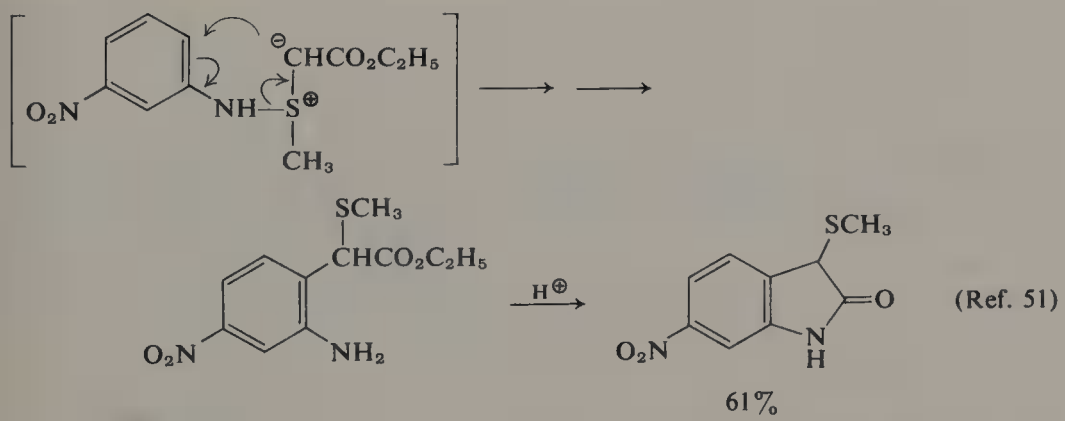
32



ship and its potential synthetic impact. The ready availability of such species and the facility of the [2.3]shift have led to the successful development of a new general synthesis of heterocycles.[49–52]

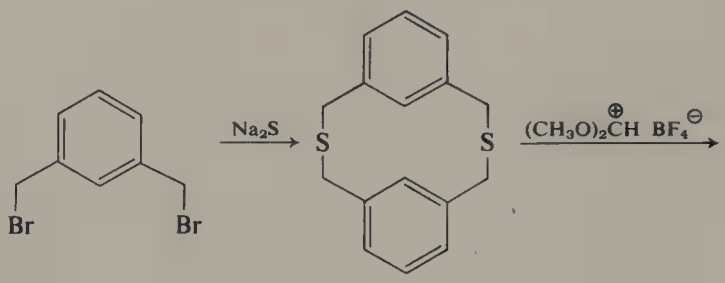


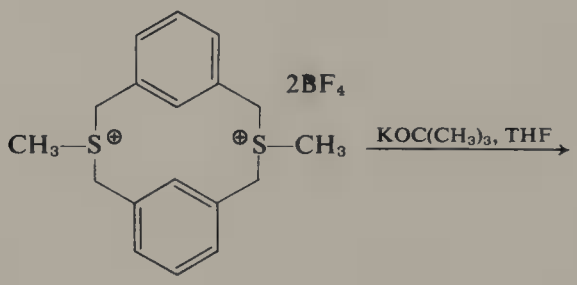
33



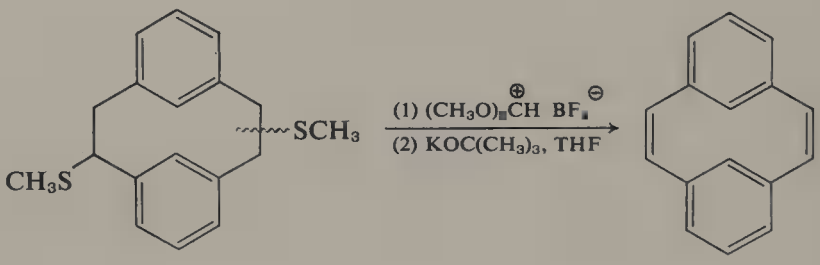
61%

The 1,2-shift of sulfur ylides has had even more limited applications. However, the synthesis of cyclophanes of all kinds stands as a spectacular illustration of its potential.[53] The general approach to this class of compounds involves alkylation of a sulfide or bissulfide with an oxonium salt and then

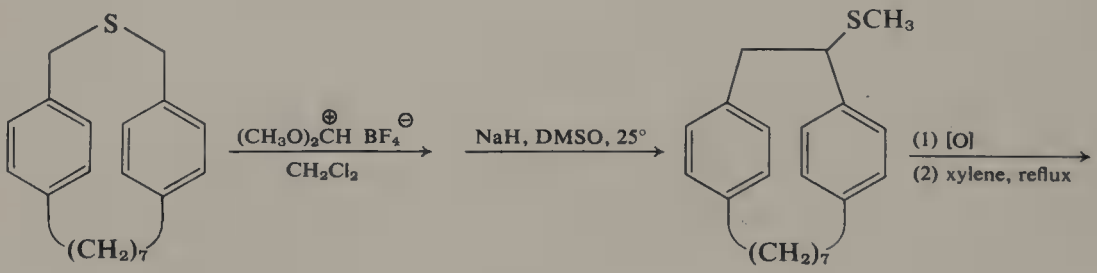

Br
Br
Na2S
S
S
(CH3O)2CH BF4

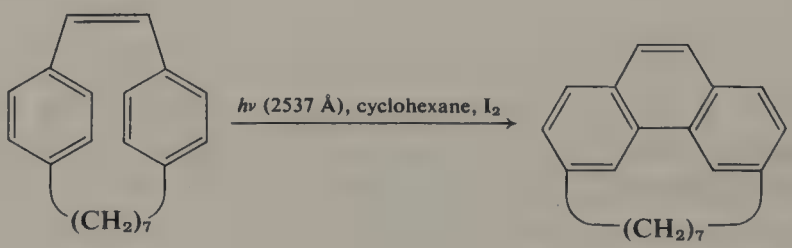

2BF4
CH3—S
S—CH3
KOC(CH3)3, THF

100%

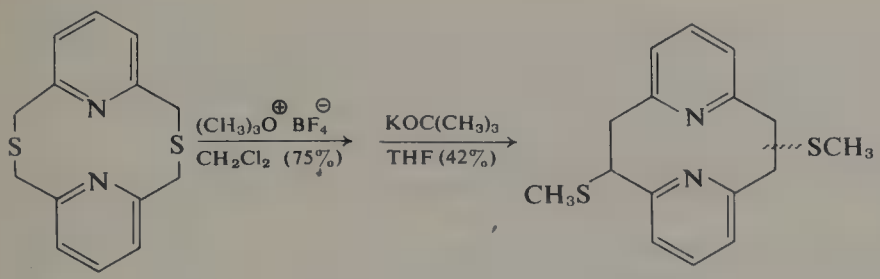

SCH3
CH3S
(1) (CH3O)2CH BF4
(2) KOC(CH3)3, THF

93%

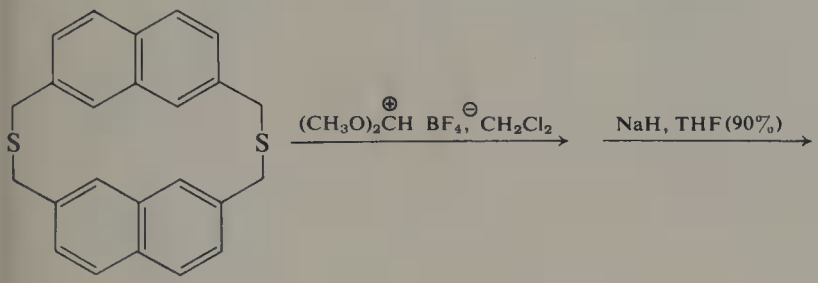

S
(CH2)7
(CH3O)2CH BF4
CH2Cl2
NaH, DMSO, 25°
SCH3
(CH2)7
(1) [O]
(2) xylene, reflux

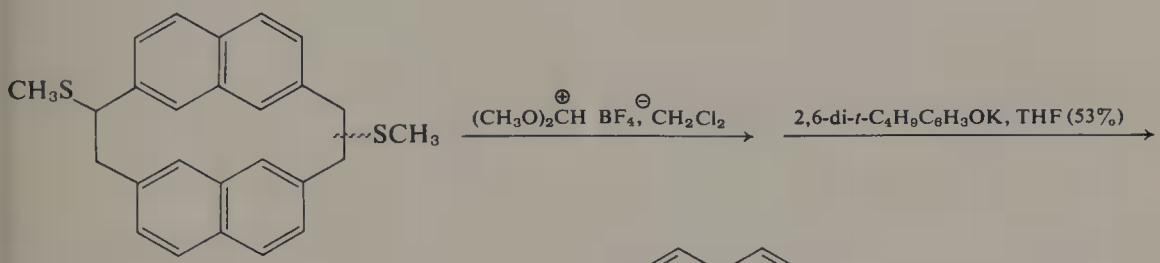

(CH2)7
hν (2537 Å), cyclohexane, I2
(CH2)7

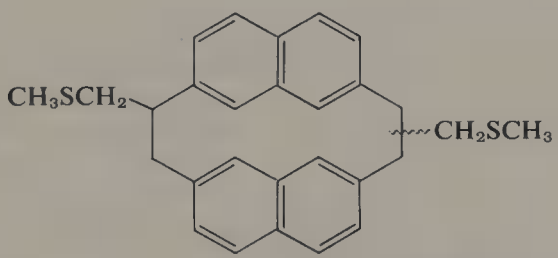
(Ref. 17)



(Ref. 54).







(Ref. 32)

treatment of the latter with base to cause the 1,2-shift. The resultant sulfide can be alkylated or oxidized and eliminated to form olefins or desulfurized to form the saturated hydrocarbons. This method is also very successful for the synthesis of heterocyclophanes[54,55] and tris-bridged cyclophanes.[56] The sequence is by far the most facile route to cyclophanes of virtually any structural variety as the accompanying equations illustrate.

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8

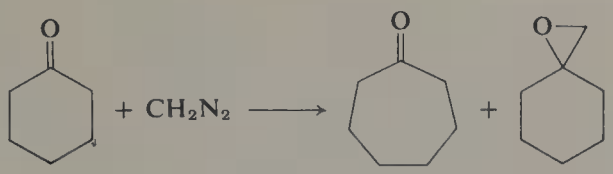
Related Synthetic Methods

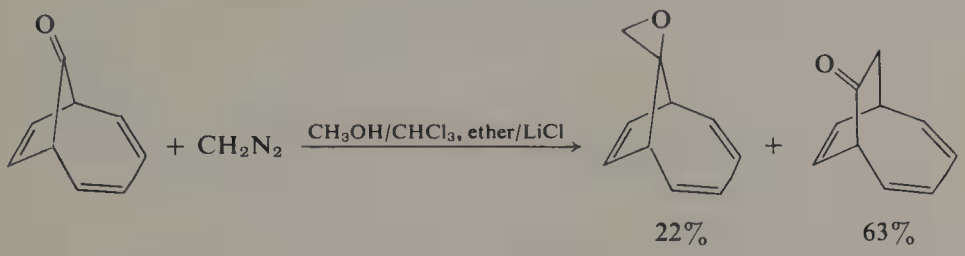
The emergence of sulfur ylides (π-sulfuranes) as synthetic intermediates depends on the alternative methods to perform similar transformations. A brief review of these alternatives places the subject of ylide chemistry in proper perspective and allows an intelligent decision to be made about when to use the ylide approach.

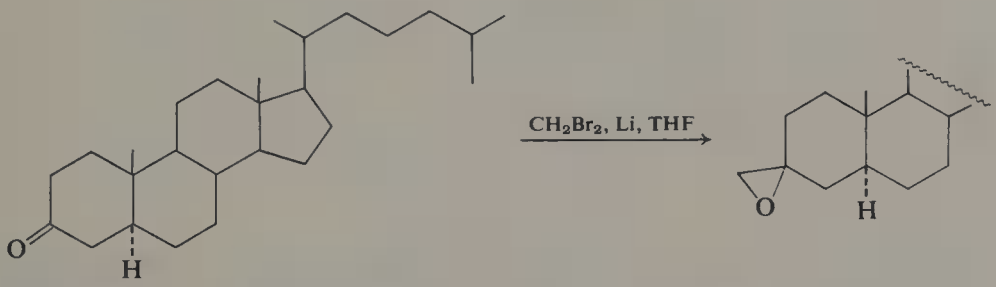
8.1. EPOXIDATIONS

The classic method to transfer a methylene group to a carbonyl group with epoxide formation involves the addition of diazomethane to an aldehyde or ketone.[1] Although in some cases good yields of epoxides can be obtained, the usual course of events involves the formation of homologated aldehyde or ketone as by-product and often as the major product. For example, cyclohexanone reacts with diazomethane to form 63% cycloheptanone and only 15% epoxide.[2] Bicyclo[4.2.1]nona-2,4,7-trien-9-one reacts similarly.[3] Competitive homologation reactions of this kind have not been found with the sulfur ylides. Furthermore, the ease of handling of the ylide compared to the explosive diazomethane normally dictates preferential use of the former.

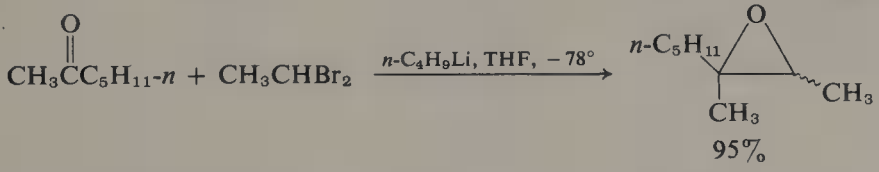
α-Haloanions also condense with carbonyl groups to give epoxides.[4] Methylene transfer is achievable by the reaction of methylene bromide with



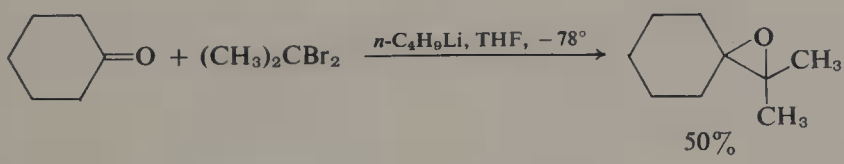




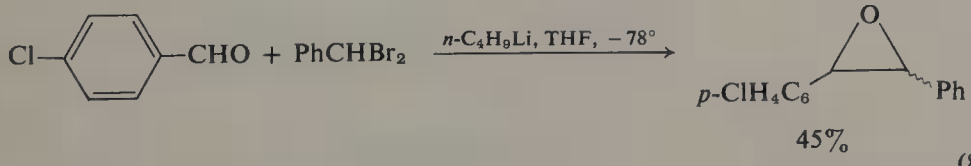
lithium dispersion or *n*-butyllithium in the presence of the carbonyl partner. 5α-Cholestan-3-one was epoxidized in 95% yield by this method; however, in most cases yields ranged from 35–53%. Equations (8.1)–(8.3) summarize successful transfers of ethylidene, isopropylidene, and benzylidene groups from the corresponding dibromides.[5] In these reactions, use of *n*-butyllithium



(8.1)



(8.2)

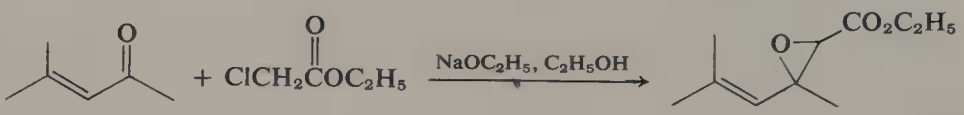


(8.3)

is preferred. The routinely lower yields and the requirement of generating the reagents, bromoalkyllithium, *in situ* utilizing a strong reducing agent or an

organolithium makes this method less attractive for routine synthetic objectives.

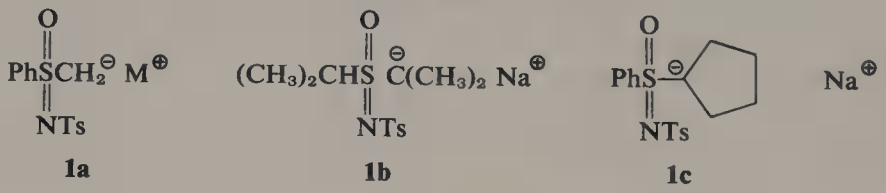
Carbonyl-stabilized α-haloanions, on the other hand, react well with aldehydes and ketones to give α,β-epoxyketones.[6] The well-known Darzens glycidic ester condensation [Eq. (8.4)] involves treatment of an α-chloro or α-bromo ester with an alkoxide in the presence of the aldehyde or ketone. Even with α,β-unsaturated ketones, such as mesityl oxide, epoxidation rather



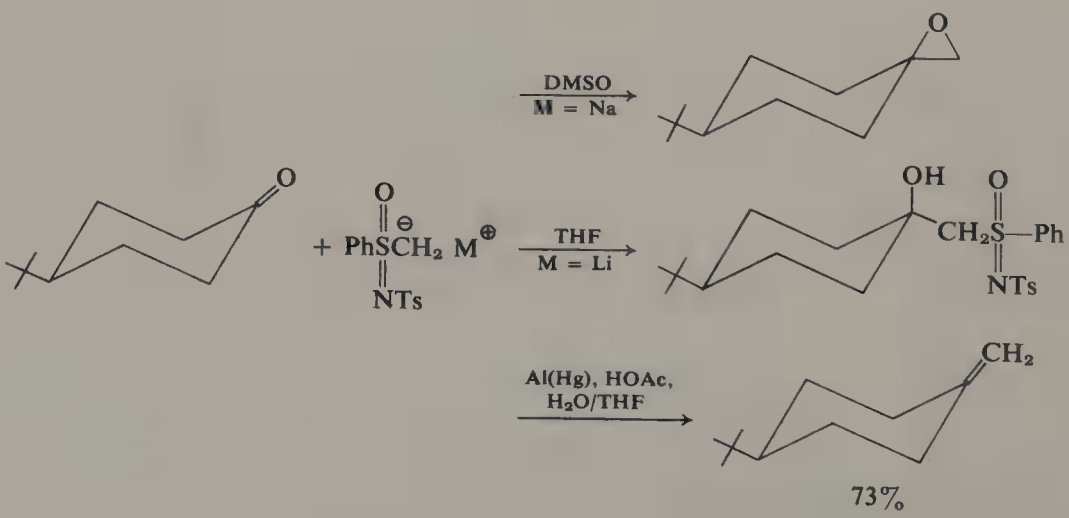
(8.4)

than cyclopropanation appears to be the rule. The combination of *n*-butyllithium and ethyl dibromoacetate is a satisfactory modification.[5] Since similar carbonyl-stabilized ylides normally fail to condense with ketones and undergo only conjugate addition with enones, the more reactive α-haloanions are preferred for these epoxidations. The use of thetin anions has not been sufficiently investigated to evaluate their merits.[7]

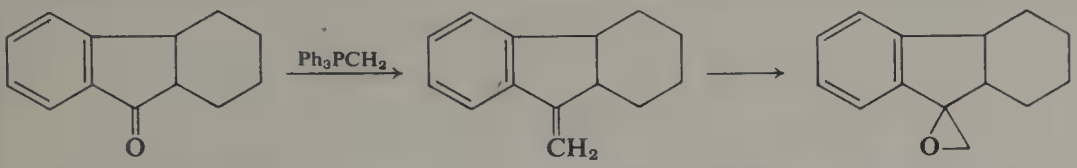
The anions of *N*-*p*-toluenesulfonyl sulfoximines **1a–1c** behave like the oxosulfonium ylides.[8,9] Alkylidene transfer to saturated ketones produces the corresponding epoxides in good yields. The intermediate carbonyl adducts can be isolated if the reaction is performed in tetrahydrofuran. Reductive cleavage produces olefins in a Wittig type reaction.[10]



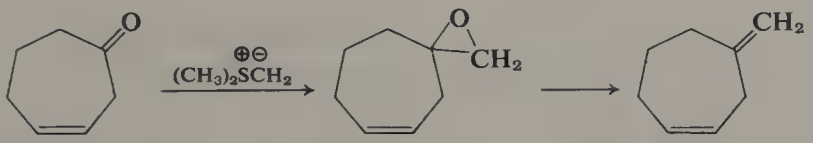
1a **1b** **1c**



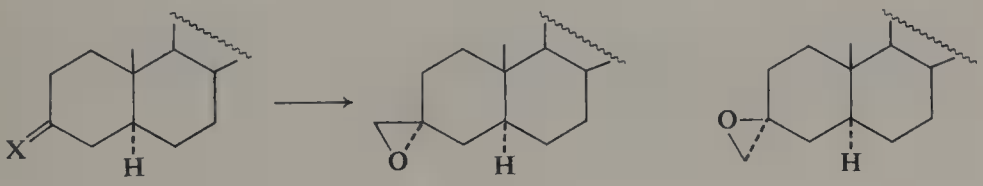
Other methods for epoxidation normally involve two steps—conversion of the ketone into an olefin followed by oxidative epoxidation. For example, hexahydrofluorenone would not condense with the sulfur ylides, but did



condense with triphenylphosphonium methylide.[11] The resulting terminal olefin could be epoxidized by normal peracid treatment. On the other hand, 3-cycloheptenone would not undergo the Wittig condensation.[12] The conversion of ketone to olefin, however, was achievable by the condensation with dimethylsulfonium methylide followed by deoxygenation to the olefin. The stereoselectivity achievable by the ylide epoxidation route normally



exceeds that achievable by olefin epoxidation. 3-Ketosteroids condense with the oxosulfonium ylides to generate the α-epoxide in 97% relative yield, whereas epoxidation of the olefin with *m*-chloroperbenzoic acid produces the same epoxide in only 85% relative yield.[13] If double bonds are present in the



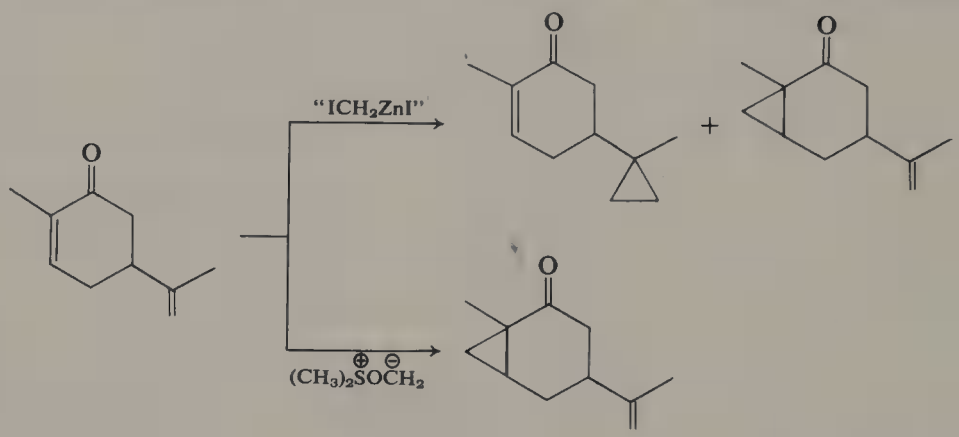
X = O, $(CH_3)_2SOCH_2$	97%	3%
X = CH_2, *m*-$ClC_6H_4CO_3H$	85%	15%

starting compound, complications of selectivity arise with the olefination–epoxidation route that do not arise with the ylide epoxidation.

8.2. CYCLOPROPANATIONS

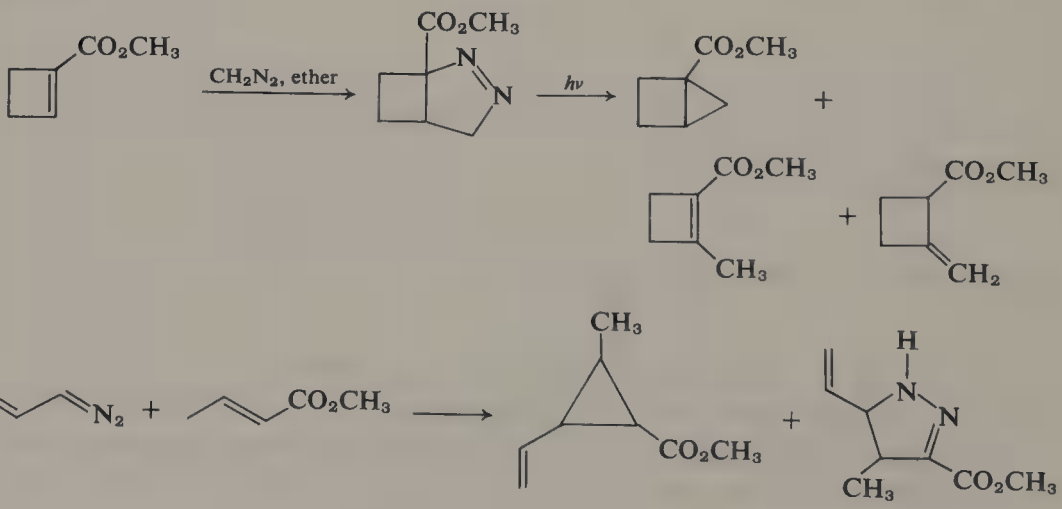
The transfer of alkylidene groups to α,β-unsaturated carbonyl systems by carbenes and carbenoids normally proceeds in low yields because of the usually high electrophilicity of such reagents.[14] However, the use of the Simmons–Smith reagent has been fairly successful.[15] The success has been

attributed to coordination of the zinc with the lone pairs on the carbonyl oxygen.[16] Unfortunately, in substrates where an isolated double bond is also present, reaction occurs at both olefins. Carvone is cyclopropanated at

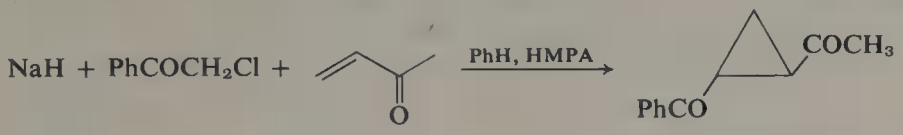


the isopropenyl and enone sites with iodomethylzinc iodide but at the enone site exclusively with dimethyloxosulfonium methylide.[17,18]

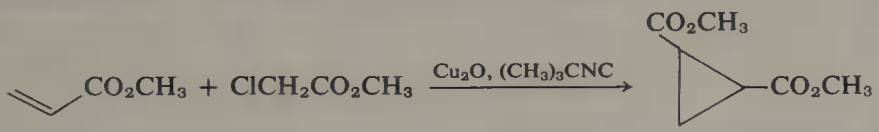
Diazoalkanes will undergo 1,3-dipolar additions to electron-deficient double and triple bonds to generate pyrazolines and pyrazoles which undergo thermal or photochemical loss of nitrogen.[19] Thus, methyl cyclobutene-1-carboxylate undergoes smooth cycloaddition with diazomethane followed by photochemical loss of nitrogen to give methyl bicyclo[2.1.0]pentane-1-carboxylate.[20] However, frequently, as in this case, olefins arising by hydrogen shift are by-products. If the intermediate pyrazoline contains a hydrogen atom alpha to the carbonl group, tautomerism may complicate the reaction. If prototropy occurs the Δ^2-pyrazoline remains inert to the cyclopropanation conditions. For example, addition of vinyldiazomethane to methyl crotonate produced the cyclopropanes in 21% yield and the Δ^2-pyrazoline in 12% yield.[21]



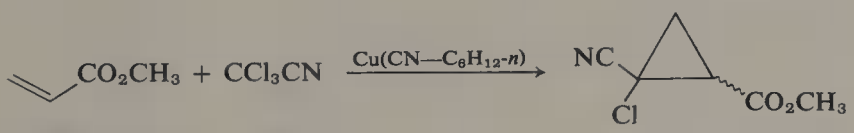
As in epoxidations, α-haloanions also have been employed in cyclopropanations; however, only in cases where the anion is also resonance stabilized. Treatment of phenacyl chloride with sodium hydride in the presence of methyl vinyl ketone produced the corresponding cyclopropane in 60% yield.[22]



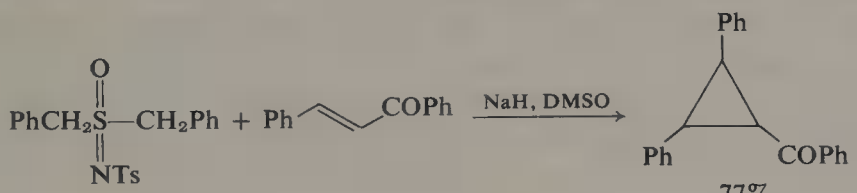
Even α-chloro esters can be used in these reactions if cuprous oxide–*t*-butylisonitrile is used as base; however, the yields are inferior to those obtained using the corresponding sulfur ylides.[23,24] Somewhat improved yields are possible with trichloromethyl derivatives and metallic copper complexed by an isonitrile.[25]



22%

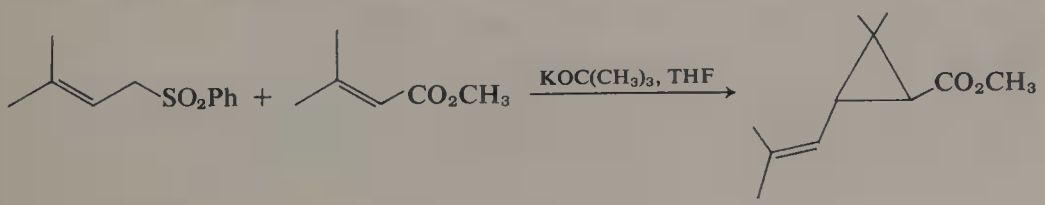


Other sulfur-stabilized anions have been employed. The anions of *N*-*p*-toluenesulfonyl sulfoximines react well with enones to give cyclopropanes.[8,9] Although no advantages exist over the ylides for methylene transfer, the alkyl- and aryl-substituted anions should be advantageous since they should exhibit greater selectivity toward cyclopropanation compared to epoxidation.



77%

The corresponding oxosulfonium ylides normally are not accessible. Sulfone-stabilized anions also enjoy limited success in cyclopropanations. An interesting synthesis of methyl chrysanthemate involved the addition of the anion of γ,γ-dimethylallylphenyl sulfone to methyl 3-methyl-2-butenoate.[26]

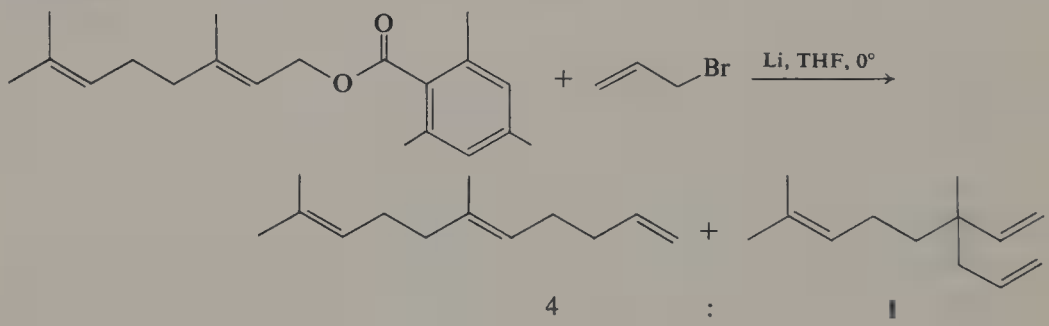


However, attempts to add this anion to methyl acrylate led only to Michael addition and no elimination to cyclopropane.[27] Presumably, the facilitation of the 1,3-elimination in the former case by the *gem*-alkyl effect accounts for its success.

These results indicate the general preference of sulfur ylides in most cases of nucleophilic cyclopropanation.

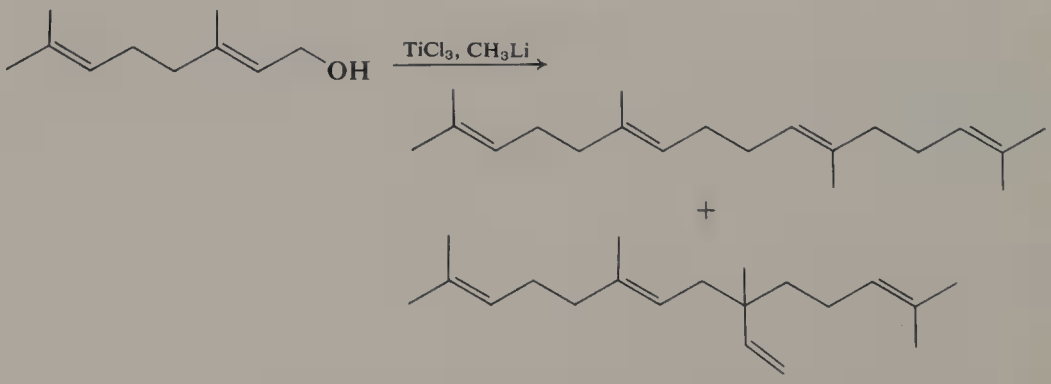
8.3. COUPLINGS

The oldest coupling procedure is the Wurtz reaction for the coupling of alkyl halides; however, variable yields, formation of rearrangement products, and nonapplicability for mixed couplings make this method unattractive for the synthesis of 1,5-dienes.[28,29] Reasonable yields of mixed coupling products can be obtained by treatment of allyl bromides and allyl mesitoates with lithium.[28]



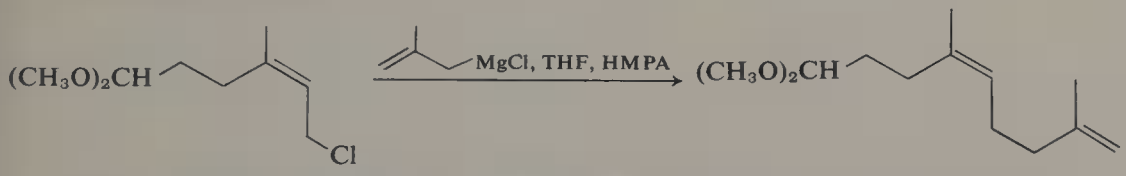
Product yield 60%

Titanium trichloride and tetrachloride have been used for coupling allylic alcohols. Alkoxides are treated with titanium tetrachloride, reduced with potassium metal, and the resultant titanium(II) alkoxides coupled by pyrolysis. In this manner squalene was produced in 40% yield from farnesol.[30] Alternatively, the addition of geraniol to titanium trichloride and methyllithium produces a 7:1 mixture of primary and tertiary coupling products in

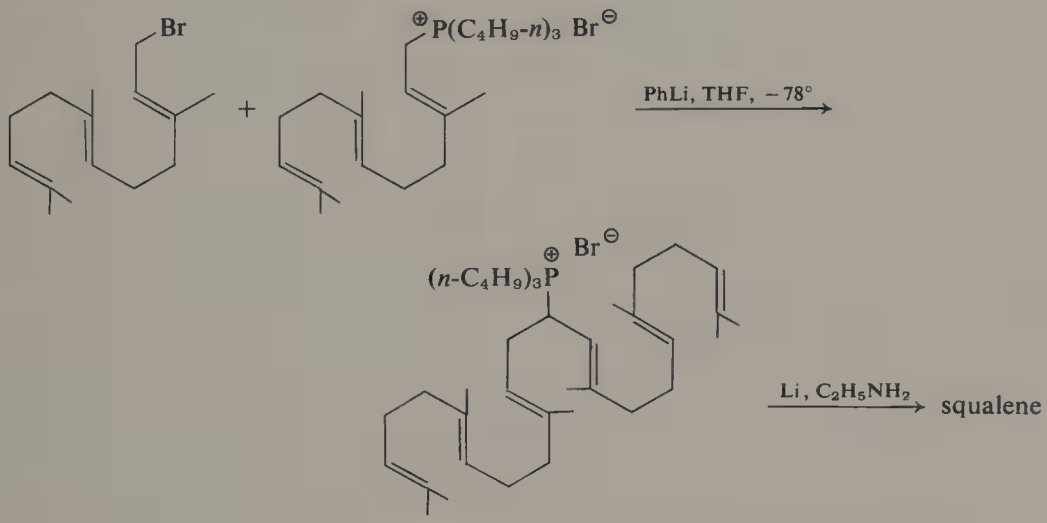


71% yield.[31] This latter method is comparable to the sulfur ylide-induced coupling. However, use of equimolar quantities of two different allyl alcohols led to statistical mixtures of symmetrical and unsymmetrical coupling products.

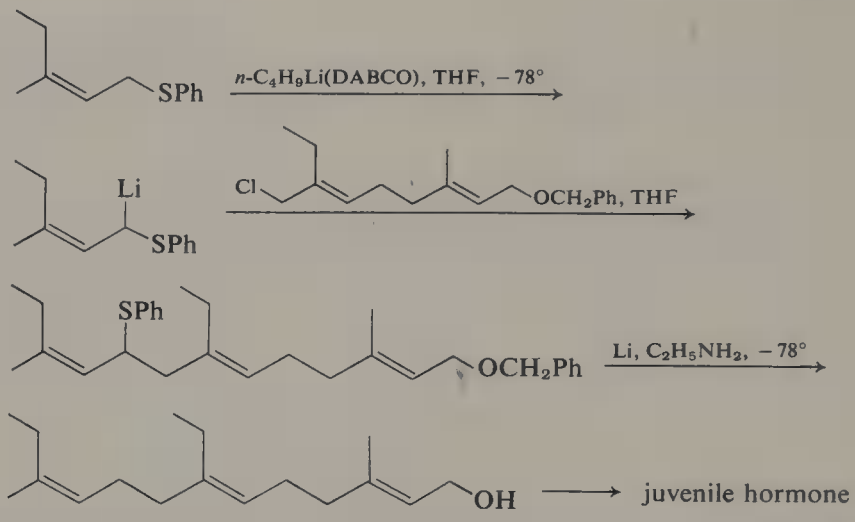
Under certain conditions Grignard reagents undergo coupling with allylic halides. Thus, methallylmagnesium chloride was coupled with a *cis*-allylic chloride in tetrahydrofuran and hexamethylphosphortriamide as solvent producing stereospecifically the *cis*-1,5-diene in high yield. Likewise the *trans*-allylic chloride coupled in 95% yield giving only the trans product.[32] However, most allyl Grignard couplings are not reported to occur with this specificity or yield.



Phosphonium ylides can be alkylated with allyl bromides followed by reduction of the resultant phosphonium salt to yield 1,5-dienes stereospecifically. Farnesyl bromide and the corresponding tri-*n*-butyl phosphonium salt were coupled and the product salt reduced with lithium in ethylamine yielding 65% of all *trans*-squalene. This method seems to be general and does not give rearranged products.[33]

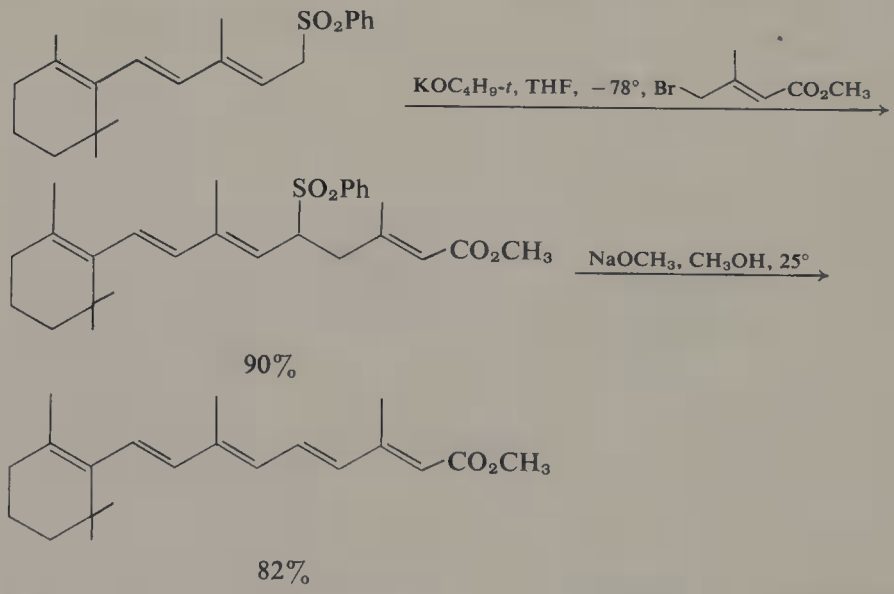


Replacement of the phosphonium center as the anion-stabilizing group with a sulfide has been highly successful. Metalation of a phenyl allyl sulfide occurs with *sec*-butyllithium[34] or *n*-butyllithium in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO).[35] A novel approach to the juvenile hormone employed this methodology.[36] Substituting a heterocycle such as a



thiazoline for the phenyl ring facilitates metalation.[37] Reduction by dissolving metals or Raney nickel removes the anion-stabilizing group.

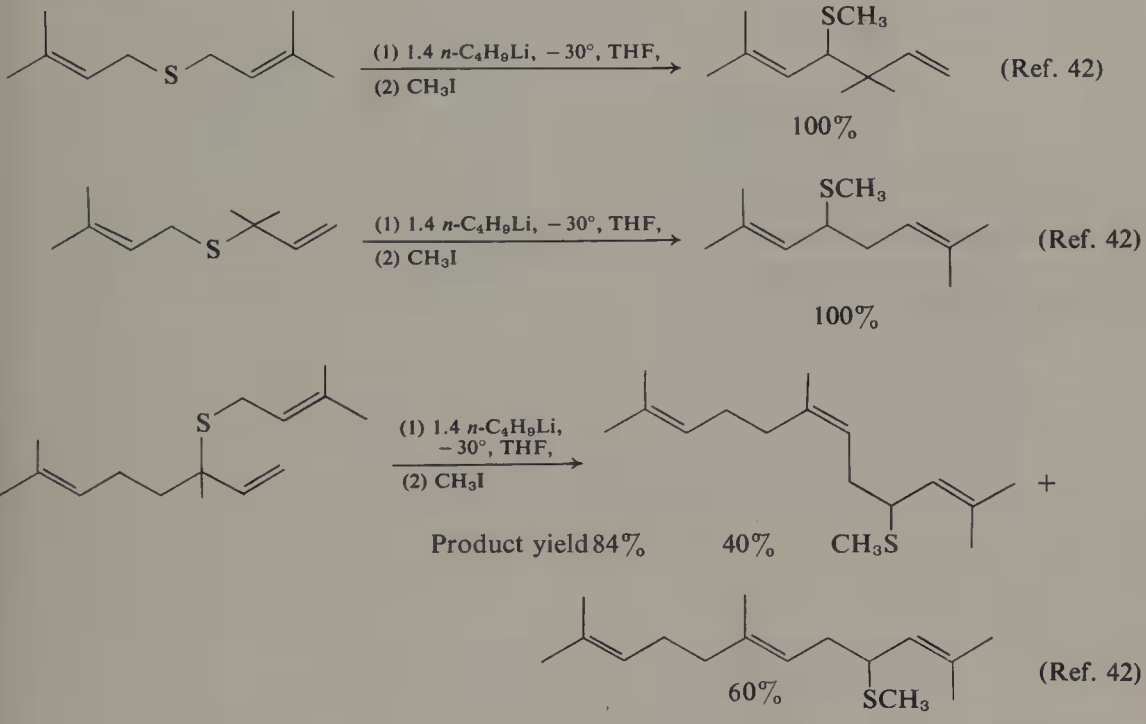
The conversion of the sulfide to a sulfone increases its electronegativity and thereby facilitates the metalation to the extent that potassium *t*-butoxide suffices as base.[38] A further advantage of the sulfone is its ability to serve as a leaving group. Thus, while reductive elimination effects net allylic coupling, base treatment allows formation of a triene. The synthesis of vitamin A ester illustrates the approach.[38]



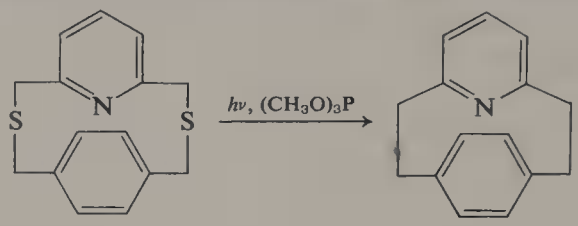
Nickel tetracarbonyl is used very successfully for coupling allyl units, especially intramolecularly to form medium-size rings. However, coupling of acyclic-substituted allyl moieties produces varying amounts of rearranged products. The nickel carbonyl coupling of farnesyl bromide produced all

trans-squalene in only 25% yield.[39] This method also suffers from its inapplicability to cross coupling.[40]

In analogy to the [2.3]sigmatropic rearrangement of sulfur ylides, anions of allylic sulfides very efficiently undergo the same rearrangement.[41,42] The only drawback of this method is the requirement of a strong base such as *n*-butyllithium. Its advantage is the ability to rearrange the sulfide directly without prior conversion to the sulfonium salt which, in some cases, has been very difficult to prepare.

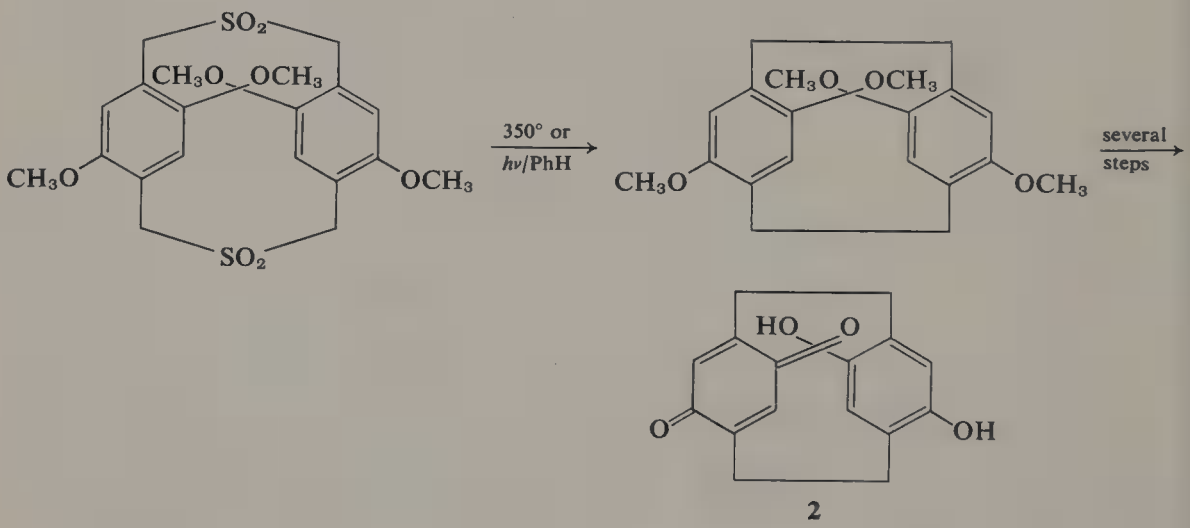


Bisallyl ethers[43] and ammonium salts[44] also undergo [2.3]sigmatropic coupling. The ether rearrangement requires an organolithium as base, whereas the ammonium salts rearrange in liquid ammonia with sodium amide. The major limitation to this method relates to the high proportion of [1,2]rearrangement in competition with the desired [2.3]rearrangement.



(Ref. 47) (8.5)

Cyclic dibenzyl sulfides serve as convenient precursors to cyclophanes.[45] Desulfurization with concomitant coupling occurs on photolysis in the presence of a phosphite[46,47] [see Eq. (8.5)]. Oxidation of the bissulfides to the disulfones followed by pyrolysis or photolysis exemplified by the synthesis of the internal quinhydrone **2**[48] serves as an alternative coupling and desulfurization method.[45]



2

Sulfur ylide rearrangements are comparable and in many cases better than the above synthetic methods; however, further experimentation is necessary to evaluate their real potential.

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9

Experimental Conditions

9.1. NONSTABILIZED YLIDES

The generation of nonstabilized ylides generally requires a strong base at low temperature. The use of a strong base such as an organometallic requires an appropriately compatible solvent. Ethers such as diethyl ether, tetrahydrofuran, or 1,2-dimethoxyethane have been used. Such solvents must be carefully dried—preferably by distillation from lithium aluminum hydride followed by a second distillation from benzophenone sodium ketyl. Since most alkylides are not appreciably stable above $-30°$, this temperature forms an upper limit for their generation. At lower temperatures, the rate of proton abstraction is slowed and the solubility of the sulfonium salts decreases. It is generally true that the solubility increases in the order ether < tetrahydrofuran < 1,2-dimethoxyethane.

The nature of the anion associated with the sulfonium center also determines solubility. Among the halides, solubility in ether solvents increases in the order iodide < bromide < chloride. However, the better solubility of the fluoroborate salts makes them preferred when available. If the sulfonium halides are in hand, a metathesis can be achieved by treatment with an equivalent amount of silver fluoroborate.

For the organometallic base, *n*-butyllithium is invariably chosen. Commercially available solutions of *n*-butyllithium in hexane may be used directly. If

complications arise because of slow proton abstraction, the use of *t*-butyllithium (also commercially available in pentane solution), lithium dialkylamides (from dialkylamines and *n*-butyllithium), lithium dichloromethide (from lithium dialkylamide and methylene chloride), or dimsylsodium (from sodium hydride and dimethylsulfoxide) may be recommended. The addition of *N,N,N′,N′*-tetramethylethylenediamine or DABCO to *n*-butyllithium generally increases its basicity relative to its nucleophilicity. It has also been reported that addition of one or two equivalents of hexamethylphosphoramide (HMPA) enhances the rate of metalation by base in enolate generation. Such methods may be applicable to ylide generation. Naturally, the use of such bases requires that all reactions be carried out under a nitrogen or argon atmosphere. Prior degassing of reaction mixtures does not appear to be necessary.

Ylide generation takes from several minutes to 1 hr. It is normally accompanied by yellow to red colorations even though solutions of simple alkylides in tetrahydrofuran should be at most pale yellow. The deeper coloration may be associated with decomposition. However, the yields of products normally appear independent of the color of the ylide solution. Only with diphenylsulfonium allylide has a higher yield of epoxide been noted when a pale yellow solution, generated using *t*-butyllithium, has been employed as compared with a deep red solution, generated with *n*-butyllithium. For nucleophilic additions, the acceptor is added at $-78°$ to prevent decomposition of the ylide. Completion of the 1,3-elimination is assured by allowing the reaction to warm to room temperature. The [2.3]sigmatropic ylide rearrangement is rapid and complete at low temperature (e.g., $-78°$).

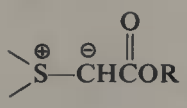
For the parent dimethylsulfonium methylide and the oxosulfonium alkylides, as well as [2.3]sigmatropic rearrangements, sodium hydride, potassium *t*-butoxide, or dimsylsodium at room temperature or slightly below may be employed. However, for dimethylsulfonium methylide this method seems less desirable because of the relatively short lifetime of the ylide at these temperatures. Only with unhindered ketones in which carbonyl addition occurs very rapidly is such a method applicable. Since the oxosulfonium alkylides are stable at room temperatures, the ease of operation makes this procedure the preferred one. Although tetrahydrofuran has been used, dimethyl sulfoxide is preferable for epoxidations and cyclopropanations if the reaction can be done at room temperature. If temperatures of $0° \pm 10°$ are required for the stability of the ylide, then mixtures of tetrahydrofuran and dimethyl sulfoxide are necessary to prevent freezing. Dimethyl sulfoxide should be dried by distillation from calcium hydride.

The use of reversible ylide generation conditions has not been sufficiently explored to permit comment on its limitations generally. Although the use of aqueous solvent systems is hampered by the limited solubility of most

organic acceptors, dimethyl sulfoxide as solvent overcomes this limitation. These conditions are suitable even with ketones and aldehydes which undergo easy aldol condensations and with hydrolyzable esters if only the stoichiometric quantity of base is employed. In the case of the cyclopropylide, the presence of the ylide acceptor stabilizes these solutions as evidenced by the rapid decomposition of the sulfonium salt under these conditions in its absence. Two-phase reactions comprised of aqueous base–benzene succeeds best when long aliphatic chains are bonded to sulfur. With ylides that undergo intramolecular [2.3]sigmatropic rearrangement, even the use of aqueous hydroxide or carbonate bases has been successful.

9.2. STABILIZED YLIDES

These ylides permit much greater flexibility of experimental conditions. Although the ylide can be generated *in situ* with the use of mild inorganic (e.g., sodium carbonate) or organic (e.g., triethylamine) bases, the use of preformed ylide is generally preferable. The decision rests with the degree of reactivity of the ylide in question. The carbonyl-stabilized ylides **1**–**3** are



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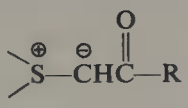

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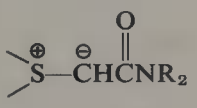
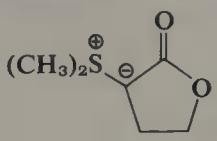


3

crystalline solids or oils which can be stored indefinitely.[1–3] Since such ylides may be hygroscopic, protection from moisture is desirable to increase their shelf-life. Although the lactone ylide **4** has been isolated as a crystalline solid,



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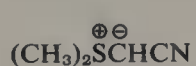


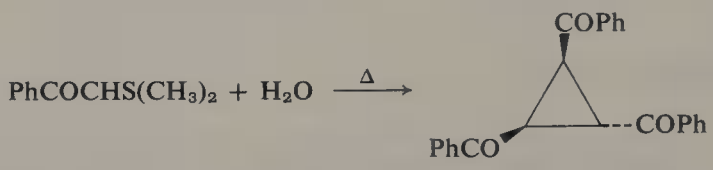
5

its limited shelf-life makes *in situ* methods more desirable if the acceptor is base-stable. With acrylonitrile *in situ* methods gave an 87% yield of cyclopropane; however, methyl vinyl ketone as acceptor required preformation of the ylide for good yields.[4] The cyano ylide **5** was not obtained crystalline and was therefore employed by generating it *in situ*.[5,5a]

The choice of base for generation of the ylides depends on the nature of the stabilizing group. With the carbonyl-stabilized ylides **1** to **3** a wide range of bases including hydroxide, alkoxide, carbonate, and amines have been successful. The sulfonium salt precursor of the lactone ylide **4** underwent

decomposition under these conditions and required nonnucleophilic sodium hydride as base. For the cyano ylide **5**, *n*-butyllithium allowed generation without complications from displacement of dimethyl sulfide or addition to the nitrile.

For condensations, dryness is desirable. The sluggishness of reaction frequently necessitates temperatures up to 100° for epoxidations or cyclopropanations. At these temperatures, a proton source initiates self-condensation reactions leading to symmetrical trisubstituted cyclopropanes. For example, dimethylsulfonium phenacylide in the presence of moisture produces *trans*-1,2,3-tribenzoylcyclopropane in nearly quantitative yield.[3] Because



such side reactions become important normally only at elevated temperatures, the lower the temperature for nucleophilic alkylidene transfer the better. Temperatures of 25° or above are adequate for [2.3]rearrangements, whereas [1.2]rearrangements usually require temperatures of 100° or more.

The unreactivity of stabilized ylides allows a wide range of solvents to be used. For reactions of the ester ylides **1**, solvents such as dimethyl sulfoxide, ethanol, methanol, acetone, methylene chloride, and benzene are used. As expected for reactions involving separation of charge, reactions are faster in more polar solvents. Thus, dimethylsulfonium carbomethoxymethylide combines with dimethyl maleate at room temperature in dimethyl sulfoxide, but requires refluxing tetrahydrofuran.[2] The advantages of the dipolar aprotic solvents in terms of rates of reaction are diminished in practice because they are difficult to remove from products.

9.3. EXPERIMENTAL PROCEDURES

This section consists of typical ways to prepare sulfonium salts and stabilized and nonstabilized ylides and to utilize such compounds in nucleophilic epoxidations and cyclopropanations and rearrangements. In parentheses after the title of each procedure appears the experimental technique the procedure exemplifies.

Very few complete experimental procedures for the rearrangement reactions of sulfur ylides have appeared in the literature. The following procedures are indicative of what has been done, but optimal conditions for rearrangements have not been approached.

9.3.1. Sulfonium Salts

9.3.1.a. *Carbethoxymethyldimethylsulfonium Bromide* (Alkylation of Dialkyl Sulfide).[2] A solution of 265 g (1.59 moles) of ethyl bromoacetate and 114 g (1.84 moles) of dimethyl sulfide in 500 ml of acetone was stored in a water bath at 25° for 3 days. A white solid crystallized. Filtration gave 326 g (90%) of the sulfonium bromide, m.p. 78–°80° (dec.). The nmr spectrum showed singlets at δ3.5 (6H) and 5.3 (2H), a triplet at δ1.3 (3H), and a quartet at δ4.3 (2H).

9.3.1.b. *Cyanomethyldimethylsulfonium Fluoroborate* (Disproportionation followed by Methylation).[5] A solution of 38.6 g (0.231 mole) of iodoacetonitrile and 110 ml (1.5 moles) of dimethyl sulfide in 200 ml of acetone was refluxed for 13 hr. The reaction was cooled, poured into 500 ml of ether, and filtered to yield 46.8 g (98%) of trimethylsulfonium iodide. The filtrate was concentrated *in vacuo* and distilled at 64°–65° at 12 mm to yield 18.0 g (88%) of methylthioacetonitrile. Its infrared spectrum (CCl_4) showed nitrile stretch at 2250 cm^{-1}. The nmr spectrum (CCl_4) showed singlets at δ2.30 (3H) and 3.30 (2H).

To a solution of 14.1 g (0.163 mole) of methylthioacetonitrile in 41 ml of acetonitrile at 0° was added 25.4 g (0.171 mole) of trimethyloxonium fluoroborate. *Caution!* A very exothermic reaction occurs. The reaction was stirred 10 min, poured into ether, and filtered. The crystals collected were recrystallized from methanol–acetonitrile to yield 18.0 g (59%) of sulfonium fluoroborate, m.p. 151.5°–152.5°. Its infrared spectrum (Nujol mull) showed nitrile absorption at 2260 cm^{-1}. Its nmr spectrum (CD_3CN) showed singlets at δ3.00 (6H) and 4.40 (2H).

9.3.1.c. *Ethyldiphenylsulfonium Fluoroborate* (Use of Silver Salts, Normal Addition).[6] A solution of 4.65 g (25 mmoles) of diphenyl sulfide in 19.5 g (125 mmoles) of ethyl iodide was protected from light with aluminum foil and from moisture with a calcium chloride drying tube. Over a period of 0.5 hr, 4.88 g (25 mmoles) of silver fluoroborate was added. The reaction mixture became warm and a precipitate of silver iodide formed. After allowing the reaction to stand overnight at room temperature, the precipitate was removed by filtration and washed with methylene chloride. The combined filtrates were evaporated *in vacuo*. Washing the resulting oil with ether induced crystallization. The sulfonium fluoroborate (8.78 g, 86% yield) was recrystallized from *n*-butanol, m.p. 76°–77°.

9.3.1.d. *Allyldiphenylsulfonium Fluoroborate* (Use of Silver Salts, Inverse Addition).[7] Under nitrogen 24.8 g (0.127 mole) of silver fluoroborate was

slowly dissolved in 40 ml of dry acetone. Then 157 g of diphenyl sulfide was added to the solution. The flask was wrapped in aluminum foil and immersed in a 0° bath. To the stirred brown slurry 17.0 g (0.140 mole) of allyl bromide was rapidly added via syringe. The bath was removed after 5 min. Soon a yellow-green solid formed in the colorless solution. After approximately 2 hr, the solution began to turn light yellow. (The yellow color accompanies decomposition of the salt. The reaction was therefore terminated when the color change was noted.) The reaction mixture was filtered, and the silver bromide was washed with methylene chloride. The organic fractions were combined, and the volume was reduced *in vacuo* to yield a dark red oil. Ether (200 ml) was added to the oil, and the mixture was vigorously shaken to induce solidification. The solid mass was broken up with a stirring rod, a few milliliters of methylene chloride added, and the mixture shaken. After a few minutes of shaking, the solid material was an offwhite color. The solid was filtered and recrystallized by dissolving in methylene chloride and reprecipitating with ether to yield 34.4 g (85%) of the desired salt (m.p. 70°–72°). The infrared spectrum ($CHCl_3$) showed aromatic absorption at 1640 cm^{-1} and fluoroborate absorption at 875 and 682 cm^{-1}. The ultraviolet spectrum (C_2H_5OH) showed λ_{max} (ϵ) at 235 sh (ϵ9530), 259(1400), 267(1680), and 273 nm (1300). Its nmr spectrum ($CDCl_3$) showed absorptions at δ4.80 (2H, d, J = 6.0 Hz), 5.28–5.95 (3H, m), and 7.5–7.8 (10H, m).

9.3.1.e. *Cyclopropyldiphenylsulfonium Fluoroborate* (Ylide Alkylation).[8] A solution of diphenyl sulfide (93.0 g, 0.50 mole), 1-chloro-3-iodopropane (347 g, 1.70 moles), and 200 ml of nitromethane was stirred at room temperature under nitrogen. The flask was wrapped with aluminum foil to shield it from light. Silver fluoroborate (78.0 g, 0.40 mole) was added in one portion. Initially the temperature rose to 40°, then gradually fell to room temperature. No external cooling was necessary. After 16 hr, 200 ml of methylene chloride was added and the mixture was filtered through a sintered glass funnel prepared with a pad of 35 g of Fluorosil to remove finely divided silver and silver salts. The solid was washed with methylene chloride (100 ml) and the methylene chloride portions were combined. The methylene chloride solution was evaporated until a solid appeared, then 1 liter of ether was added to precipitate the sulfonium salt. The crystals were collected, washed with ether, and dried *in vacuo* at 25°. The yield of 3-chloropropyldiphenylsulfonium fluoroborate was 122.1 g (87%), m.p. 104°. The nmr spectrum ($CDCl_3$) showed absorption at δ2.21 (2H, d of d, J = 8.0, 6.5 Hz), 3.73 (2H, t, J = 6.5 Hz), 4.27 (2H, broadened t, J = 8.0 Hz), 7.5–8.1 (10H, two multiplets in 3:2 ratio).

A suspension of 3-chloropropyldiphenylsulfonium fluoroborate (118.7 g, 0.339 mole) in THF (500 ml) was placed in a 2-liter flask under nitrogen.

Then 5 g portions of a 55% sodium hydride–mineral oil dispersion (15.2 g, 0.350 mole) were added in 0.5-hr intervals. The resulting mixture was stirred at room temperature for 24 hr. A solution of 25 ml of 48% aqueous fluoroboric acid, 15 g of sodium fluoroborate, and 400 ml of water was added to destroy residual hydride and swamp out chloride ion. After 5 min, methylene chloride (300 ml) was added and the methylene chloride layer removed. The organic layer was extracted with 100 ml of water. This water layer was combined with the first aqueous layer and the combined water layers extracted with an additional 100 ml of methylene chloride. The methylene chloride portions were combined, dried over sodium sulfate, and evaporated *in vacuo* until precipitation occurred. The salt was completely precipitated on addition of ether (1 liter). The crystals were collected, washed with ether, and recrystallized from absolute ethanol (approximately 400 ml). After drying *in vacuo* the yield was 83.5 g (79%), m.p. 139°. Its nmr spectrum ($CDCl_3$) showed absorptions at δ1.32–1.70 (4H, m), 3.43–3.95 (1H, m), 7.40–8.17 (10H, two multiplets in 3:2 ratio).

9.3.2. Ylides

9.3.2.a. *Dimethyloxosulfonium Methylide* (An Oxosulfonium Ylide).[9] Method A (in DMSO). Sodium hydride (0.58 g of 50% mineral oil dispersion, 12 mmoles) was freed of mineral oil by three washings and decantings with petroleum ether (b.p. 40°–60°) under a nitrogen atmosphere. After the last washing, the system was evacuated to remove the last traces of the petroleum ether. The vacuum was broken by introduction of nitrogen and 20 ml of dimethyl sulfoxide (distilled from calcium hydride at 64° at 4 mm) was added. Powdered trimethyloxosulfonium iodide (2.64 g, 12 mmoles), equivalent to the sodium hydride, was added portionwise. Vigorous evolution of hydrogen ensued which ceased after 15–20 min to give a milky white reaction mixture.

Method B (in THF). Sodium hydride (0.32 mole) free of mineral oil was prepared as described above. To the resulting gray solid, 500 ml of tetrahydrofuran (distilled from lithium aluminum hydride) was added and 38.4 g (0.30 mole) of trimethyloxosulfonium chloride added all at once. With stirring, the mixture was heated to reflux with rapid evolution of hydrogen at first, then cessation, continued evolution after 2–3 hr, and completion after 3–4 hr as evidenced by cessation of gas evolution and formation of a milky white suspension. The mixture was cooled and filtered in a dry box through a large Büchner funnel fitted with a matting of Celite filter aid directly into a storage flask which was maintained under a nitrogen atmosphere. The flask was sealed with rubber stoppers. The solution of ylide can be stored at 0° or below for several weeks without appreciable decomposition. Before use, samples of the solution may be withdrawn via hypodermic syringe, added to

distilled water, and titrated with standard hydrochloric acid to the phenolphthalein end point to determine the ylide concentration.

9.3.2.b. *Dimethylsulfonium Methylide* (Use of Methylsulfinyl Carbanion, Irreversible Conditions).[9] Sodium hydride (0.10 mole) was washed with petroleum ether (b.p. 40°–60°) to remove the mineral oil as described (see Section 9.3.2.a) and mixed with 100 ml of dimethyl sulfoxide (distilled from calcium hydride). The mixture was stirred at 50° for 3.5 hr at which time hydrogen evolution ceased. The solution was cooled and transferred to dry bottles for storage. Addition of 0.5 ml of mineral oil to each bottle provides a protective layer toward air oxidation. With triphenylmethane as indicator, titration utilizing cyclohexanone indicated the solution of sodium methylsulfinyl carbanion to be 1.06 *M*. Refrigeration of the solution at 0° resulted in solidification which enhanced its shelf-life. An aliquot of this solution was diluted with an equal volume of tetrahydrofuran (distilled from lithium aluminum hydride) and cooled in an ice–salt bath. A solution of trimethylsulfonium iodide in dimethyl sulfoxide (800 ml of solvent per mole of salt) was added at such a rate that the internal temperature did not exceed 5°. After the addition of the salt was complete, the mixture was stirred an additional minute longer before adding the acceptor.

9.3 2.c. *Diphenylsulfonium Isopropylide* (*in situ* Preparation by Alkylation, Lithium Dichloromethide Base).[10] A solution of 3.0 g (0.01 mole) of diphenylethylsulfonium fluoroborate and 0.85 g (0.01 mole) of methylene chloride in 100 ml of dry 1,2-dimethoxyethane (distilled from lithium aluminum hydride) under nitrogen was cooled to −70° and treated with 0.011 mole of a cold solution of lithium diisopropylamide (reagent prepared freshly by the addition of 7.0 ml of 1 6 *M* *n*-butyllithium in hexane to 1.12 g of diisopropylamine in 10 ml of 1,2-dimethoxyethane at −70°). The yellow-green solution which resulted became cloudy after 10 min. After 30 min at −70° the solution was treated with 1.50 g (0.0105 mole) of methyl iodide and the reaction mixture maintained at −70° to −50° for 2 hr, at the end of which time 0.011 mole of lithium diisopropylamide solution was again added at −70°. An orange color was produced rapidly and the solution was stirred an additional hour. The resulting solution contains approximately 0.010 mole of ylide.

9.3.2.d. *Diphenylsulfonium Allylide* (Use of Organolithium Base at Low Temperature).[7] A slurry of 1.0 g (3.18 mmoles) of allyldiphenylsulfonium fluoroborate in 50 ml of dry tetrahydrofuran (distilled from lithium aluminum hydride and benzophenone sodium ketyl) was prepared under nitrogen. It was placed in a cooling bath at −78° for 0.5 hr whereupon 2.37 ml (3.50 mmoles) of a 1.48 *N* solution of *n*-butyllithium in hexane or preferably

2.00 ml (3.25 mmoles) of a 1.6 *N* pentane solution of *t*-butyllithium was added dropwise. With the former base, the solution became deep red-orange during the addition; whereas, with the latter base, it turned golden yellow.

9.3.2.e. *Dimethylsulfonium Carboethoxymethylide* (Isolation of a Stable Ylide).[2] A solution of 163 g (0.71 mole) of carboethoxymethyldimethylsulfonium bromide in 565 ml of chloroform under nitrogen was stirred vigorously at 5°–10° with ice bath cooling and treated in one portion with a mixture of 425 ml of saturated aqueous potassium carbonate solution (prepared by dissolving 650 g of potassium carbonate hydrate in 500 ml of water, adding 170 ml of anhydrous carbonate, stirring overnight, and filtering) and 56.6 ml of 12.5 *N* aqueous sodium hydroxide solution. The reaction mixture was warmed to 15°–20° and held there an additional 15 min. After removal of salt by filtration, the filtrate was separated and the upper chloroform layer was dried 2 hr over anhydrous potassium carbonate. Removal of solvent *in vacuo* at 25° (1 mm) gave a light yellow oil, n_D^{25} 1.5253–1.5263, with a constant weight of 100 g (95% yield). The infrared spectrum ($CHCl_3$) showed the carbonyl band at 1600 cm^{-1}. The ultraviolet spectrum showed λ_{max}^{nm} (ϵ) at 256 (4020) in ethanol and 267 (7800) in isooctane. The nmr spectrum ($CDCl_3$) showed a triplet at δ1.2 (3H), a quartet at δ3.9 (2H), and a singlet with a shoulder δ2.7–2.8 (7H). The ylide was stored at −10° using a bottle fitted with a Teflon-lined screw cap and wrapped with tape. It could be distilled by a molecular distillation at 40° (0.003 mm) with an 80% recovery.

9.3.3. Epoxidations

9.3.3.a. *Methylenecycloheptane Oxide* (Oxosulfonium Ylide with Saturated Ketone).[9] A solution of the ylide was prepared under nitrogen from 0.30 mole of sodium hydride, 66 g (0.30 mole) of trimethyloxosulfonium iodide, and 200 ml of dimethyl sulfoxide. Cycloheptanone (22.4 g, 0.20 mole) was added dropwise at room temperature over a period of 20 min and stirring continued at this temperature for 18 hr and then at 50° for 1 hr. After cooling, the reaction mixture was poured into 400 ml of cold water and the product extracted with seven 100-ml portions of ether. The combined extracts were washed once with 50 ml of water, dried over anhydrous sodium sulfate, and evaporated; the yellow residue was distilled at reduced pressure to yield 17.9 g (71.1%) of colorless methylenecycloheptane oxide, b.p. 63° (14 mm). The infrared spectrum (neat) showed absorptions at 3.35 (s), 3.45 (m), 6.85 (m), 9.95 (w), 10.55 (w), and 11.25 (w) μm. The nmr spectrum (neat) showed signals at δ1.62 (12H) and 2.43 (2H).

9.3.3.b. *4-Phenylbutadiene-1-oxide* (Sulfonium Ylide with Unsaturated Aldehyde, Alkoxide Base).[6] A mixture of 13.2 g (0.10 mole) of cinnamaldehyde and 22 g (0.14 mole) of trimethylsulfonium bromide was stirred under a nitrogen atmosphere with 60 ml of dry dimethyl sulfoxide (distilled from calcium sulfate) for 15 min to effect solution. Dropwise addition of a solution of 14 g of potassium *t*-butoxide in 60 ml of dry dimethyl sulfoxide was made over a 30–45 min period while cooling the reaction mixture with water. After an additional 15 min of stirring, 300 ml of water was added while maintaining the reaction at room temperature by occasional cooling in an ice–salt bath. The cloudy solution was extracted three times with 500 ml of ether and the extracts washed three times with 400 ml of water. After drying over anhydrous sodium sulfate, the residue was distilled at 55° (0.001 mm) to give 5.84 g (40%) of epoxide.

9.3.3.c. *1,3-Diphenyl-trans-1,3-butadiene 3,4-oxide* (Sulfonium Ylide with Unsaturated Ketone, Methylsulfinyl Carbanion as Base).[9] A solution of the ylide in dimethyl sulfoxide–tetrahydrofuran was prepared as previously described from 6.50 g (0.032 mole) of trimethylsulfonium iodide and 20 ml (0.032 mole) of 1.6 *M* solution of sodium methylsulfinyl carbanion in dimethyl sulfoxide. After addition of the salt was complete, the mixture was stirred 1 min and 6.24 g (0.03 mole) of benzalacetophenone in 10 ml of tetrahydrofuran was added at a moderately rapid rate. Stirring was continued for several minutes at ice–salt temperature and then for 30–60 min with the bath removed. The reaction mixture was diluted with three volumes of water and the product extracted with pentane. The pentane extracts were washed with water and dried over anhydrous potassium carbonate Removal of solvent *in vacuo* left 6.7 g (quantitative yield) of oxirane as a pale yellow oil. A 1.23 g sample was evaporatively distilled at 130° (0.05 mm) from 50 mg of of potassium carbonate to yield 1.07 g (87% recovery) of pale yellow oil. The infrared spectrum ($CHCl_3$) showed absorptions at 5.90 (w), 5.98 (m), 6.20 (m), 6.30 (w), and 6.66 (s). The ultraviolet spectrum (cyclohexane) exhibited a maximum at 256 nm (ϵ20,100). The nmr spectrum (CCl_4) showed a pair of doublets centered at δ2.92 (2H, $J = 6.5$ Hz), and phenyl multiplets at δ7.00–7.58 (10H).

9.3.3.d. *Cyclopropylidenecyclopentane Oxide* (Reversible Ylide Generation Conditions).[11] A solution of 7.85 g (25.0 mmoles) of cyclopropyldiphenylsulfonium fluoroborate and 2.10 g (25 mmoles) of cyclopentanone in 40 ml of commercial dimethyl sulfoxide was prepared under nitrogen. Powdered potassium hydroxide (pellets ground with mortar and pestle, 2.80 g, 50 mmoles) was added rapidly to the reaction mixture and the stirring continued for 4 hr. The dimethyl sulfoxide mixture was extracted with two

50 ml portions of pentane. The pentane extracts were washed with saturated aqueous sodium bicarbonate solution, dried over anhydrous sodium sulfate, and evaporated *in vacuo* to yield a mixture of diphenyl sulfide and oxaspiropentane. Reduction of the pressure to 0.5 mm allowed flash distillation of the oxaspiropentane from the diphenyl sulfide at room temperature. In this way, 2.91 g (94% yield) of cyclopropylidenecyclopentane oxide was obtained as a colorless oil. Its infrared spectrum (CCl_4) shows strong absorptions at 3.25, 9.28, 9.79, 10.01, 10.58, 10.78, and 11.09 μm. Its nmr spectrum exhibits a multiplet for the cyclopropyl protons at δ0.59–1.08 (4H) and a broad singlet for the cyclopentyl protons at δ1.80. Its mass spectrum shows a molecular ion at *m/e* (relative intensity) 124 (16) as well as fragment ions at 96 (16), 82 (19), and 67 (100).

9.3.3.e. *Ethyl 2,3-Epoxy-3-methyllevulinate* (Stable Ylide).[2] A solution of 8.6 g (0.10 mole) of diacetyl in 25 ml of benzene was added dropwise with with stirring over 2 hr to a solution of 14.8 g (0.10 mole) of dimethylsulfonium carboethoxymethylide in 100 ml of benzene heated to 45°–50°. After 1 hr at 45°–50° and 18 hr at 25°, the mixture was distilled in a Claisen flask at 56°–57° (1 mm) to give 8.6 g (50%) of ethyl 2,3-epoxy-3-methyllevulinate, n_D^{25} 1.4327. Its nmr spectrum ($CDCl_3$) showed singlets at δ1.5 (3H), 2.3 (3H), and 3.5 (1H) as well as a triplet (J = 7 Hz) at δ1.2 (3H) and a quartet (J = 7 Hz) at δ4.2 (2H).

9.3.4. Cyclopropanations

9.3.4.a. *1-Methyl-4-isopropenylbicyclo[4.1.0]heptan-2-one* (Oxosulfonium Ylide with Enone).[9] A solution of the ylide was prepared under nitrogen as previously described from 0.021 mole of sodium hydride, 4.62 g (0.021 mole) of trimethyloxosulfonium iodide, and 25 ml of dimethyl sulfoxide. A solution of 3.0 g (0.02 mole) of freshly distilled carvone (b.p. 104°–105° at 10 mm) in 5 ml of dimethyl sulfoxide was added with stirring and slight cooling in a water bath. The reaction mixture was stirred at room temperature for 2 hr, then at 50° for 1 hr, poured into 80 ml of cold water, and extracted with ether. The ether extracts were washed twice with water, dried over anhydrous sodium sulfate, and evaporated to leave a pale yellow liquid. Distillation gave 2.65 g (81.3%) of the cyclopropyl ketone as a colorless liquid, b.p. 109°–110° (10 mm). The infrared spectrum (neat) showed absorptions at 5.90 (s), 6.06 (m), and 8.90 (m). The nmr spectrum showed a multiplet centered at δ0.8 (1H), a sharp singlet at 1.15 (3H), a sharp singlet at 1.68 (3H) with less intense overlapping multiplets at 1.25–2.60 (10H), and a singlet at 4.70 (2H).

9.3.4.b. *1,3-Dimethylcyclothymine* (Oxosulfonium Ylide with Enamide, Tetrahydrofuran Solvent).[12] A solution of the ylide under nitrogen was

prepared by refluxing a mixture of 0.133 mole of sodium hydride with 17.1 g (0.133 mole) trimethyloxosulfonium chloride in 200 ml of tetrahydrofuran for 2 hr. To the resulting milky suspension, 14.4 g (0.103 mole) of 1,3-dimethyluracil was added and the reaction mixture gently refluxed for 4 hr. The solution was cooled to room temperature, filtered, and the precipitate was washed thoroughly with fresh tetrahydrofuran. The combined filtrate and washings were evaporated *in vacuo* to leave a yellow oil. Distillation under reduced pressure gave a slightly yellow liquid, b.p. 110°–120° (0.5 mm), which solidified on cooling to yield 10.5 g (66%). The product could be further purified by column chromatography on silica gel first with benzene–acetone (20:1) followed by a second chromatography with chloroform–acetone (20:1) as eluting solvents. This purification gave cyclothymine as colorless plates, m.p. 43°–46°. The infrared spectrum (Nujol) showed absorptions at 1700 and 1660 cm^{-1}. The ultraviolet spectrum (C_2H_5OH) showed strong end absorption with slight shoulders at (log ϵ) 250 (3.09) and 223 (3.43) nm. Its nmr spectrum ($CDCl_3$) exhibited multiplets at δ0.77 (1H), 1.36 (1H), 2.12 (1H), and 2.97 (1H) and a singlet at δ3.14 (6H). In deuterium oxide the latter signal splits into two peaks of equal intensity at δ3.02 and 3.08. The mass spectrum (80 eV) shows prominent peaks at *m/e* 154, 97, 69, 68, and 42.

9.3.4.c. *1-Phenyl-2,2-dimethylcyclopropanecarboxylic Acid* (Substituted Ylide with Enoate).[13] A solution of diphenylsulfonium isopropylide was prepared as previously described (Section 9.3.2.c) by first generating diphenylisopropylsulfonium iodide from 60.0 g (0.199 mole) of diphenylethylsulfonium fluoroborate, 0.146 mole of lithium diisopropylamide (from 15.75 ml of diisopropylamine and 73 ml of a 2.0 *M* solution of *n*-butyllithium in hexane), dissolved in 75 ml of 1,2-dimethoxyethane, 12 ml of methylene chloride, and 21.2 g (0.149 mole) of methyl iodide followed by addition of another 0.146 mole of lithium diisopropylamide in 75 ml of anhydrous 1,2-dimethoxyethane. The entire procedure was executed under nitrogen at −80°. To this vigorously stirred solution at −80°, 17.6 g (0.109 mole) of methyl α-phenylacrylate was added all at once. Over a 4-hr period, the mixture was allowed to come to room temperature. Filtration removed the precipitated salts which were washed with additional dimethoxyethane. The filtrate and washings were concentrated *in vacuo*, dissolved in 250 ml of 10% methanolic potassium hydroxide, and refluxed for 8 hr. The resulting mixture was cooled, concentrated under vacuum, diluted with water, and extracted with ether. The aqueous layer was acidified to Congo red with 15% aqueous hydrochloric acid solution and subsequently extracted with ether. These ether extracts were dried and concentrated *in vacuo* to give 18.7 g (90.5%) of cyclopropyl acid as a solid mass. Recrystallization from pentane produced acid, m.p. 104.5°–106.5°. Its infrared spectrum (CCl_4) showed carboxylic acid

absorptions between 3.00–4.40 and 5.94 μm. The nmr spectrum (CCl_4) showed a singlet at δ13.00 (1H), a multiplet at δ7.20 (5H), a doublet (J = 4.5 Hz) at 1.67 (1H), a singlet at δ1.31 (3H), a doublet (J = 4.5 Hz) at δ1.10 (1H), and a singlet at δ0.80 (3H).

9.3.4.d. *Methyl Spiropentanecarboxylate* (Reversible Ylide Generation Conditions).[14] A solution of cyclopropyldiphenylsulfonium fluoroborate (1.57 g, 5.0 mmoles) and 0.43 g (5.0 mmoles) of methyl acrylate in 30 ml of dimethyl sulfoxide was prepared under nitrogen at room temperature. To the stirred solution, 0.28 g (5.0 mmoles) of powdered potassium hydroxide was added in one portion. After stirring 1.25 hr, an equal volume of water was added and the mixture extracted two times with 50 ml portions of ether. The ether was washed with 50 ml of water and dried over anhydrous sodium sulfate. After evaporation of solvent *in vacuo*, an oil (1.053 g) remained which consisted of an approximately 50:50 mixture of diphenyl sulfide and methyl spiropentanecarboxylate (approximately 83% yield). A small sample was further purified by collection from a 5-ft 5% SE 30 on a Chromosorb W vpc chromatographic column. Its infrared spectrum (CCl_4) showed carbonyl absorption at 1726 cm^{-1}. The nmr spectrum showed a pseudosinglet at δ0.87 (4H), a multiplet at δ1.00–2.58 (3H), and a singlet at δ3.50 (3H). Its mass spectrum (70 eV) showed in addition to the molecular ion at *m/e* 126 prominent ions at *m/e* 95, 93, 79, 67, and 59.

9.3.4.e. *Ethyl 2-Formylcyclopropanecarboxylate* (Preformed Stabilized Ylide with Enal).[2] To a stirred solution of 14.8 g (0.10 mole) of dimethylsulfonium carboethoxymethylide in 100 ml of refluxing dry acetone was added dropwise over a 5-min period 7.0 ml (0.10 mole) of acrolein. After an additional 10 min, distillation in a Claisen flask removed the solvent and allowed isolation of the product by distillation *in vacuo*, b.p. 45° (< 1 mm). In this way, 9.0 g (63%) of ethyl 2-formylcyclopropanecarboxylate was produced as an 83:17 mixture of trans-cis isomers, n_D^{25} 1.4488. Vapor phase chromatographic analysis was performed utilizing a 10-ft column packed with 5% XF-1150 on Chromosorb W. The infrared spectrum ($CHCl_3$) showed carbonyl absorption at 5.85 μm. The nmr spectrum ($CDCl_3$) showed a triplet at δ1.3 (3H), a quarter at δ4.2 (2H), a multiplet at δ1.5–2.5 (4H), and a singlet at δ9.3 (1H).

9.3.4.f. *1-Benzoyl-1,2-dimethylcyclopropane* (Aminooxosulfonium Ylide with *in Situ* Michael Acceptor Generation).[15] *n*-Butyllithium [3.61 ml (6.0 mmoles) of a 1.6 *M* solution in hexane] was added at room temperature under a nitrogen atmosphere to 1.80 g (6.0 mmoles) of (dimethylamino)ethyl-*p*-tolyloxosulfonium fluoroborate in 10 ml of dimethyl sulfoxide to generate

the ethylide. To the reaction was added a solution of 0.957 g (5.0 mmoles) of α-methyl-β-dimethylaminopropiophenone in 2 ml of dimethyl sulfoxide. After stirring for 21 hr at 25°, the reaction was poured into 50 ml of water and extracted three times with 25 ml of pentane. The combined organic extracts were washed with water to remove any unreacted Mannich base. The solution was dried over anhydrous magnesium sulfate, concentrated, and the residue passed over a column of silica gel eluting with a 5:95 ether–pentane mixture to yield 644 mg (74%) of a yellow oil. The infrared spectrum (neat) showed a carbonyl band at 1670 cm^{-1}. The nmr spectrum (CCl_4) showed δ7.8–7.2 (m, 5H), 1.6–0.8 (m, 8H), and 0.3–1 (m, 1H).

9.3.4.g. *2-Cyano-1-(2'-hydroxyethyl)-1-cyclopropanecarboxylic Lactone (in situ* Generation of Stabilized Ylide with Unsaturated Nitrile).[4] A suspension of mineral oil-free sodium hydride (27.4 mmoles) in 75 ml of dry tetrahydrofuran (distilled from lithium aluminum hydride) was prepared by washing sodium hydride with petroleum ether (b.p. 40°–60°) as previously described. To this suspension, 6.6 g (28.2 mmoles) of dimethyl(2-γ-butyrolactone)sulfonium fluoroborate was added. After just a few minutes of additional stirring 2.97 g (56.0 mmoles) of acrylonitrile was added all at once and stirring continued for 8 hr at room temperature. The reaction mixture was then quenched by pouring into water and was extracted with ethyl acetate. The organic phase was dried over magnesium sulfate and the solvent removed *in vacuo* to yield 3.4 g (87%) of the lactone. A small amount was further purified by preparative layer chromatography utilizing silica gel PF 254 and chloroform as the eluting solvent. The infrared spectrum (CCl_4) showed nitrile absorption at 4.45 μm and carbonyl absorption at 5.67 μm. The nmr spectrum (CCl_4) showed triplets (J = 7.4 Hz) at δ4.48 (2H) and 2.50 (2H) and multiplets at δ2.07 (1H) and 1.55 (2H). The mass spectrum (70 eV) showed a molecular ion at *m/e* 137 and prominent peaks at *m/e* 109, 84, 79, 66, and 55.

9.3.5. [2.3]Sigmatropic Rearrangements

9.3.5.a. *4-Methylthio-2,5,5-trimethyl-2,6-heptadiene* (1,5-diene with *n*-Butyllithium as Base).[16] To a −70° solution of 156 mg (0.58 mmole) of methyl (bisdimethylallyl)sulfonium fluoroborate in 4 ml of tetrahydrofuran was added dropwise 0.5 ml (0.8 mmole of *n*-butyllithium) of a 1.6 *M* solution of *n*-butyllithium in hexane. The resulting orange solution was stirred 2 hr at −70°, 45 min at 0°, poured over ice, and extracted twice with 4-ml portions of pentane. The combined pentane extract was dried over magnesium sulfate, filtered, and evaporated *in vacuo*. The residual yellow oil was vacuum distilled yielding 87.8 mg (83%) (b.p. 30° at 0.3 mm) of 4-methylthio-2,5,5-

trimethyl-2,6-heptadiene. The nmr spectrum (CCl_4) showed the following resonances: δ1.07 (singlet, 6H), 1.64 (doublet, J = 1.5 Hz, 3H), 1.82 (doublet, J = 1.5 Hz, 3), 1.86 (singlet, 3H), 3.18 (doublet of doublets, J = 10.5, 1.0 Hz, 1H), 4.92 (doublet of doublets, J = 11.0, 1.5 Hz, 1H), 4.95 (two doublet of doublets, J = 17.5, 10.0, 1.5 Hz, 2H) and 5.90 (doublet of doublets, J = 18.0 and 10.0 Hz, 1H).

9.3.5.b. *3-Methylthiohex-1,5-diene* (1,5-Diene with Sodium Hydroxide as Base).[17] To 0.02 mole of methyl diallylsulfonium monomethylsulfate in 30 ml of water was added 15 ml of 2 *N* sodium hydroxide causing a milky suspension. The mixture was vigorously shaken for several minutes and allowed to stand 2 hr forming two phases. The colorless organic phase was dried with calcium chloride and purified by gas liquid phase chromatography (2 m × 2 cm column at 135° packed with 15% dinonyl phthalate on kieselguhr). In this manner a 9.5:1 ratio of 3-methylthiohex-1,5-diene (45–50%, b.p. 153°) and 3-allylthiohex-1,5-diene (5%, b.p. 180°) was obtained. 3-Methylthiohex-1,5-diene shows the following nmr resonances: δ1.92 (multiplet, 3H), 3.0 (multiplet, 1H), 2.3 (triplet, 2H), and 4.7–6.2 (multiplet, 6H).

9.3.5.c. α-(*Methylthio*)*methoxystyrene* (Vinyl Ether from a Carbonyl-Stabilized Ylide).[18] 2-(Dimethylsulfuranylidene)acetophenone (3.8 g, 0.02 mole) was added to water (45 ml) and refluxed for 5 hr. The cooled mixture was extracted with two 50-ml portions of ether and the ether extracts concentrated to give 2.5 g (66%) of α-(methylthio)methoxystyrene. The nmr spectrum ($CDCl_3$) showed singlets at δ2.08 and 4.88, doublets at 4.73 (J = 3 Hz) and 4.20 (J = 3 Hz), and a multiplet at 7.40.

9.3.5.d. *1-Adamantyl 4-Pent-1-enyl Sulfide* (Homoallylic Sulfide with Potassium *t*-Butoxide–Crown Ether as Base).[19] 1-Adamantylallylethylsulfonium fluoroborate (80.0 mg, 0.247 mmole) was dissolved in 10 ml of dry benzene at 25° and potassium *t*-butoxide; dicyclohexyl-18-crown-6-ether[20] (1.20 ml of 0.20 *N* solution in *t*-butyl alcohol, 0.24 mmole) was added. After stirring 16 hr the mixture was poured into 50 ml of water and extracted four times with ether to afford, after drying and evaporating *in vacuo*, 194.5 mg of oil. The oil was analyzed by vapor phase chromatography (11 ft, 5% SE-30 on Chromosorb W, 159°) with *n*-butyl phthalate as internal standard. 1-Adamantylethyl sulfide (7-min retention time, 17.4% yield) and 1-adamantylallyl sulfide (10-min retention time, 1.8% yield) were identified by peak enhancement from coinjections with known samples. A third product (17-min retention time, 74.4% yield) was identified as 1-adamantyl-4-pent-1-enyl sulfide: nmr (CCl_4) 3.8–4.5 (multiplet, 1H), 4.9 and 5.2 (singlets, 2H), 7.30 (multiplet, 1H), 7.79 (triplet of multiplets, 2H), 7.8–8.5 (multiplet, 15H),

and 8.78 (doublet, $J = 6.5$ Hz, 3H). The infrared spectrum (CCl_4) shows a double-bond absorption at 1632 cm^{-1}. The mass spectrum shows major fragmentation at *m/e* (70 eV) 236 (7), 135 (100), and 69 (12).

9.3.6. [1.2]Rearrangement

9.3.6.a. *Tristrimethylthio[2.2.2](1,3,5)-cyclophane* (Steven's Rearrangement).[21] A mixture of 5.0 g (7.8 mmoles) of the trissulfonium salt of 2,11,20-trithia[3.3.3](1,3,5)-cyclophane and 1.02 g (42.5 mmoles) of washed sodium hydride in 100 ml of tetrahydrofuran was stirred at room temperature for 24 hr. Water was added to destroy the excess sodium hydride, the mixture was filtered, and the filtrate was concentrated. The resulting yellow oil was chromatographed over silica gel using a 20% benzene–petroleum ether (30°–60°) solution for elution. Concentration of the eluate gave 1.23 g (42%) of the cyclophane as a colorless oil. The nmr spectrum ($CDCl_3$) showed the following resonances: δ6.35–6.55 (m), 5.68–5.98 (m), 3.77–4.33 (m), 3.05–3.68 (m), 1.92–2.55 (m), and 2.15 (s, 9H).

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Appendix: Tabular Survey

The tables that appear in this appendix resulted from an exhaustive literature search through August, 1973 with occasional references published thereafter. Unpublished work from the authors' laboratory and other laboratories was included to help minimize the dating of the tables. Although an attempt was made to be complete, difficulties in searching such a topic may have led to some examples being overlooked.

The tables have been divided to permit most efficient use by the chemist. Tables A.I and A.II represent nucleophilic epoxidations with methylides of ketones and aldehydes, respectively. Within these tables, the acceptors are arranged according to molecular formula. Table A.III consists of nucleophilic epoxidations of both aldehydes and ketones by substituted (stabilized and nonstabilized) ylides. The sequence is determined, first, by the formula of the alkylidene group being transferred and, second, by the molecular formula of the acceptor.

Table A.IV consists of nucleophilic cyclopropanations with methylene transfer to all structural types of acceptors arranged according to molecular formula of the acceptor. Table A.V consists of nucleophilic cyclopropanations with alkylidene transfer arranged, first, according to formula of the alkylidene group being transferred and, second, by the molecular formula of the acceptor. Table A.VI consists of [2,3]sigmatropic rearrangements and Table A.VII of Stevens' rearrangements of sulfonium salts. In these tables the examples are arranged according to molecular formula of the sulfonium cation.

In tables involving methylene transfer, the ylide employed is designated as follows

A_1	Dimethylsulfonium methylide from iodide salt
A_2	Dimethysulfonium methylide from chloride salt
A_3	Dimethylsulfonium methylide from bromide salt
B_1	Dimethyloxosulfonium methylide from iodide salt
B_2	Dimethyloxosulfonium methylide from chloride salt
C_1	Racemic phenyl(dimethylamino)oxosulfonium methylide
C_2	Optically active phenyl(dimethylamino)oxosulfonium methylide
C_3	Optically active *p*-tolyl (dimethylamino)oxosulfonium methylide
C_4	Methyl(dimethylamino)oxosulfonium methylide
C_5	Optically active (dimethylamino)oxosulfonium methylide
C_6	Optically active (diethylamino)phenyloxosulfonium methylide

The following abbreviations for common solvents, reagents, and substituents have been used throughout the tables.

DMSO	Dimethyl sulfoxide
THF	Tetrahydrofuran
DME	1,2-Dimethoxyethane
DMF	Dimethylformamide
Ph	Phenyl
Ms	Methane sulfonate
THP	Tetrahydropyranyl or tetrahydropyran

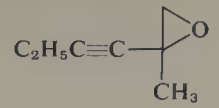
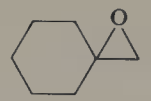
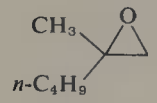
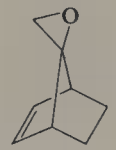
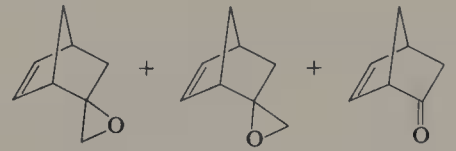
Tables A.I—A.VII

(pages 160–319)

TABLE A.I

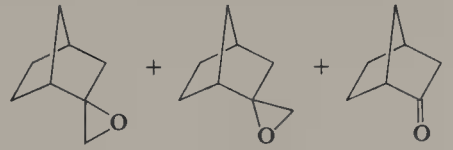
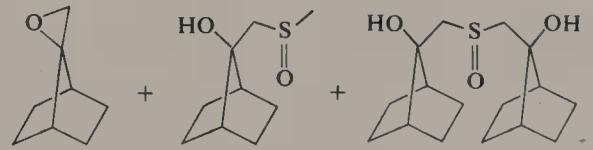
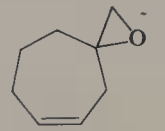
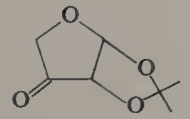
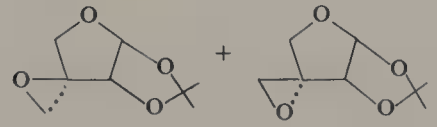
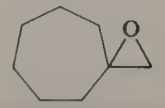
Epoxidations with Methylides: Ketones

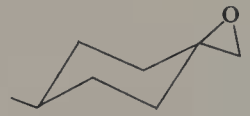
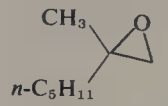
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
C_3				
Acetone	A_3	$KOC(CH_3)_3$, DMSO, 25°	$(CH_3)_2C$(O) (50)	1
	Polymer—S(CH$_3$)(⊕)—⊖CH$_2$	Unstated	(Good)	2
C_4				
2-Butanone	A_3	$KOC(CH_3)_3$, DMSO, 25°	H_3C, H_5C_2, O (39)	1
C_5				
3-Pentyn-2-one	A	Unstated	$CH_3C{\equiv}C$, O, CH_3 (25)	3
Cyclopropyl methyl ketone	A	$NaCH_2SCH_3$, DMSO/THF, −5° (20 min), 25° (1 hr)	(unstated)	4
Tetrahydrothiopyran-4-one	B	Unstated	O, S (75)	5
3-Methyl-2-butanone	A_3	$KOC(CH_3)_3$, DMSO, 25°	CH_3, CH_3, CH_3, O (40)	1
3-Pentanone	A_3	$KOC(CH_3)_3$, DMSO, 25°	C_2H_5, C_2H_5, O (43)	1

C_6					
3-Hexyn-2-one	A	Unstated		(30)	3
Cyclohexanone	A_3	$KOC(CH_3)_3$, DMSO, 25°		(74)	1
	A_1	Electrolysis, DMSO, 25°		(10)	6
	n-$C_{12}H_{25}\overset{\oplus}{S}(CH_3)_2\ Cl^{\ominus}$	NaOH, H_2O/PhH, 25° (10 hr)		(88)	7
	n-$C_{12}H_{25}\overset{\oplus}{S}(CH_3)_2\ I^{\ominus}$	NaOH, H_2O/PhH, 25° (10 hr)		(27)	7
2-Hexanone	A_3	$KOC(CH_3)_3$, DMSO, 25°		(60)	1
C_7					
Norborn-2-en-7-one	B_1	NaH, DMSO, 25° (1 hr)		(40–72)	8, 9
					8
Norborn-5-en-2-one	B_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO, 25°	8.0 : 3.4 : 1	(70)	
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −15°	1 : 16	(60)	8

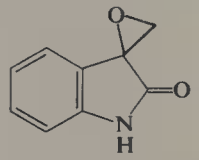
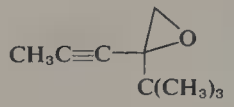
(continued)

TABLE A.I (*continued*)

Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
2-Norbornanone				
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −10°	1 : 20 : 28 (70)	8
	B_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO, 25°	5 : 44 : 1 (67)	8
7-Norbornanone				
	B_1	NaH, DMSO, 25° (1 hr)	(54) (11) (4)	10
3-Cycloheptanone	A	Unstated	 (unstated)	11
				
	B_1	NaH, DMSO, 25° (1 hr)	6 : 1 (poor)	12, 13
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, 0° (30 min), 25° (1 hr)	(0) (17)	13
Cycloheptanone	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (59)	1

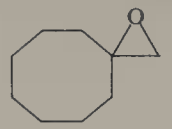
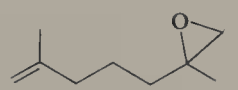
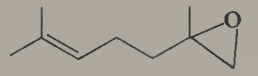
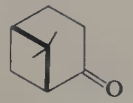
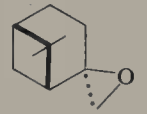
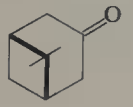
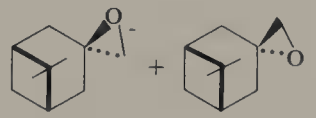
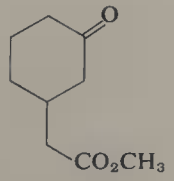
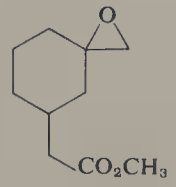
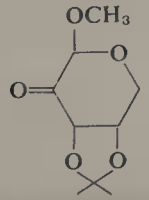
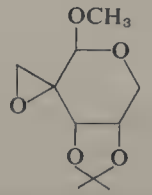
	B_1	NaH, DMSO, 50° (1 hr)	(71.7)		14
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0° (10 min), 25° (30–60 min)	(97.2)		14
	C_4	NaH, DMSO, 50° (overnight)	(42)		15
3-Methylcyclohexanone	A_3	$KOC(CH_3)_3$, DMSO, 25°	(69)		1
4-Methylcyclohexanone	C_4	NaH, DMSO, 50° (8 hr)		(42)	15
2-Heptanone	A_3	$KOC(CH_3)_3$, DMSO, 25°		(70)	1

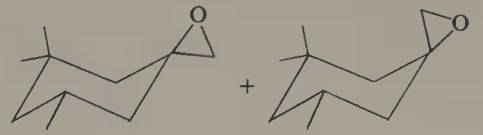
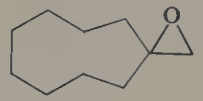
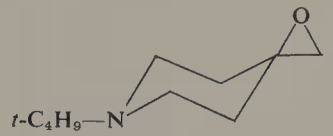
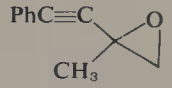
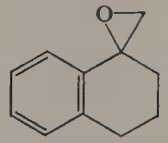
C_8

Isatin	A_1	Unstated		(97)	16
	B_1	Unstated	(84)		16
Acetophenone	C_2	NaH, DMSO, 25°	1-Methyl-1-phenyloxirane	(38)	17
	A_1	Electrolysis, DMSO, 25°		(7)	6
		NaOH, H_2O, CH_2Cl_2, $(n\text{-}C_4H_9)_4NI$, 50° (72 hr)		(36)	130
	$n\text{-}C_{12}H_{25}\overset{\oplus}{S}(CH_3)_2\ Cl^{\ominus}$	NaOH, H_2O/PhH, 25° (10 hr)		(85)	7
2,2-Dimethylhex-4-yn-3-one	A	Unstated		(50)	3

(*continued*)

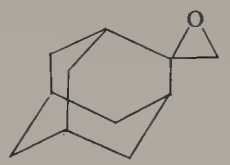
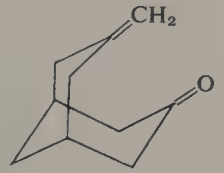
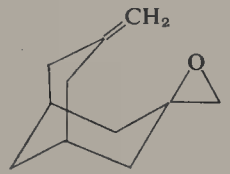
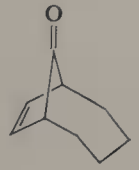
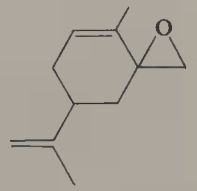
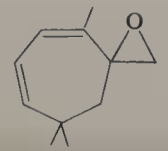
TABLE A.I (*continued*)

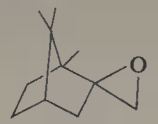
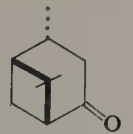
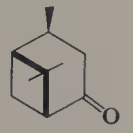
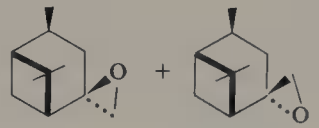
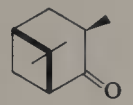
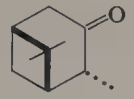
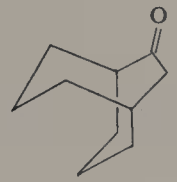
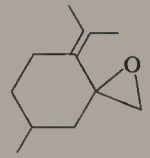
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
Cyclooctanone	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (53)	1
6-Methyl-6-hepten-2-one	B	Unstated	 (unstated)	18
6-Methyl-5-hepten-2-one	B_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, unstated	 (60–71)	18a
C_9				
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, −10° to −15° (1–2 hr)	 (80)	19
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, −10° to −15° (1–2 hr)	 1.5 : 1 (70)	19
	B_1	NaH, DMSO, 25° (1 hr), 40°–50° (1 hr)	 (61)	20
	B	Unstated	 (unstated)	21

3,3,5-Trimethylcyclohexanone	B_2	NaH, THF, reflux (16 hr)		(78)			14, 128
							
	A_1	n-C_4H_9Li, THF, 0° (10 min), 25° (30–60 min)	1	:	1	(88.2)	14
	A_1	n-C_4H_9Li, THF, 0° (30 min)	Only		0	(unstated)	128
Cyclononanone	A_3	$KOC(CH_3)_3$, DMSO, 25°		(73)			1
1-t-Butyl-4-piperidone	B_1	NaH, DMSO, 25° (overnight)		(53)			22
C_{10}							
4-Phenyl-3-butyn-2-one	A	Unstated		(30)			3
1-Tetralone	B	Unstated		(unstated)			23
Cyclopropylphenylketone	A	Unstated	1-Cyclopropyl-1-phenyloxirane	(78)			24
Isopropylphenylketone	A	Unstated	1-Isopropyl-1-phenyloxirane	(86)			24

(continued)

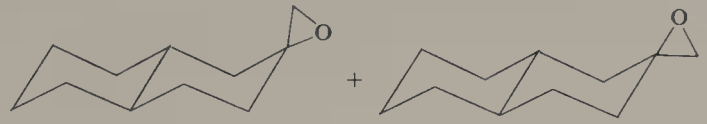
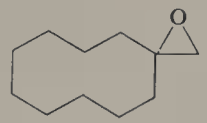
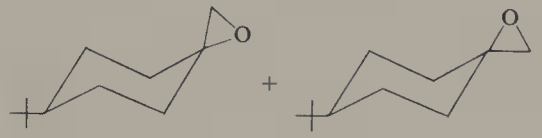
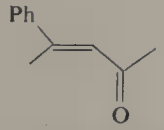
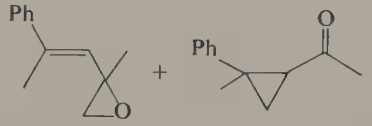
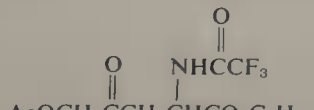
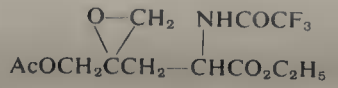
TABLE A.I (*continued*)

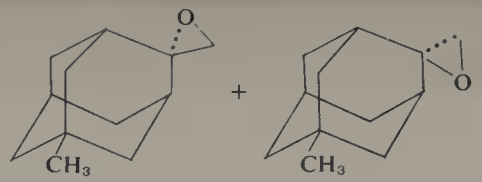
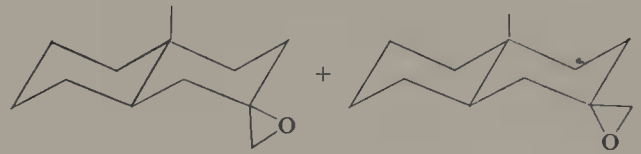
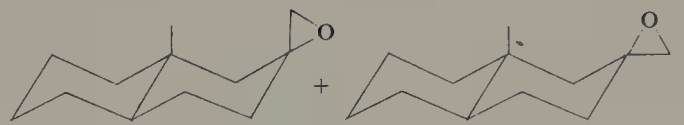
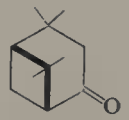
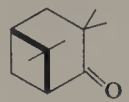
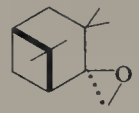
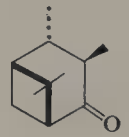
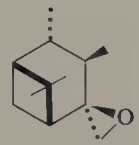
Ketone	Ylide	Reaction conditions	Products (Yield, %)[a]	References
Adamantanone	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, THF/DMSO, 0° (20 min), 25° (2 hr)	 (70)	26
	B_1	NaH, DMSO, 50° (12 hr)	(70)	26
	B_1	NaH, DMSO, 25° (20 hr), 50° (1 hr)	(96)	27
	B_1	NaH, DMSO, 25° (1 hr), 55° (1.5 hr)	(91)	28
	B	Unstated	 (60)	29
	B_1	NaH, DMSO, 25° (20 hr), 50° (2 hr)	 (89)	14
Carvone	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0° (10 min), 25° (30–60 min)	 (89.1)	14
Eucarvone	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0° (10 min), 25° (30–60 min)	 (93.5)	14

Camphor		n-$C_{12}H_{25}\overset{\oplus}{S}(CH_3)_2\ Cl^{\ominus}$ NaOH, H_2O/PhH, 25° (10 hr)		(40)	7
	A$_1$	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −10° to −15° (1–2 hr)		(75)	19
	A$_1$	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −10° to −15° (1–2 hr)	 9 : 1	(95)	19
	A$_1$	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −10° to −15° (1–2 hr)		(80)	19
	A$_1$	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −10° to −15° (1–2 hr)		(90)	19
	A or B	Unstated	No reaction		31
Pulegone	A$_1$	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, 0° (10 min), 25° (30–60 min)		(90)	14

(continued)

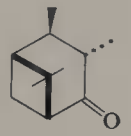
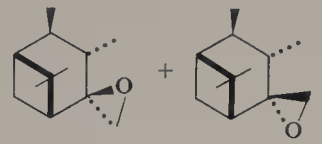
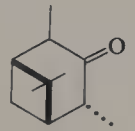
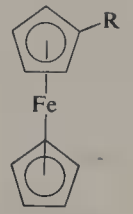
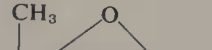
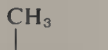
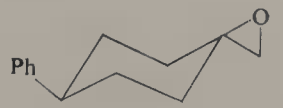
TABLE A.I (*continued*)

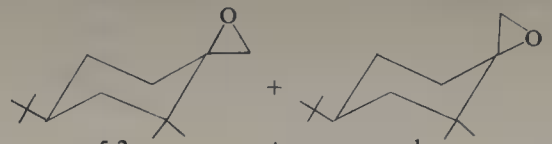
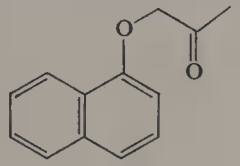
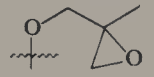
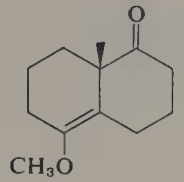
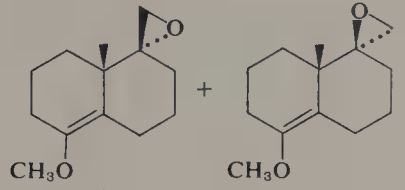
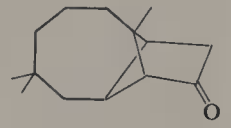
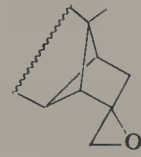
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
trans-2-Decalone				
	B_1	Unstated	1 : 9	32
	A_1	Unstated	1.5 : 1	32
Cyclodecanone	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (87)	1
4-*t*-Butylcyclohexanone	C_1	NaH, DMSO, 25° (20 hr)	 (84)	33
	B_2	NaH, THF, reflux (1 hr)	(89.2)	14
	C_4	NaH, DMSO, 50° (4 hr)	(72)	15
	A_1	*n*-C_4H_9Li, THF, 0° (10 min), 25° (30–60 min)	 (77.3)	14
C_{11} 	B_1	NaH, DMSO	 (unstated)	34
p-Vinylpropiophenone	A_1	$KOC(CH_3)_3$	1-*p*-Vinylphenyl-1-methyloxirane (unstated)	35
	B_2	NaH, THF, 25°, then 50° (2 hr)	 (49)	36

5-Methyl-2-adamantanone							
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$ THF/DMSO, 0° (20 min), 25° (2 hr)	49	:	51	(unstated)	26
	B_1	NaH, DMSO, 50° (12 hr)	53	:	47	(unstated)	26
10-Methyl-2-decalone	B_1	Unstated					32
			1	:	9		
9-Methyl-2-decalone	B_1	Unstated					32
			1	:	19		
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −10° to −15° (1–2 hr)				(88)	19
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO, THF, −10° to 15° (1–2 hr)				(unstated)	19
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO, THF, −10° to −15° (1–2 hr)				(85)	19

(continued)

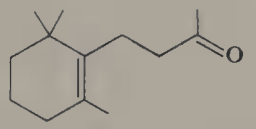
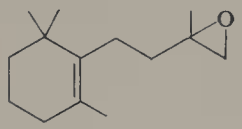
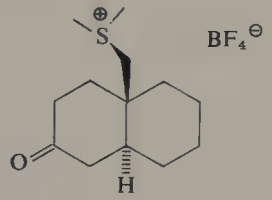
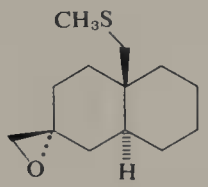
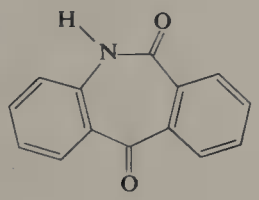
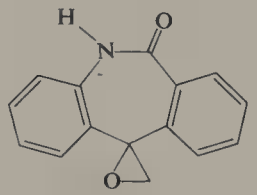
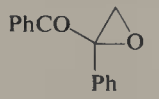
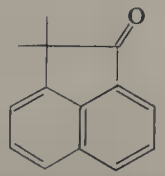
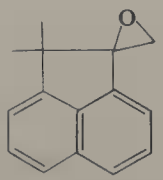
TABLE A.I (*continued*)

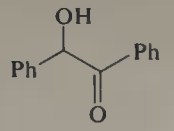
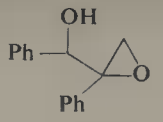
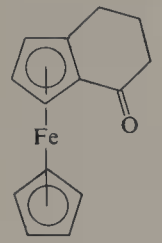
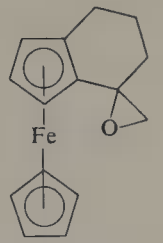
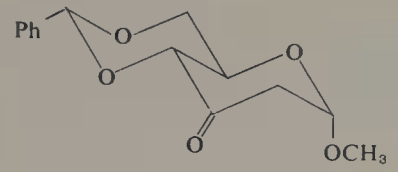
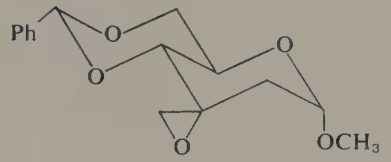
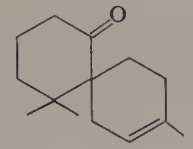
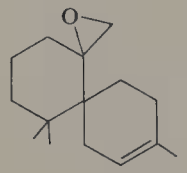
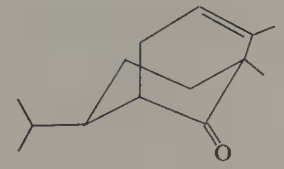
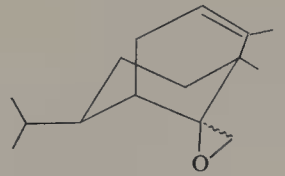
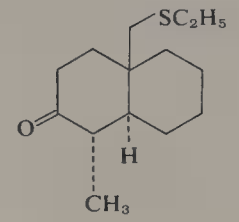
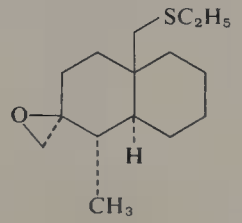
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	A_1	 $NaCH_2SCH_3$, DMSO, THF, $-10°$ to $-15°$ (1–2 hr)	 1 : 1.2	(88)	19
	A_1	 $NaCH_2SCH_3$, DMSO, THF, $-10°$ to $-15°$ (1–2 hr)		(80)	19
C_{12} Ferrocenyl methyl ketone	A_1	 $NaCH_2SCH_3$, DMSO/THF, $-15°$ (5 min), 25° (30 min)	 R = 	(70)	37
	B_1	NaH, DMSO, 55° (1.5 hr)	R =  (40), R =  (80)		37
4-Phenylcyclohexanone	B_1	NaH, DMSO, 50° (1 hr)		(71.7)	14
	B_2	NaH, THF, reflux (1 hr)		(73.4)	14
cis-2-Acetoxy-4-*t*-butylcyclohexanone	B	Unstated		(unstated)	38

2,2-Dimethyl-4-*t*-butylcyclohexanone	B_1	NaH, DMSO, 25° (22.5 hr), 65° (3 hr), 25° (21 hr)	 5.2 : 1	(54)	39
C_{13}					
p-Bromobenzophenone	B_1	NaH, DMSO, 25° (1 hr), 50°–55° (2 hr)	1-Phenyl-1-*p*-bromophenyloxirane	(98)	40, 41
Benzophenone	A_3	NaH, DMSO, 25°	1,1-Diphenyloxirane	(84)	1
	B_1	NaH, DMSO, 50° (1 hr)		(89.9)	14
	A_1	Electrolysis, DMSO, 25°		(40)	6
		$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, 0° (10 min), 25° (30–60 min)		(83.6)	14
		NaOH, H_2O/CH_2Cl_2, $(n\text{-}C_4H_9)_4NI$, 50° (72 hr)		(18)	130
[1-^{14}C]Benzophenone	B_1	NaH, DMSO, 25°	[1-^{14}C] 1,1-Diphenyloxirane	(96)	42
	B_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO 60° (2 hr)		(unstated)	43
	B	DMSO	 9 : 1	(86)	44
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, 0° (2 hr)		(85)	45

(*continued*)

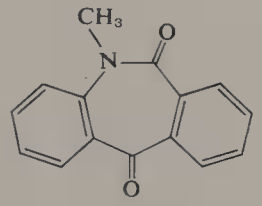
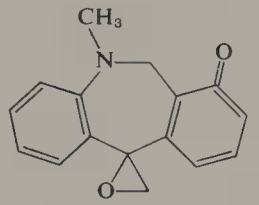
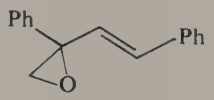
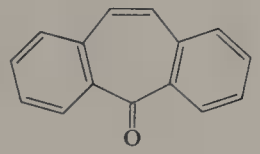
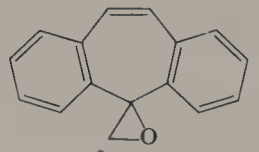
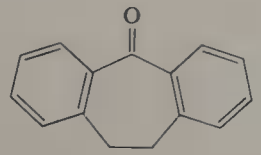
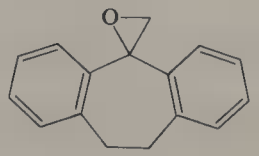
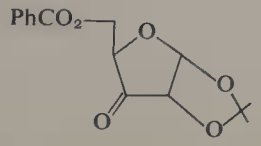
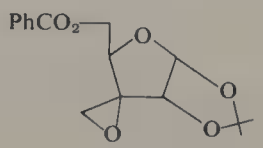
TABLE A.I (*continued*)

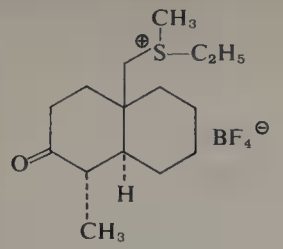
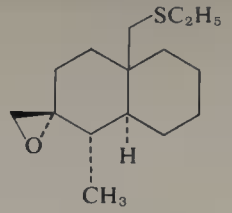
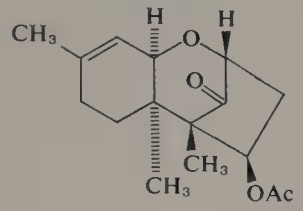
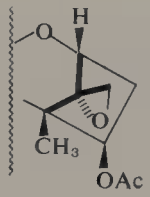
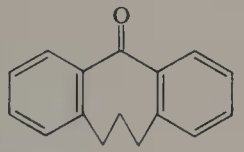
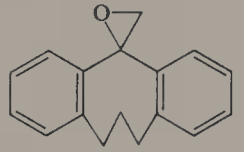
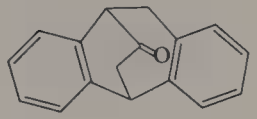
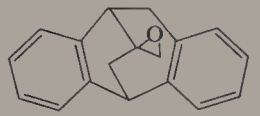
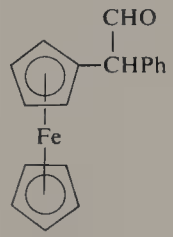
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_1	NaH, DMSO, 25° (18 hr), 50° (1 hr)	 (67)	46
		$KOC(CH_3)_3$	 (unstated)	47
C_{14} 	A_1	NaH, DMSO, 25° (3.5 hr)	 (75–86)	48
	A_1	$NaCH_2SCH_3$, DMSO/THF, −10°	 (60)	49
	B_1	$NaCH_2SCH_3$, DMSO	(40)	49
	B_1	NaH, DMSO, 50°–60° (4.5 hr)	 (30)	50

	B_1	$NaCH_2SCH_3$, DMSO		(80)	49
	A_1	$NaCH_2SCH_3$, DMSO/THF, $-5°$ (0.5 hr)		(33–52)	51
	B	Unstated		(65)	21
	A	Unstated		(94)	52
	A_1	$NaCH_2SCH_3$, DMSO, 0° (10 min), 25° (30 min)		(95)	53
	A	Unstated			54

(continued)

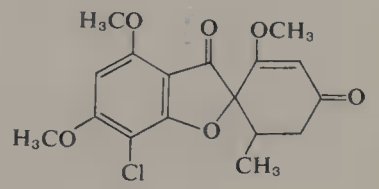
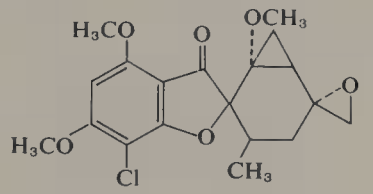
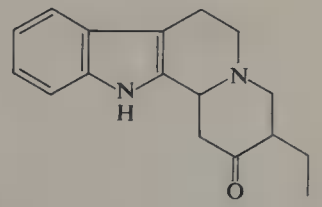
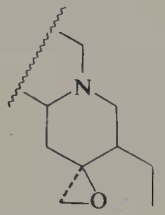
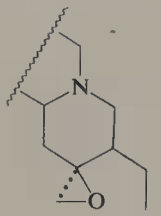
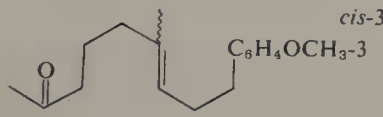
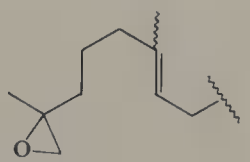
TABLE A.I (*continued*)

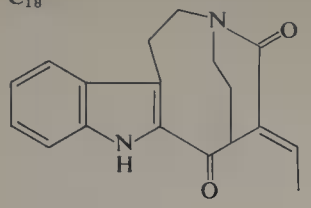
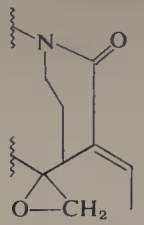
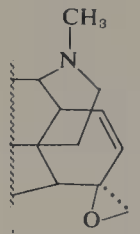
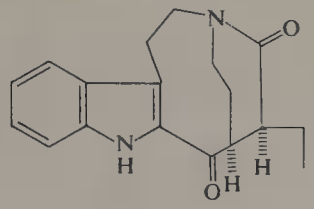
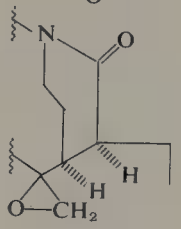
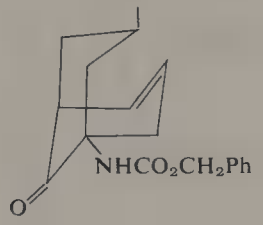
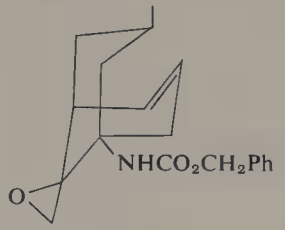
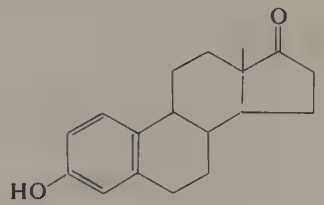
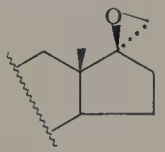
Ketone	Ylide	Reaction Conditions	Products (Yields, %)[a]	References
C_{15}				
	A_1	NaH, DMSO, 25° (3.5 hr)	 (74–80)	48
Benzalacetophenone	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0° (10 min), 25° (30–60 min)	 (87)	14
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0° (30 min), 25° (1 hr)	 (91)	55
	B_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO, 25° (1 hr), 50°–55° (1 hr)	(42)	55
	B_1	*n*-C_4H_9Li, DMSO, 50° (3 hr)	(86)	56
	A_1	NaH, DMSO, 25° (3.5 hr)	 (90)	48
	B	Unstated	 (unstated)	21

		$KOC(CH_3)_3$, PhH, 25°		(50)	54
C_{16}					
	A_1	*n*-C_4H_9Li, THF, 0° (30 min)		(22)	57
	A_1	NaH, DMSO, 25° (3.5 hr)		(98)	48
C_{17}					
	B_1	NaH, DMSO, 35° (1.3 hr), 25° (overnight)		(95)[b]	58
Ferrocenyl phenyl ketone	A_1	 $NaCH_2SCH_3$, DMSO/THF, −15° (5 min), 25° (30 min)		(72)	37
	B_1	NaH, DMSO, 55° (1.5 hr)	No reaction		37

(*continued*)

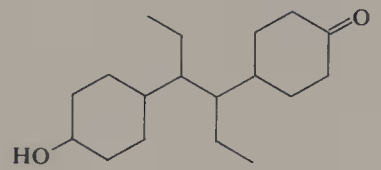
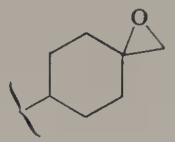
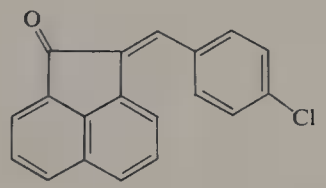
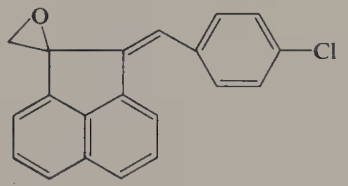
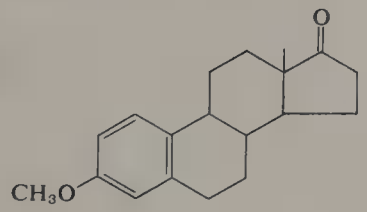
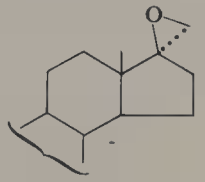
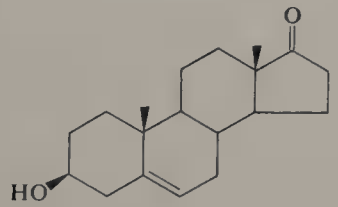
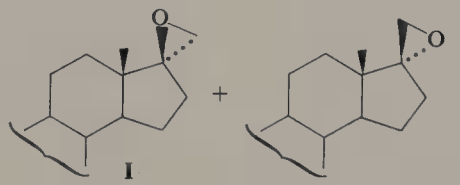
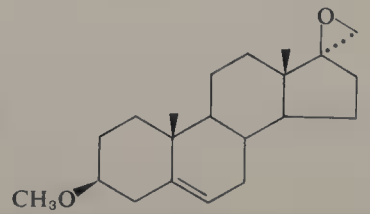
TABLE A.I (*continued*)

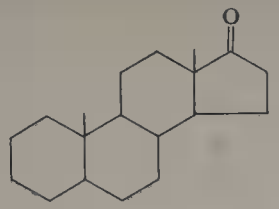
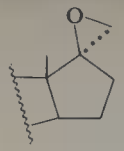
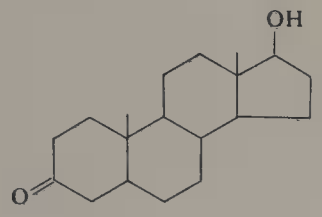
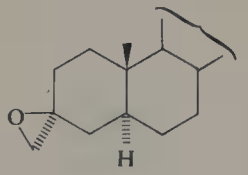
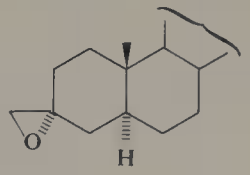
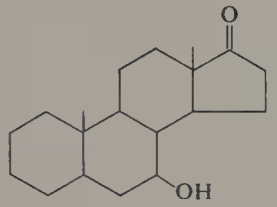
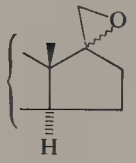
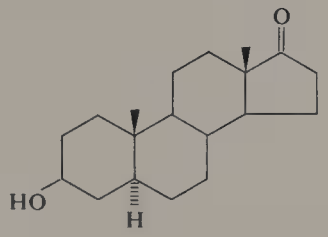
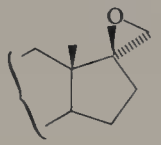
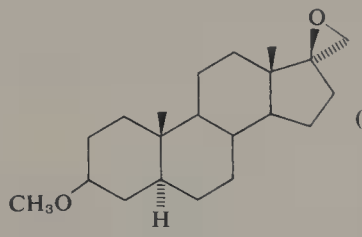
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B	NaH, DMSO, 25° (1 hr)	 (unstated)	59
	B_1	NaH, DMSO, 25° 60° (45 min)	 (88)	60
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, −10° (2 hr), 25° (2 hr)	 (88)	60
 *cis*-3	B_1	NaH, DMSO, 25° (15 min), 50° (1 hr)	 (50)	61
trans-3	B_1	NaH, DMSO, 25° (15 min), 50° (1 hr)	(64)	61

C_{18} 	A	Unstated		(unstated)	62
Codeinone	B_2	NaH, THF, 55° (1 hr), 25° (overnight)		(6)	129
	A	Unstated		(unstated)	63
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, 0° (1 hr), 25° (1 hr)		(66)	64
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −5° (2 hr)		(high)	65

(continued)

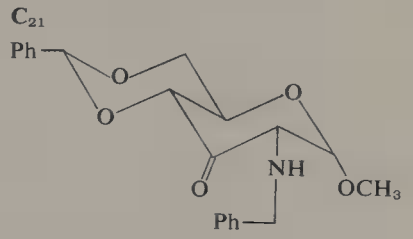
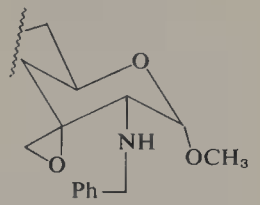
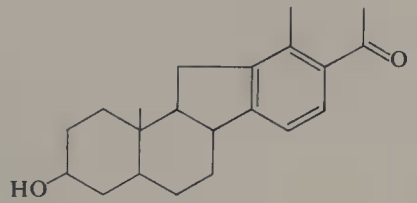
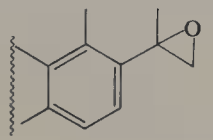
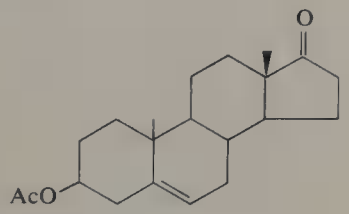
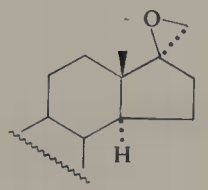
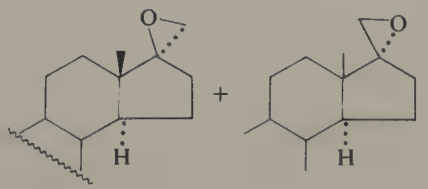
TABLE A.I (*continued*)

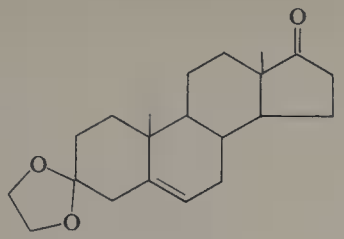
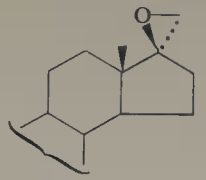
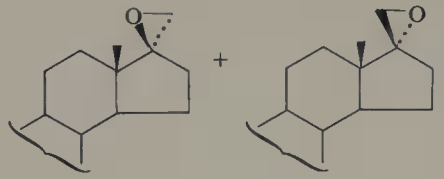
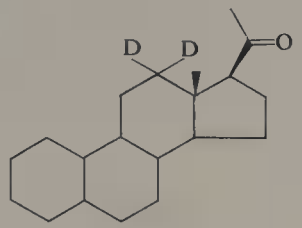
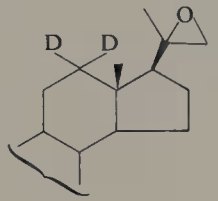
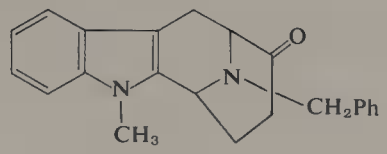
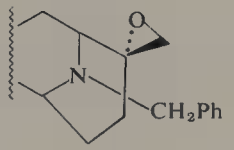
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_1	NaH, DMSO, 50° (1.5 hr)	 (100)	66
C_{19} 	A_1	$KOC(CH_3)_3$, DMSO, 25° (1 hr)	 (85)	67
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, −5° (2 hr)	 (90)	65
	B_1	NaH, DMF	 I (41) + (7)	68, 69
	A_1	KNH_2, DMSO	I +  (unstated)	70

	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, $-5°$, 20° (15 hr)		(84)	71
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 25° (16 hr), 50° (2 hr)	 +  2 : 1	(79)	65
	B_1	NaH, DMSO, 21° (16 hr), 50° (2 hr)	(—)	(63)	72
	B	Unstated		(unstated)	73
	A_1	KNH_2, DMSO	 + 	(unstated)	70

(*continued*)

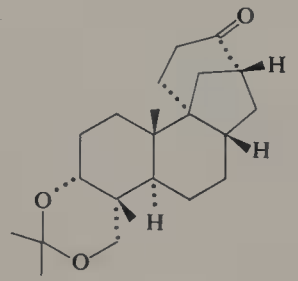
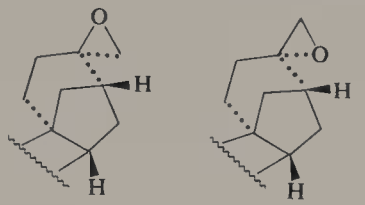
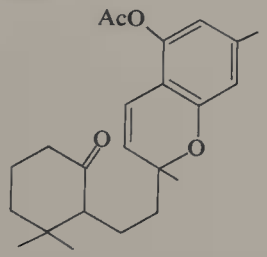
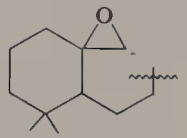
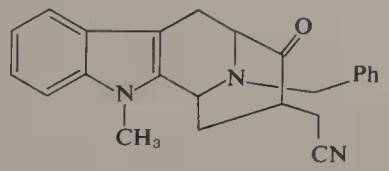
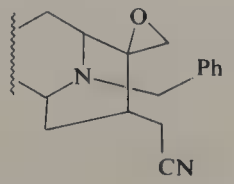
TABLE A.I (*continued*)

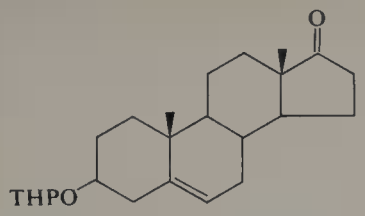
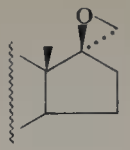
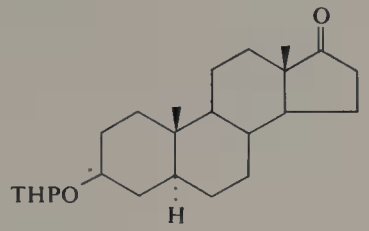
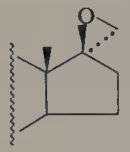
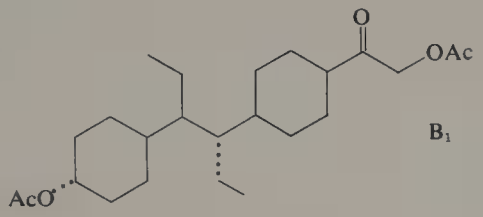
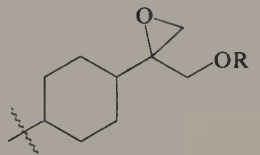
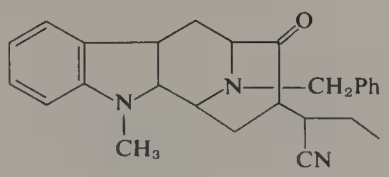
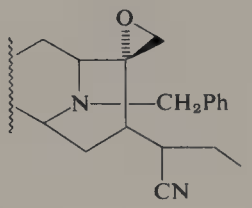
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
C_{21} 	B_1	NaH, DMSO, 50° (4 hr), 25° (12 hr)	 (64)	74
	A	Unstated	 (unstated)	75
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0° (45 min)	 (quantitative)	73
	A	Unstated	(75–90)	69
	B_1	NaH, DMF, 25° (16 hr)	 (98)	73

	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, $-5°$, 20° (15 hr)		(88)	71
	B_1	NaH, $\overset{O}{\overset{\|}{S}}$MSO, 20° (4 hr), 55° (3 hr)	 2 : 1	(96)	76
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 25° (1.5 hr)		(unstated)	77
C_{22} 	A or B	Unstated		(96)	78

(continued)

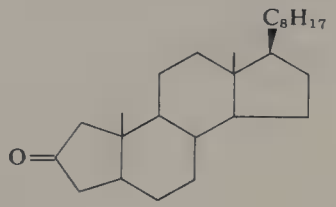
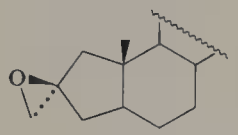
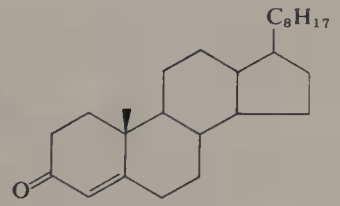
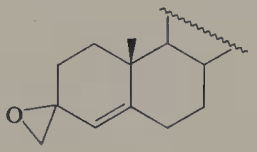
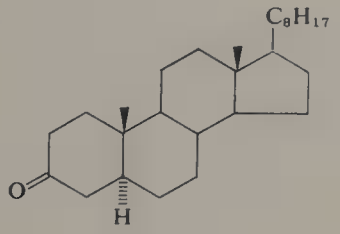
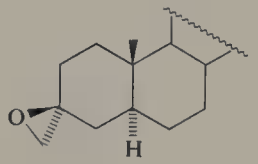
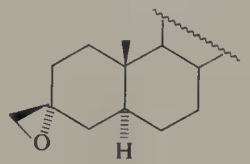
TABLE A.I (*continued*)

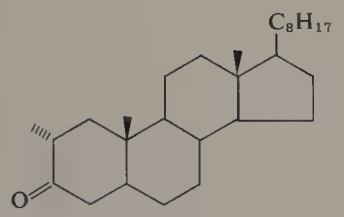
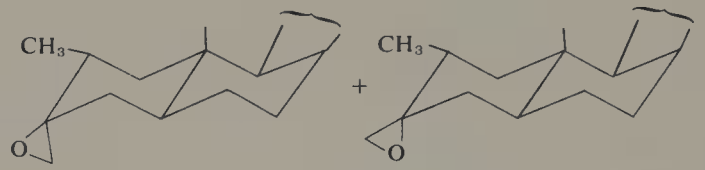
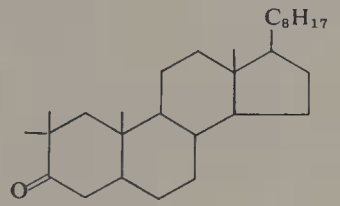
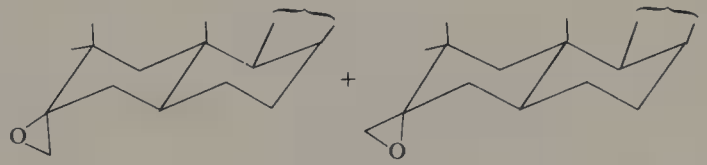
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	A_1	NaH, DMSO/THF, 0° (15 min), 25° (30 min)	 1 : 1	78a
	B_1	NaH, DMSO/THF, 25° (2 hr), 50° (45 min)	(20)	78a
C_{23} 	A	DMSO		(unstated) 79
C_{24} 	B_1	NaH, DMSO, 25° (4 hr)		(70) 80

	A_1	KNH_2, DMSO	 (80)	70
	A_1	KNH_2, DMSO	 (unstated)	70
	B_1	NaH, DMSO/THF, 25° (overnight)	 R = H (50) R = Ac (12)	80a
C_{26} 	A or B	Unstated	 (unstated)	78

(*continued*)

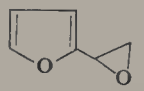
TABLE A.I (*continued*)

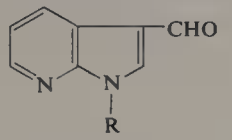
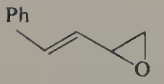
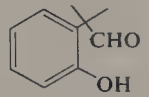
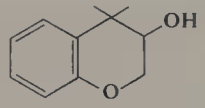
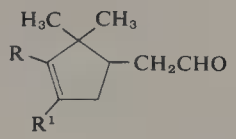
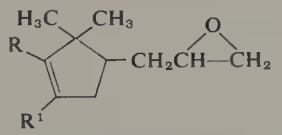
Ketone	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_1	NaH, DMSO/THF, 25° (10 min), 95° (24 hr)	 (unstated)	81
C_{27}				
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0° (19 min), 25° (30–60 min)	 (90.5)	14
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, −5° (0.5 hr)	 +  (82–92)	65, 82
			2 : 1	
	B_1	NaH, DMSO/THF, 25° (16 hr), 50° (2 hr)	0 : Only (80)	65
	B_1	NaH, DMSO/THF, 25° (1 hr), 50° (1 hr)	1 : 32 (85)	82

C_{28} 							
	B_1	NaH, DMSO/THF, 25° (1 hr), 50° (1 hr)	1	:	32	(83)	82
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −10° (10 min), 25° (1 hr)	1	:	3	(81)	82
C_{29} 							
	B_1	NaH, DMSO/THF, 25° (1 hr), 50° (1 hr)	1	:	16	(82)	82
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, −10° (10 min), 25° (1 hr)	2	:	1	(93)	82

[a] When the products obtained under various reaction conditions are the same, the structural formulas are not repeated. Only the yields (%) are given.
[b] Yield for further transformation product, not of epoxide.

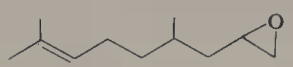
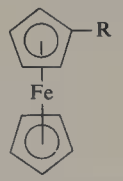
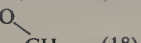
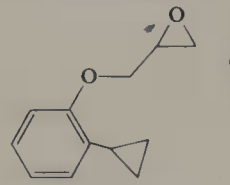
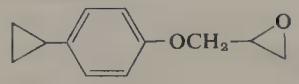
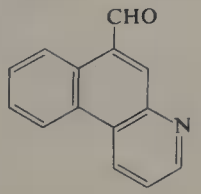
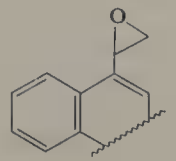
TABLE A.II
Epoxidations with Methylides: Aldehydes

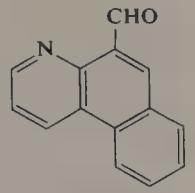
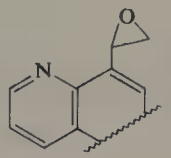
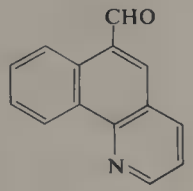
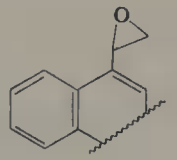
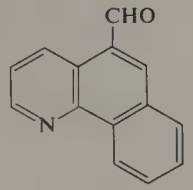
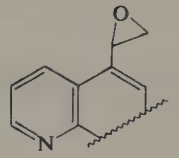
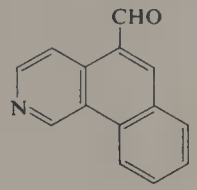
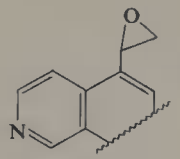
Aldehyde	Ylide	Reaction conditions	Products (Yields, %)[a]	References
C_4				
Isobutyraldehyde	A_3	$KOC(CH_3)_3$, DMSO, 25°	Isopropyloxirane (30)	1
C_5				
Furfuraldehyde	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (25)	1
C_7				
3,4-Dichlorobenzaldehyde	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, ice-salt bath	3,4-Dichlorophenyloxirane (68)	83
p-Chlorobenzaldehyde	C_1	NaH, THF, 25° (5 hr)	*p*-Chlorophenyloxirane (60)	33, 84
	C_3	NaH, DMSO, 25° (12 hr)	(74)	17
	C_4	NaH, DMSO, 50° (2 hr)	(62)	15
	C_5	NaH, DMSO, 25° (overnight)	(51)	17
Benzaldehyde	A_3	NaH, DMSO, 25°	Phenyloxirane (65)	1
	C_3	NaH, DMSO, 25° (25 hr)	(60, 20% opt. yield)	17
	C_4	NaH, DMSO, 50° (2 hr)	(57)	15
	$n\text{-}C_{12}H_{25}\overset{\oplus}{S}(CH_3)_2Cl^{\ominus}$	NaOH, H_2O/PhH, 25° (10 hr)	(86)	7
	B_1	NaOH, H_2O/CH_2Cl_2, 50° (48 hr)	(20–30)	130
	A_1	Electrolysis, 25°	(28)	6
		Electrolysis, DMSO, 25°	(32)	6
	B_2	NaH, THF, 55° (2.5 hr)	(55.6)	14
	A_2	NaOH, PhH/H_2O/n-C_3H_7OH, 70° (1 hr)	(68)	85
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0° (10 min), 25° (30 min)	(75.4)	14
		NaOH, H_2O/CH_2Cl_2, $(n\text{-}C_4H_9)_4NI$, 50° (48 hr)	(90)	130

		$KOC(CH_3)_3$, DMSO, 25°	(65)	86
n-Heptanal	C_2	NaH, DMSO, 25° (2 hr)	*n*-Hexyloxirane (39)	17
	C_4	NaH, DMSO, 50° (4 hr)	(37)	15
C_8				
p-Methoxybenzaldehyde	A_3	$NaNH_2$, DMSO, 25°	*p*-Methoxyphenyloxirane (58)	1
o-Methoxybenzaldehyde	B	Unstated	*o*-Methoxyphenyloxirane (80)	87
	A	Unstated	No reaction	88
C_9				
Cinnamaldehyde	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (40)	1
	A_1	$NaOH, H_2O/CH_2Cl_2, (n\text{-}C_4H_9)_4NI$, 50° (48 hr)	(85)	130
C_{10}				
4-Cyclopropylbenzaldehyde	A_1	 DMSO/THF, 0°	4-Cyclopropylphenyloxirane (79)	89
	B	Unstated	 (70)	25
	B_1	NaH, DMSO, 25° (1 hr), 50° (05. hr)	 $R = H, R^1 = CH_3$ (55) $R = CH_3, R^1 = H$ (68)	90, 91

(*continued*)

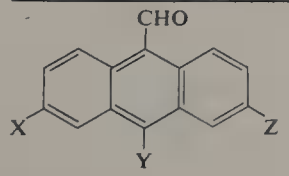
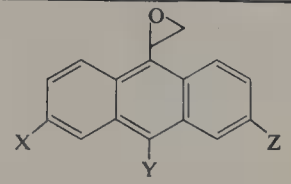
TABLE A.II (*continued*)

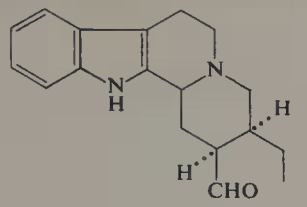
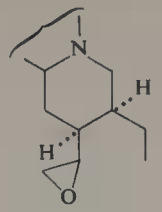
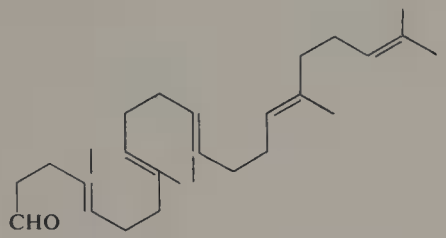
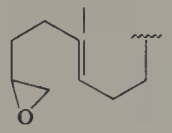
Aldehyde	Ylide	Reaction conditions	Products (Yields, %)[a]	References
3,7-Dimethyl-6-octenal	A_1	Unstated	 (51)	92
C_{11}				
Ferrocenyl carboxaldehyde				
	A_1	$NaCH_2SOCH_3$, DMSO/THF $-15°$ (5 min), 25° (30 min)	R = CH_2CHO (64)	37
	B_1	NaH, DMSO, 55° (1.5 hr),	R = CH_2COCH_3 (27) + R = $COCH_3$ (10) + R =  (18)	37
o-Cyclopropylphenoxyacetaldehyde	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0°	 (44)	89
p-Cyclopropylphenoxyacetaldehyde	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0°	 (unstated)	89
C_{14}				
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, ice-salt bath	 (49)[b]	83

	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, ice-salt bath	 (71)[b]	83
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, ice-salt bath	 (65)[b]	83
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, ice-salt bath	 60[b]	83
	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, ice-salt bath	 (27)[b]	83
m-Benzyloxybenzaldehyde	B_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO	*m*-Benzyloxyphenyloxirane (80)	93
C_{15}				
9-Phenanthraldehyde	A_1	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO/THF, ice-salt bath	9-Phenanthryloxirane (70)[b]	83

(*continued*)

TABLE A.II (*continued*)

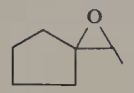
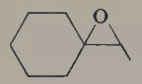
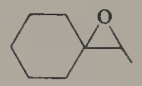
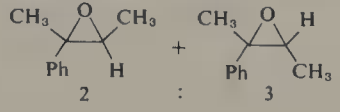
Aldehyde	Ylide	Reaction conditions	Products (Yields, %)[a]	References
				
			1	
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, ice-salt bath	X = Y = Z = H (68)[b]	83
X = Z = H, Y = Br	A	Unstated	X = Z = H, Y = Br (67)	94
X = Z = H, Y = Cl	A	Unstated	X = Z = H, Y = Cl (96)	94
X = Y = Cl, Z = H	A	Unstated	No reaction	94
X = Z = Br, Y = Cl	A	Unstated	No reaction	94

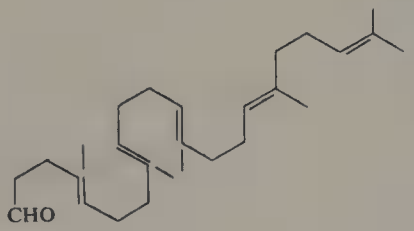
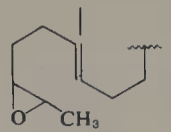
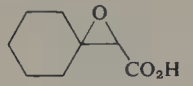
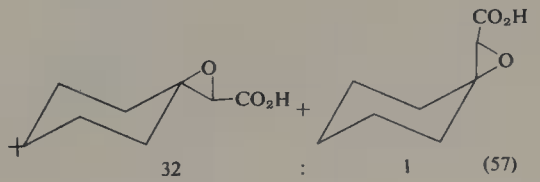
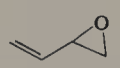
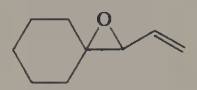
C_{18} 	B_1	NaH, DMSO, 25° (15 min), 60° (30 min)	 (unstated)	60
C_{27} 		Unstated		(60–80)

[a] When the products obtained under various reaction conditions are the same, the structural formulas are not repeated. Only the yields (%) are given.
[b] Yield of transformation product after further reaction of crude epoxide.

TABLE A.III

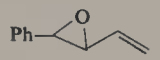
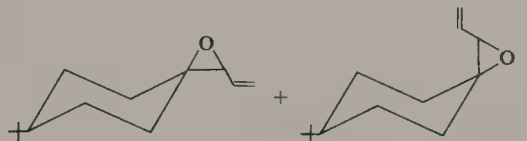
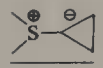
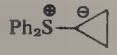
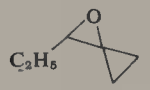
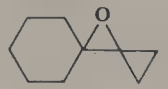
Epoxidations with Substituted Ylides

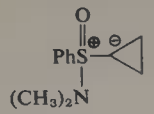
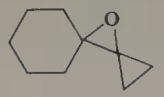
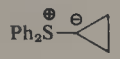
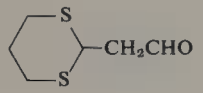
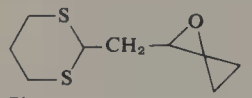
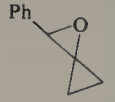
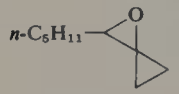
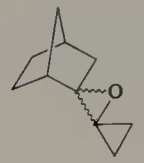
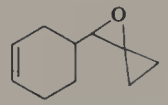
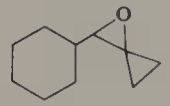
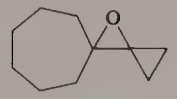
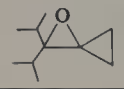
Ylide	Carbonyl	Reaction conditions	Products (Yields, %)[a]	References
$\diagdown$SCHCH$_3$				
Ph_2SCHCH_3	Cyclopentanone	$LiN(C_2H_5)_2$, THF, −76°	 (65)	96
	Cyclohexanone	PhLi, THF, −76°	 (50)	96
		n-C_4H_9Li, THF, −76°	(30–50)	96
		$(CH_3)_3CLi$, THF, −76°	(74)	96
		$LiN(C_2H_5)_2$, THF, −76°	(71)	96
$(C_2H_5)_2SCHCH_3$	Cyclohexanone	$LiN(C_2H_5)_2$, THF, −76°	 (unstated)	96
4-$CH_3C_6H_4S(O)CHCH_3$ $\vert$ $N(CH_3)_2$	4-Chlorobenzaldehyde	NaH, DMF, 0°–5° (86 hr), 25° (1 hr)	1-(4′-Chlorophenyl)-2-methyloxirane *cis*:*trans*, 1:1 (78)	97
Ph_2SCHCH_3	Benzaldehyde	$LiN(C_2H_5)_2$, THF, −76°	1-Phenyl-2-methyloxirane *cis*:*trans*, 1:1 (85)	96
	Benzaldehyde	Electrolysis, DMSO, 25°	1-Phenyl-2-methyloxirane (10)	96
$(C_2H_5)_2SCHCH_3$	Benzaldehyde	NaOH, H_2O/ PhH/C_2H_5OH (2 hr)	1-Phenyl-2-methyloxirane *cis*:*trans*, 4:1 (70)	85
4-$CH_3C_6H_4S(O)CHCH_3$ $\vert$ $N(CH_3)_2$	Benzaldehyde	NaH, DMF, 0°–5° (86 hr), 25° (1 hr)	1-Phenyl-2-methyloxirane *cis*:*trans*, 3:2 (67)	97
	Acetophenone	NaH, DMF, 0°–5° (4 days), 25° (1 day)	 (62)	97

	4-*t*-Butylcyclohexanone	NaH, DMF, 0°–5° (4 days), 25° (1 day)		(88)	97
		NaH, DMSO, 25° (72 hr)		(64)	17
$(C_2H_5)SCHCH_3$		Unstated	 *cis*:*trans*, 1:1	(60–80)	95, 97a
$\diagdown SCHCO_2^{\ominus}$					
$(CH_3)_2SCHCO_2^{\ominus}$	Cyclohexanone	NaH, DMSO, 25°		(67)	98
	4-*t*-Butylcyclohexanone	NaH, DMSO, 25°	 32 : 1	(57)	98
$\diagdown SCHCH{=}CH_2$					
$(CH_3)_2SCHCH{=}CH_2$	Formaldehyde	NaOH, H_2O/PhH/CH_3OH, 68° (2 hr)		(7)	85
$Ph_2SCHCH{=}CH_2$	Cyclohexanone	*n*-C_4H_9Li, THF, −76° (1 hr), 25° (1 hr)		(52–56)	99
		$(CH_3)_3CLi$, THF		(80)	99

(*continued*)

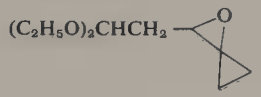
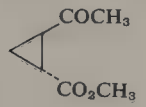
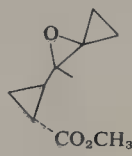
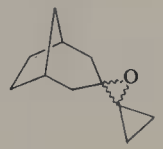
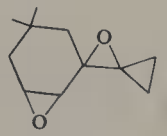
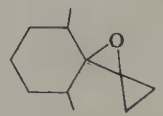
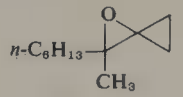
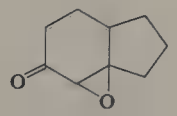
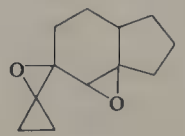
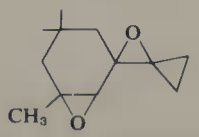
TABLE A.III (*continued*)

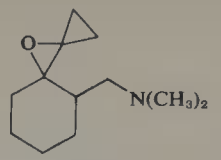
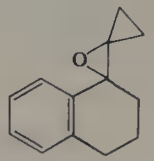
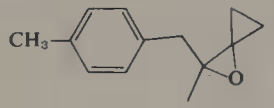
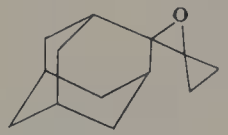
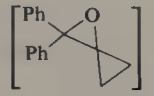
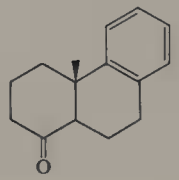
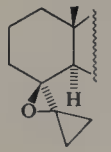
Ylide	Carbonyl	Reaction conditions	Products (Yields, %)[a]	References
$(CH_3)_2SCHCH{=}CH_2$	Benzaldehyde	NaOH, H_2O/isopropanol, 68° (2.5 hr)	 (73)	85
		NaOH, $H_2O/PhCH_3$, 25° (16.5 hr)	(60)	85
$Ph_2SCHCH{=}CH_2$	4-*t*-Butylcyclohexanone	*n*-C_4H_9Li, THF, −78° (1 hr), 25° (1 hr)	 4 : 1 (49)	99
				
	Propanal	KOH, DMSO, 25° (2 hr)	 (100)	100
	Cyclopropylmethyl ketone	KOH, DMSO, 25° (4 hr)	 (86)	101
	Cyclopentanone	KOH, DMSO, 25° (3 hr)	 (94)	100
	Cyclohexanone	KOH, DMSO, 25° (4 hr)	 (81–97)	100
		$KOC(CH_3)_3$, DMSO, 25°	(94)	100
		$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DME/DMSO, −40° (15 min), 25° (30 min)	(61)	100, 102

	Cyclohexanone	NaH, DMSO, 25° (72 hr)	 (25)	97
		$NaCH_2SCH_3$, DME/DMSO, −45° (20 min), 25°	 (80)	103
	Benzaldehyde	$NaCH_2SCH_3$, DME/DMSO, −45° (15 min) 25° (30 min)	 (70)	100, 102
	Hexanal	KOH, DMSO, 25° (0.5 hr) KOH, DMSO, 25° (1.5 hr)	(87)  (92)	100 100
	2-Norbornanone	$NaCH_2SCH_3$, DME/DMSO, −40° (15 min), 25° (30 min)	 (65)	100, 102
		KOH, DMSO, 25° (10 hr)	(92)	100
	3-Cyclohexenecarboxaldehyde	KOH, DMSO, 25°	 (80)	100
	Cyclohexanecarboxaldehyde	KOH, DMSO, 25°	 (89)	100
	Cycloheptanone	KOH, DMSO, 25°	 (44)	100
	Diisopropyl ketone	KOH, DMSO, 25°	 (59)	100

(*continued*)

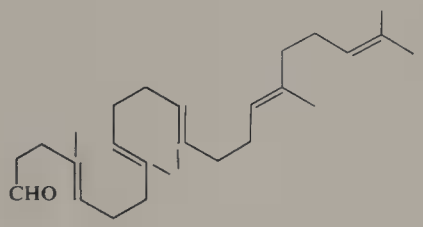
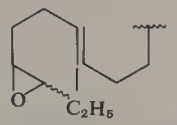
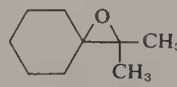
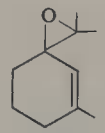
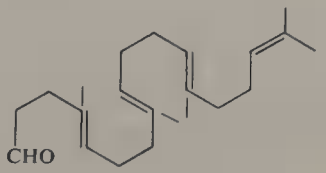
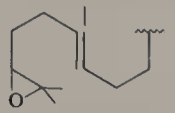
TABLE A.III (*continued*)

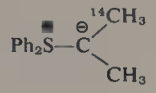
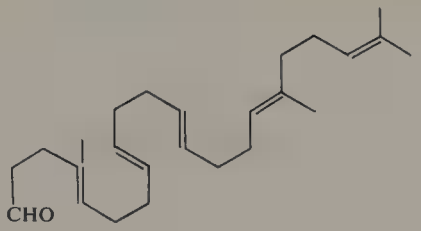
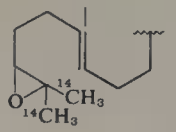
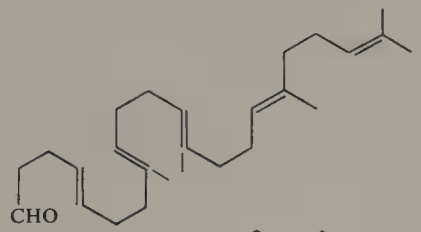
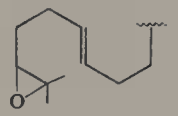
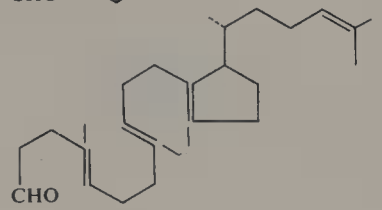
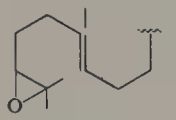
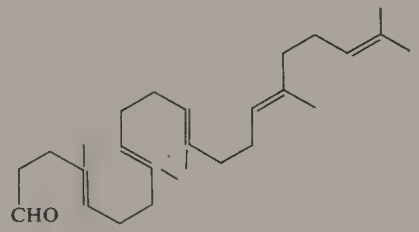
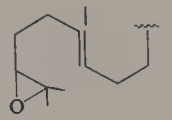
Ylide	Carbonyl	Reaction conditions	Products (Yields, %)[a]	References
	3,3-Diethoxypropanal	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DME/DMSO, −45° (20 min), 25° (40 min)	 (91)	103
		$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DME/DMSO, −40° (1 hr)	 (87)	104
	Bicyclo[3.2.1]octen-3-one	KOH, DMSO, 25°	 (44)	101
	5,5-Dimethyl-2,3-epoxycyclohexanone	KOH, DMSO, 25°	 (96)	105
	2,6-Dimethylcyclohexanone	KOH, DMSO, 25° (27.5 hr)	 (100)	106
	2-Octanone	KOH, DMSO, 25° (18 hr)	 (92)	100
		KOH, DMSO, 25°	 (85)	105
	3,5,5-Trimethyl-2,3-epoxycyclohexanone	KOH, DMSO, 25°	 (88)	105

2-Dimethylaminomethylcyclohexanone	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DME, 45° (30 min), 25° (30 min)		(81)	103
1-Tetralone	KOH, DMSO, 25°		(69)	101
p-Tolylacetone	KOH, DMSO, 25° (1 hr)		(94)	107
Adamantanone	KOH, DMSO, 25° (overnight)		(92)[b]	27
4-*t*-Butylcyclohexanone	KOH, DMSO, 25°		(70)	100
Benzophenone	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DME/DMSO, −40° (5 min), 25° (30 min)		(75)	101, 102
	KOH, DMSO, 25° (4 hr)		(91)	101
	KOH, DMSO, 25° (4 hr)		(95)	101, 106

(*continued*)

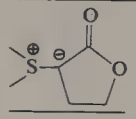
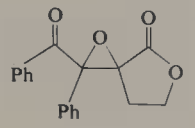
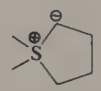
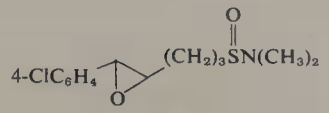
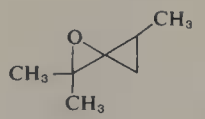
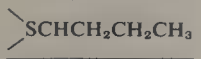
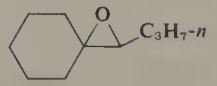
TABLE A.III (*continued*)

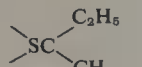
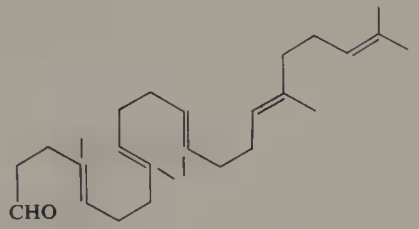
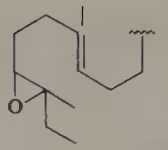
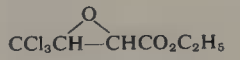
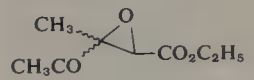
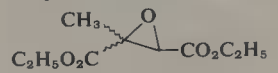
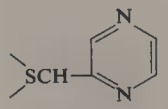
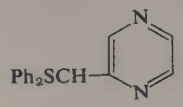
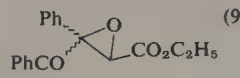
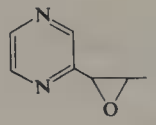
Ylide	Carbonyl	Reaction conditions	Products (Yields, %)[a]	References
$\diagdown SCHCH_2CH_3$				
$Ph_2SCHCH_2CH_3$		Unstated	 *cis*:*trans*, 1:1 (60–80)	95
$\diagdown SC(CH_3)_2$				
$Ph_2SC(CH_3)_2$	Cyclohexanone	$LiN(i\text{-}C_3H_7)_2$, DME, −70° (1 hr), −30° to −50° (2 hr)	 (74–82)	108
		$(CH_3)_3CLi$, THF, −70°	(55–60)	108
	Benzaldehyde	$LiN(i\text{-}C_3H_7)_2$, DME, −70° (2 hr)	1,1-Dimethyl-2-phenyloxirane (74–82)	108
		$(CH_3)_3CLi$, THF, −70°	(55–60)	108
	3-Methyl-2-cyclohexenone	$LiN(i\text{-}C_3H_7)_2$, DME, 70° (2 hr)	 (unstated)	109
	n-Heptanal	$LiN(i\text{-}C_3H_5)_2$, DME, −70° (2 hr)	1,1-Dimethyl-2-*n*-hexyloxirane (74–82)	108
	n-Dodecanal	$LiN(i\text{-}C_3H_7)_2$, DME, −70° (2 hr)	1,1-Dimethyl-2-*n*-undecyloxirane (74–82)	108
	Benzophenonone	$LiN(i\text{-}C_3H_7)_2$, DME, −70° (14 hr)	1,1-Dimethyl-2,2-diphenyloxirane (37)	108
			α-Methyl-α-phenylpropiophenone (49)	108
		Unstated	 (unstated)	110

		Unstated		(unstated)	111
$Ph_2SC(CH_3)_2$		Unstated		(63–65)	112, 113
		Unstated		(80)	114
		Unstated		(34)	95

(*continued*)

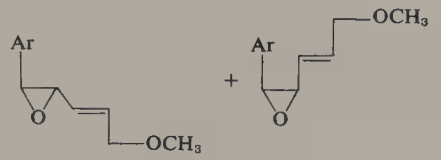
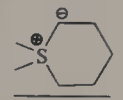
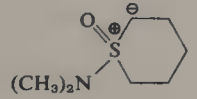
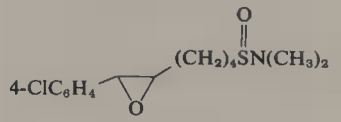
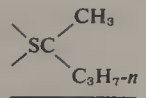
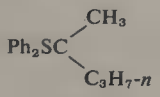
TABLE A.III (*continued*)

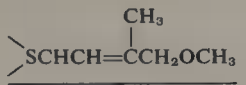
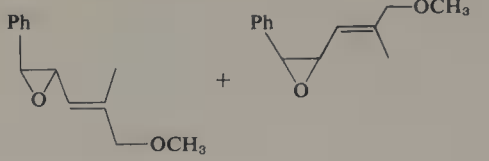
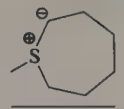
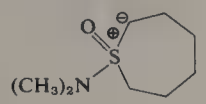
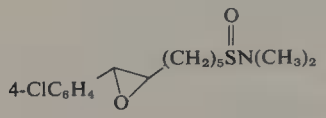
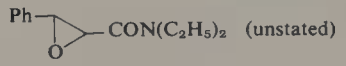
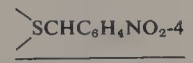
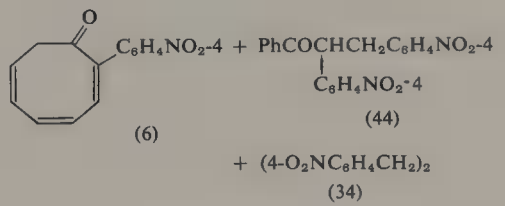
Ylide	Carbonyl	Reaction conditions	Products (Yields, %)[a]	References
	Benzil	THF, 25° (2.5 hr), 84° (2 hr)	 (13)	115
	4-Chlorobenzaldehyde	NaH, DMSO, 25°	 (66)	116
	Acetone	KOH, DMSO, 25° (1 hr)	 (100)	100
	Cyclopentanone	KOH, DMSO, 25° (1 hr)	 (83)	100
	4-*t*-Butylcyclohexanone	KOH, DMSO, 25° (4 hr)	 (95)	100
				
$Ph_2SCHC_3H_7$-*n*	Cyclohexanone	$LiN(i\text{-}C_3H_7)_2$, THF, −76°	 (81)	96

	4-Nitrobenzaldehyde	n-C_4H_9Li, THF, $-70°$	 (40) $4\text{-}O_2NC_6H_4—CH_2OH$ (53)	117
 $Ph_2SC(C_2H_5)CH_3$	Benzaldehyde	$LiN(i\text{-}C_3H_7)_2$, THF, $-76°$	1-Phenyl-2-n-Propyloxirane *cis*:*trans*, 1.0 : 1.5 (61)	96
		Unstated	 *cis*:*trans*, 1:1 (60–80)	95
$(CH_3)_2SCHCO_2C_2H_5$		Unstated	*cis*:*trans*, 2:1 (unstated)	118
	Trichloracetaldehyde	PhH, 25° (24 hr)	 (22)	119
	Biacetyl	PhH, 40°–50° (3 hr), 25° (18 hr)	 (50)	119
	Ethyl pyruvate	Acetone, reflux (0.5 hr)	 (42)	119
 	Benzil	PhH, 40°–50° (2 hr), 25° (18 hr)	 (92)	119
	Acetaldehyde	DME, 25°	 (33)[b]	120

(continued)

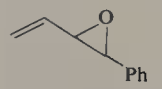
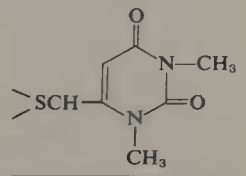
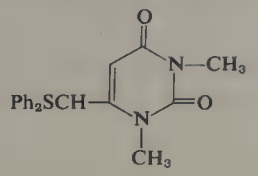
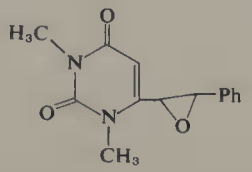
TABLE A.III (*continued*)

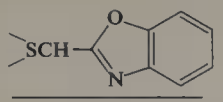
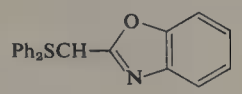
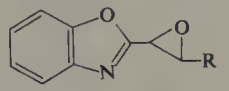
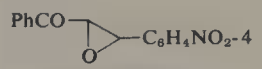
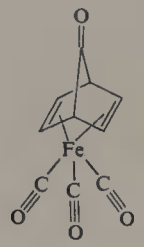
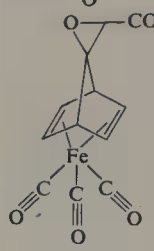
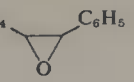
Ylide	Carbonyl	Reaction conditions	Products (Yields, %)[a]	References
$(CH_3)_2SCHCH{=}CHCH_2OCH_3$				
	p-Nitrobenzaldehyde	$NaOCH_3$, CH_3OH, $-78°$	Ar = *p*-$O_2NC_6H_4$, 2.4 : 1 (69)	127
	Benzaldehyde	$NaOCH_3$, CH_3OH, $-78°$	Ar = Ph, 3 : 1 (79)	127
	1-Naphthaldehyde	$NaOCH_3$, CH_3OH, $-78°$	Ar = 1-napthyl, 1.9 : 1 (78)	127
	9-Anthraldehyde	$NaOCH_3$, CH_3OH, $-78°$	Ar = 9-Anthryl, >9 : 1 (65)	127
				
	4-Chlorobenzaldehyde	NaH, DMSO, 25°	 (80)	116
				
	Benzaldehyde	$LiN(i\text{-}C_3H_7)_2$, DME, $-76°$	1-Methyl-1-*n*-propyl-2-phenyloxirane (unstated)	108

					
	Benzaldehyde	$NaOCH_3$, CH_3OH, $-78°$	 1 : 1	(37)	127
					
	4-Chlorobenzaldehyde	NaH, DMSO, 25°		(66)	116
					
$(CH_3)_2SCHCON(C_2H_5)_2$	Benzaldehyde	Unstated	 (unstated)		122
					
$(CH_3)_2SCHC_6H_4NO_2$-4	Tropone	NaH, THF, $-40°$	 (6) (44) (34)		122

(continued)

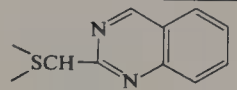
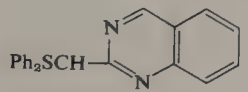
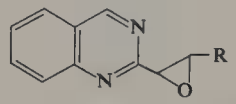
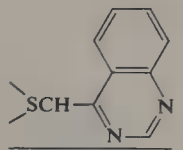
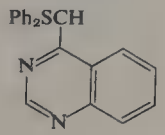
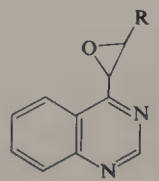
TABLE A.III (*continued*)

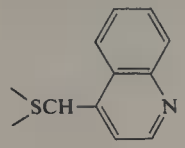
Ylide	Carbonyl	Reaction conditions	Products (Yields, %)[a]	References
>SCHPh				
$(CH_3)_2SCHPh$	Formaldehyde	NaOH, $H_2O/PhCH_3$, 84° (10 min)	Phenyloxirane (84)	85
	Acetaldehyde	NaOH, H_2O/PhH, 64° (30 min)	1-Methyl-2-phenyloxirane (48)	85
		n-C_4H_9Li, THF, −50°	(48)	117
	Acrolein	NaOH, H_2O/PhH, 70° (15 min)	 (16)	85
	Acetone	NaOH, H_2O/hexane, 50° (1 hr)	1,1-Dimethyl-2-phenyloxirane (57)	85
	p-Chlorobenzaldehyde	n-C_4H_9Li, THF, −50°	*trans*-1-*p*-Chlorophenyl-2-phenyloxirane (63)	117
	p-Nitrobenzaldehyde	n-C_4H_9Li, THF, −50°	*trans*-1-*p*-Nitrophenyl-2-phenyloxirane (72)	117
	Benzaldehyde	NaOH, H_2O/ethanol, 65° (1 hr)	*trans*-1,2-Diphenyloxirane (45)	85
		n-C_4H_9Li, THF, −50°	(58)	117
		Electrolysis, 25°	(40)	6
$(HOCH_2CH_2)_2SCHPh$	Benzaldehyde	NaOH, H_2O, 70°–80°	*trans*-1,2-Diphenyloxirane (19)	85
$(CH_3)_2SCHPh$	Acetophenone	NaOH, H_2O/hexane, 30°–60° (2 hr)	*trans*-1,2-Diphenyl-1-methyloxirane (45)	85
	4-nitroacetophenone	n-C_4H_9Li, THF, −50°	*trans*-2-*p*-Nitrophenyl-1-methyl-1-phenyloxirane (44)	117
				
	Benzaldehyde	DME, 25°	 (52)	120

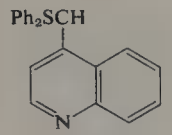
				120
				
	Propanal	DME, 25°	R = C_2H_5 (62)	120
	Benzaldehyde	DME, 25°	R = C_6H_5 (70)	120
				
$(CH_3)_2SCHCOPh$	4-Nitrobenzaldehyde	THF, reflux (27 hr)	 (10)	123
		$(C_2H_5)_3N$, DMSO, 0° (5.5 hr)	 (unstated)	124
				
$(CH_3)_2SCHC_6H_4CH_3$-4	Benzaldehyde	Electrolysis, 25°	$(4\text{-}CH_3C_6H_4CH_2)_2$ + 4-$CH_3C_6H_4CH{=}CHC_6H_5$ (8) (14) + 4-$CH_3C_6H_4$  (13)	6

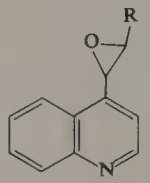
(continued)

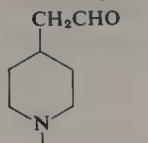
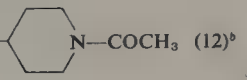
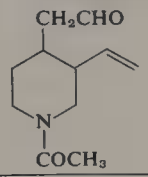
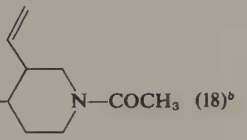
TABLE A.III (*continued*)

Ylide	Carbonyl	Reaction conditions	Products (Yields, %)[a]	References
				
				
	Propanal	DME, 25°	R = C_2H_5 (65)	120
	Benzaldehyde	DME, 25°	R = C_6H_5 (19)[b]	120
				
				
	Acetaldehyde	DME, 25°	R = CH_3 (36)[b]	120
	Propanal	DME, 25°	R = C_2H_5 (50)	120
	Benzaldehyde	DME, 25°	R = C_6H_5 (48)	120



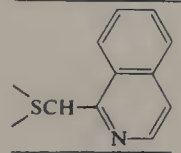
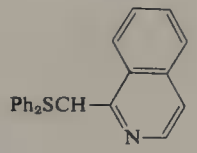
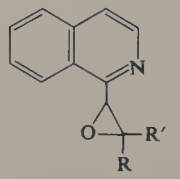
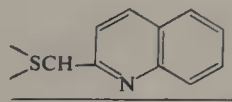
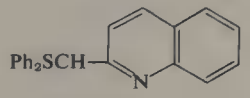
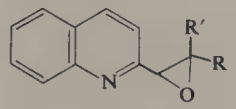


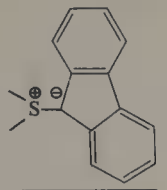


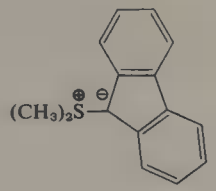
Propanal	DME, 25°	$R = C_2H_5$ (62)	120
Benzaldehyde	DME, 25°	$R = C_6H_5$ (58)	120
	DME, 25°	$R = CH_2$—  (12)[b]	125
	DME, 25°	$R = CH_2$—  (18)[b]	125

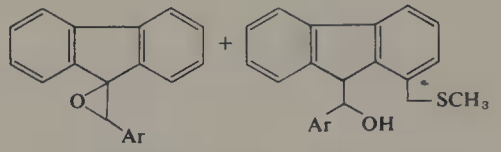
(continued)

TABLE A.III (*continued*)

Ylide	Carbonyl	Reaction conditions	Products (Yields, %)[c]	References
				
				
	Propanal	DME, 25°	R = C_2H_5, R′ = H (42)	120
	Cyclohexanone	DME, 25°	R = R′ = $(CH_2)_5$ (60)[b]	120
	Benzaldehyde	DME, 25°	R = C_6H_5, R′ = H (65)	120
				
				
	Propanal	DME, 25°	R = C_2H_5, R′ = H (37)	120
	Acetone	DME, 25°	R = R′ = CH_3 (17)	120
	Cyclohexanone	DME, 25°	R = R′ = $(CH_2)_5$ (52)[b]	120
	Benzaldehyde	DME, 25°	R = C_6H_5, R′ = H (47)	120



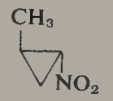
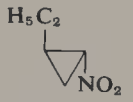
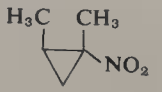
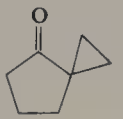
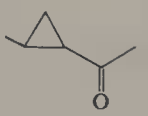
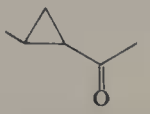
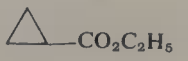
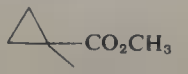


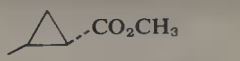
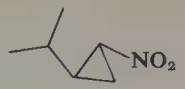
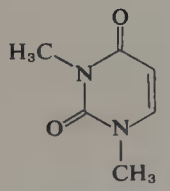
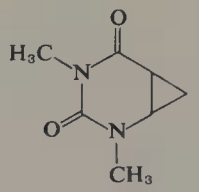
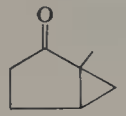
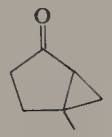
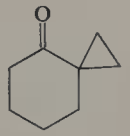


2,4-Dichlorobenzaldehyde	CH_2Cl_2, reflux (3 hr)	Ar = 2,4-$Cl_2C_6H_3$, (30)	(33)	126
4-Nitrobenzaldehyde	CH_2Cl_2, reflux, (3 hr)	Ar = 4-$O_2NC_6H_4$, (40)	(25)	126
2-Nitrobenzaldehyde	CH_2Cl_2, reflux (3 hr)	Ar = 2-$O_2NC_6H_4$, (30)	(35)	126
3-Nitrobenzaldehyde	CH_2Cl_2, reflux (3 hr)	Ar = 3-$O_2NC_6H_4$, (36)	(22)	126
4-Cyanobenzaldehyde	CH_2Cl_2, reflux (3 hr)	Ar = 4-NCC_6H_4, (33)	(29)	126

[a] When the products obtained under various reaction conditions are the same, the structural formulas are not repeated. Only the yields (%) are given.
[b] Yield of further transformation product after further reaction of crude epoxide.

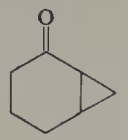
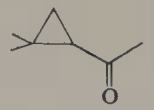
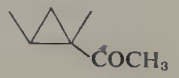
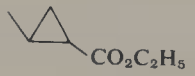
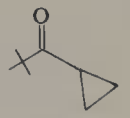
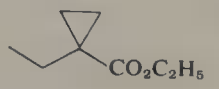
TABLE A.IV
Cyclopropanation with Methylides

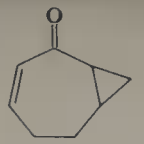
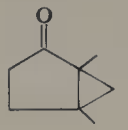
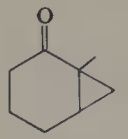
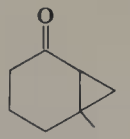
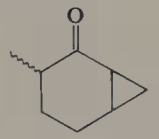
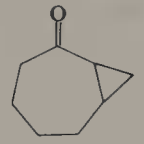
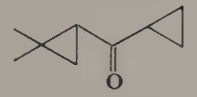
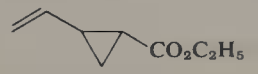
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
C_3				
1-Nitro-*trans*-1-propene	B_1	NaH, DMSO, 10° (1 hr), 50° (4 hr), 25° (12 hr)	 (31)	131
C_4				
Butadiene	A	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, −5° to 0°	 (30)	132
1-Nitro-1-butene	B_1	NaH, DMSO, 10° (1 hr), 50° (4 hr), 25° (12 hr)	 (40)	131
2-Nitro-*cis*-2-butene	B_1	NaH, DMSO, 10° (1 hr), 50° (4 hr), 25° (12 hr)	 (37)	131
C_5				
2-Bromocyclopentanone	B_1	NaH, DMSO, 25° (2 hr)	 (30)	133, 134
3-Penten-2-one				
cis	B	NaH, DMSO, 25° (overnight)	 (10)	135
trans	B	NaH, DMSO, 25° (overnight)	 (13)	135
Ethyl acrylate	B	NaH, DMSO, 25° (2 hr)	 (65)	136
Methyl methacrylate	B	NaH, DMF, 25° (1 hr)	 (20)	136

Methyl *trans*-crotonate	C_2	NaH, DMSO, 25° (16 hr)	 12% optical yield	(54)	17
1-Nitro-3-methyl-*trans*-1-butene	B_1	NaH, DMSO, 10° (1 hr), 50° (4 hr), 25° (12 hr)		(43)	131
C_6 	B_2	NaH, THF, reflux		(66)	137
$CH_3O_2CCH{=}CHCO_2CH_3$ *cis*	C_1	NaH, DMSO, 25° (1 hr)		(75)	33
	C_3	NaH, DMSO, 25° (12 hr)	18% optical yield	(56)	17
	C_3	NaH, THF, 25°	8% optical yield		17
trans	C_1	NaH, DMSO, 25° (1 hr)		(75)	33
	C_3	NaH, DMSO, 25° (12 hr)	15% optical yield	(60)	17
	C_5	NaH, DMSO, 25° (overnight)	19% optical yield	(55)	17
2-Methylcyclopent-2-enone	B	Unstated		(60)	138
3-Methylcyclopent-2-enone	B_1	NaH, DMSO		(51)	139
	B	Unstated		(82)	138
2-Bromocyclohexanone	B_1	NaH, DMSO, 25° (2 hr)		(28)	133, 134

(continued)

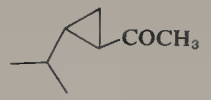
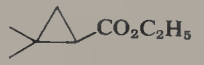
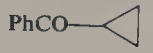
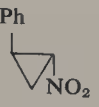
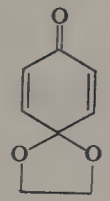
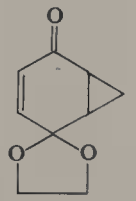
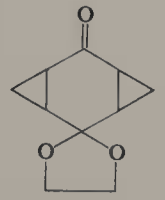
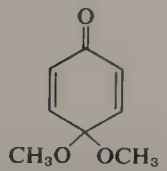
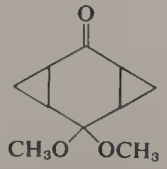
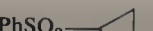
TABLE A.IV (*continued*)

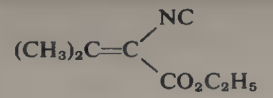
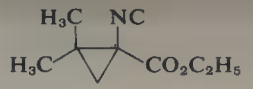
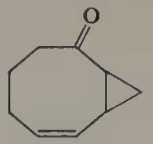
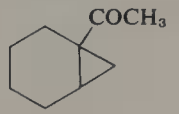
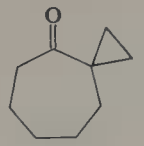
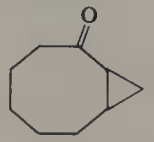
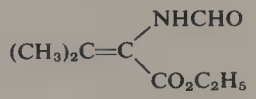
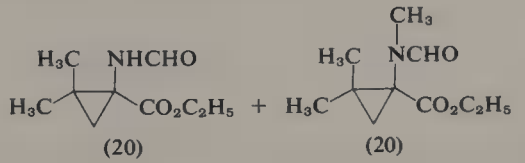
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
2-Cyclohexenone	B_1	NaH, DMSO, 50° (2 hr)	 (45)	140
4-Methyl-3-penten-2-one	C_4	NaH, DMSO, 25° (3 hr)	(60)	15
	B_1	NaH, DMSO, 25° (overnight)	 (38) (56)	135, 141
	B_1	NaH, DMF, 25° (1 hr)	(76)	136
	B_1	NaH, DMSO	(40)	34
	[illegible]	Unstated	(unstated)	142, 143
	C_4	NaH, DMSO, 25°	(62)	15
trans-3-Methyl-3-penten-2-one	B	Unstated	 (only)	144
Ethyl *trans*-crotonate	B_1	NaH, DMSO	(45)	34
	B	NaH, DMSO, 25° (2 hr)	 (60)	136
1-Bromo-3,3-dimethyl-2-butanone	B	NaH, DMF, 25° (1 hr)	(63)	136
	B_1	NaH, DMSO, 25° (2 hr)	 (33)	133, 134
Ethyl 2-bromobutyrate	B_1	NaH, DMSO, 25° (2 hr)	 (32)	133, 134
C_7				
2-Vinylpyridine	A_1	*n*-C_4H_9Li, THF, 0° (1 hr), 25° (3 hr)	2-Cyclopropylpyridine (40)	144a
4-Vinylpyridine	A_1	*n*-C_4H_9Li, THF, 0° (1 hr), 25° (3 hr)	4-Cyclopropylpyridine (45)	144a

Cyclohepta-2,6-dienone	B_1	NaH, DMSO, 0°–5° (20 min), 25° (3.5 hr)		(35)	145
2,3-Dimethylcyclopent-2-enone	B	Unstated		(40)	138
2-methylcyclohex-2-enone	B_1	NaH, DMSO		(65)	146
	B_1	NaH, DMSO, 50° (2 hr)		(76)	140
3-Methylcyclohex-2-enone	B_1	NaH, DMSO		(57)	147
6-Methyl-2-cyclohexenone	B_1	NaH, DMSO	 *cis*:*trans*, 1.8 :1	(63)	147
2-Cycloheptenone	B_1	NaH, DMSO, 25° (4 hr), 50° (1 hr)		(49)	148
$(CH_3)_2C{=}CHCCH{=}CH_2$ (O above CCH)	B	Unstated		(unstated)	149
Ethyl 2,4-pentadienoate	B_1	NaH, DMF, 25° (1 hr)		(62)	136

(*continued*)

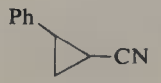
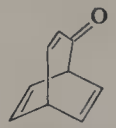
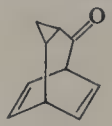
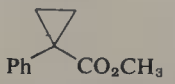
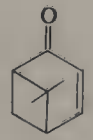
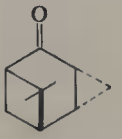
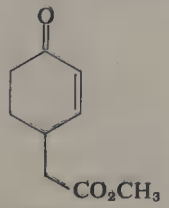
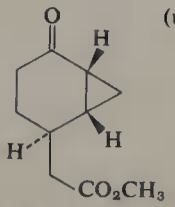
TABLE A.IV (*continued*)

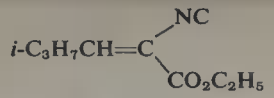
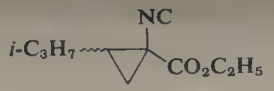
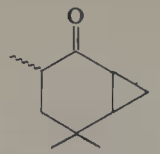
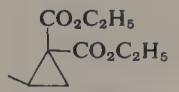
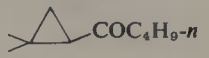
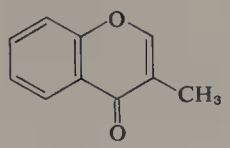
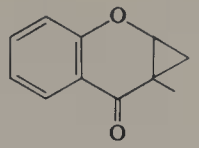
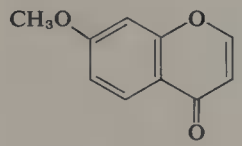
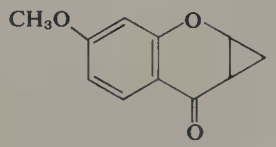
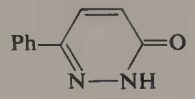
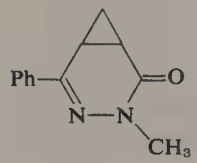
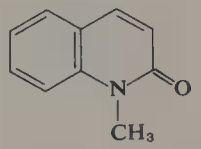
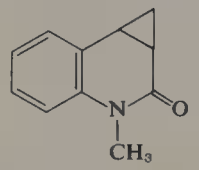
Acceptor	Ylides	Reaction conditions	Products (Yields, %)[a]	References
5-Methyl-*trans*-hex-3-enone	B	Unstated	 (35)	132
Ethyl 3-methylbutenoate	B_1	NaH, DMF, 25° (1 hr)	 (9)	136
C_8				
2-Methyl-6-vinylpyridine	A_1	*n*-C_4H_9Li, THF, 0° (1 hr), 25° (3 hr)	2-Cyclopropyl-6-methylpyridine (78)	144a
ω-Bromoacetophenone	B_1	NaH, DMSO, 25° (2 hr)	 (37)	133, 134
	C_4	NaH, DMF, 0° (12 hr), 25° (6 hr)	(25)	15
ω-Nitrostyrene	B_1	NaH, DMSO, 10° (1 hr), 50° (4 hr), 25° (12 hr)	 (44)	131
	B_1 (1 equivalent)	NaH, DMSO, 20° (2 hr), 50° (1 hr)	 (43)	150
	B_1 (excess)	NaH, DMSO, 20° (2 hr), 50° (1 hr)	 (74)	150
	B_1	NaH, DMF, 25° (16 hr)	 (unstated)	150a
$PhSO_2CH{=}CH_2$	C_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO, 25°	 (25)	84

	B_1	NaH, DMSO/THF, 25° (1 hr), 60°		(71)	151
Cycloocta-2,4-dienone	B_1	NaH, DMSO, 25° (2 hr)		(80)	151a
1-Acetylcyclohexene	B_1	NaH, DMSO, 50° (1 hr)		(53.6)	14
	B_1	NaH, DMSO		(44)	147
2-Methylenecycloheptanone	B_1	NaH, DMSO, 25° (1.5 hr)		(41)	152
2-Cyclooctenone	B	Unstated		(12)	153
Ethyl sorbate	B	NaH, DMSO, 25° (3 hr), 60° (1 hr), 25° (1 hr)		(unstated)	136
Diethyl fumarate	B	NaH, DMF, 25° (1 hr)		(42)	136
	A	Electrolysis, DMSO, 25°		(12)	6
Diethyl maleate	A	Electrolysis, DMSO, 25°		(16)	6
	B_1	NaH, DMSO/THF, 25° (1 hr), 70° (4 hr)	 (20) + (20)		151

(continued)

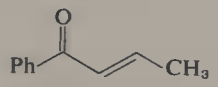
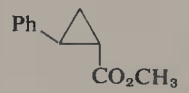
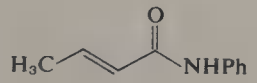
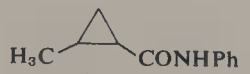
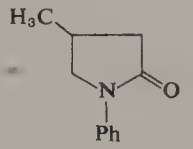
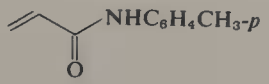
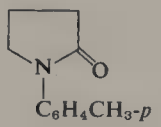
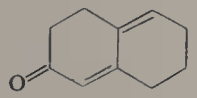
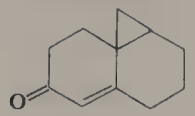
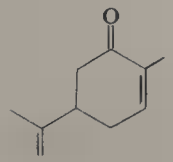
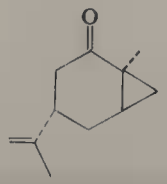
TABLE A.IV (*continued*)

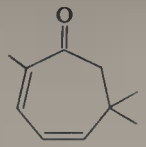
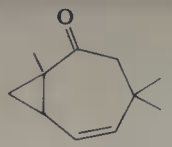
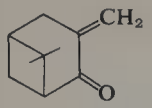
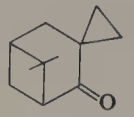
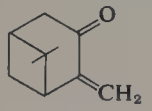
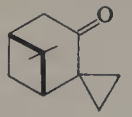
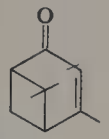
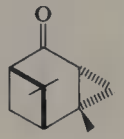
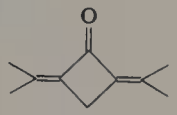
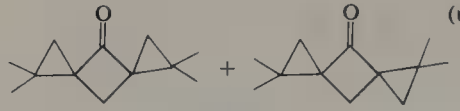
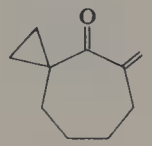
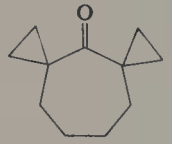
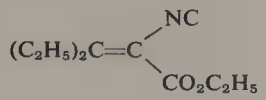
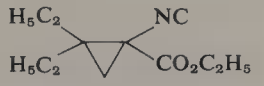
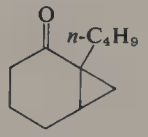
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
2-Octen-4-one	B	NaH, DMSO	 (54)	141
Ethyl 2-hexenoate	B	NaH, DMF, 25° (1 hr)	 (79)	136
C_9				
Cinnamonitrile	B_1	NaH, DMSO, 25°–30° (30 min), 55°–60° (1 hr)	 (47.5)	154
	B_1	NaH, DMSO	*trans*:*cis*, 2.8:1 (52)	155,156
	C_4	NaH, DMSO, 50° (24 hr)	*trans*:*cis*, 3.8:1 (49)	15
	B	Unstated	 (60)	156
Methyl 2-bromophenylacetate	B_1	NaH, DMSO, 25° (2 hr)	 (40)	133, 134
$PhCH{=}CHCONH_2$	B_1	NaH, DMSO	 (40)	156
	B_1	NaH, DMSO, 25°	 (80)	157
	B	Unstated	 (unstated)	157a
5-Ethyl-2-vinylpyridine	A_1	*n*-C_4H_9Li, THF, 0° (1 hr), 25° (3 hr)	2-Cyclopropyl-5-ethylpyridine (65)	144a

	B_1	NaH, DMSO/THF, 25° (1 hr), 60°	 (71)	151
4,4,6-Trimethylcyclohex-2-enone	B_1	NaH, DMSO	 (56) *cis*:*trans*, 9:1	147
Diethyl ethylidenemalonate	B_1	NaH, DMF, 25° (1 hr)	 (80)	136
2-Methyl-2-octen-4-one	B	NaH, DMSO	 (61)	141
C_{10} 	B_1	NaH, DMSO, 25°	 (72)	158
	B_1	NaH, DMSO, 25°	 (34)	158
	B_1	NaH, DMSO	 (40)	159
	B_1	NaH, DMSO, 25° (1 hr), 55° (1 hr)	 (unstated)	160

(*continued*)

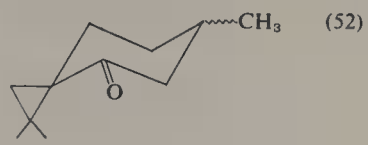
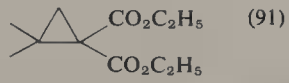
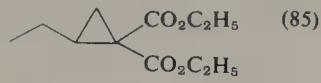
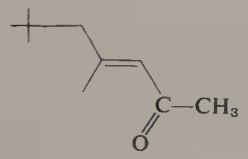
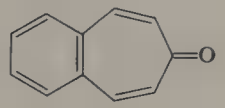
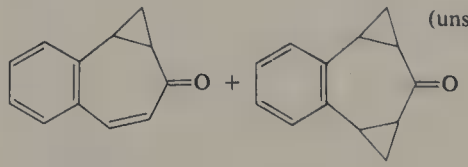
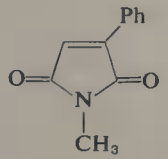
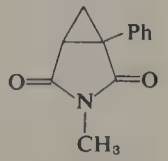
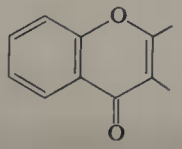
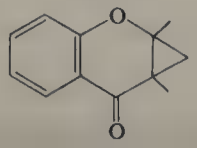
TABLE A.IV (*continued*)

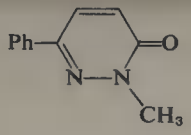
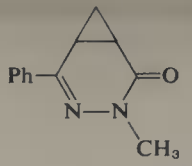
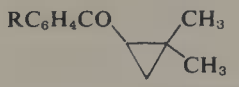
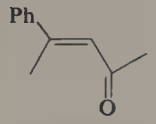
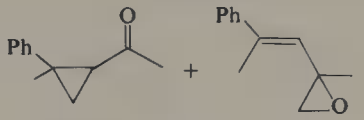
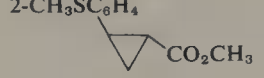
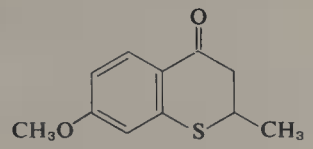
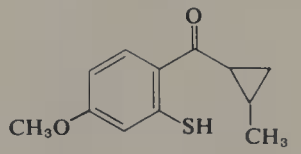
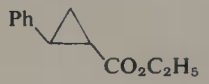
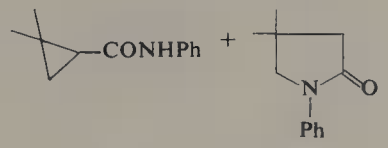
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
Benzalacetone	B_1	Unstated	 (70)	132, 144
	B_1	Unstated	 *cis*:*trans*, 1.5:1 (70)	132, 144
Methyl cinnamate	C_1	NaH, DMSO, 25° (72 hr)	 (72)	33
	C_3	NaH, DMSO	30% optical yield (76)	17
	C_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO, 25°	(70)	84
	C_4	NaH, DMSO, 25° (48 hr)	(82)	15
	B_1	NaH, DMSO	 (11) +  (80)	155, 156
	C_4	NaH, DMSO, 25° (24 hr)	 (unstated)	15
	B_1	NaH, DMSO, 25° (3 hr)	 (30)	161
	B_1	NaH, DMSO, 50° (1 hr)	 (81.3)	14, 162

	B_1	NaH, DMSO, 50° (1 hr)		(88.4)	14, 163
	B_1	NaH, DMSO, 25°		(80)	157
	B_1	NaH, DMSO, 25°		(80)	157
	B_1	NaH, DMSO, 25°		(78)	157
	B_1	Unstated		(unstated)	164
	B_1	NaH, DMSO, 25° (1 hr)		(unstated)	152
	B_1	NaH, DMSO/THF, 25° (1 hr), 60°		(71)	151
2-*n*-butylcyclohex-2-enone	B_1	NaH, DMSO, 25° (2 hr), 50° (1 hr)		(65)	165

(*continued*)

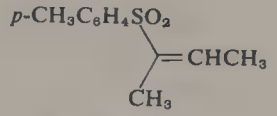
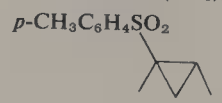
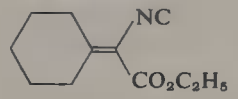
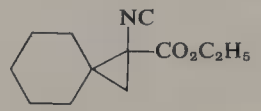
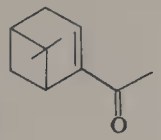
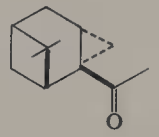
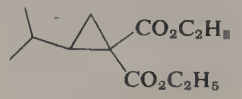
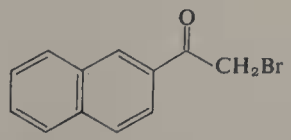
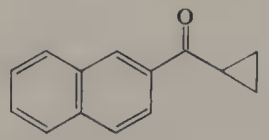
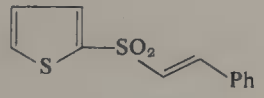
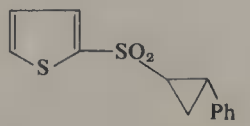
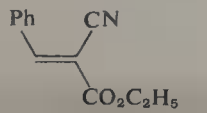
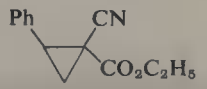
TABLE A.IV (*continued*)

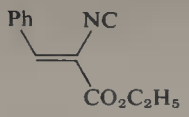
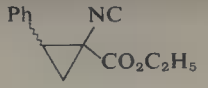
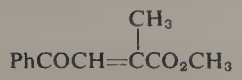
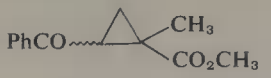
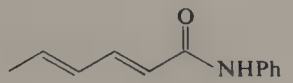
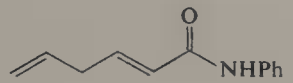
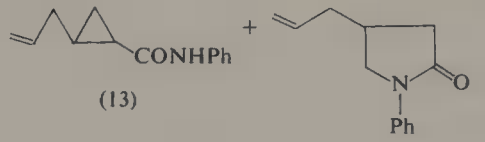
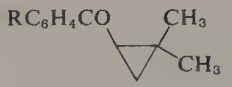
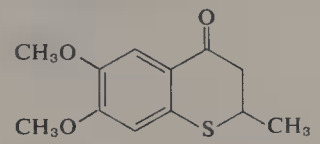
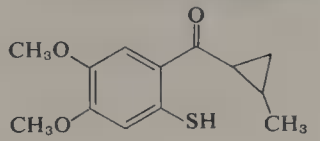
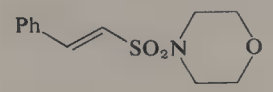
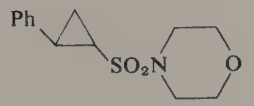
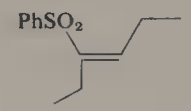
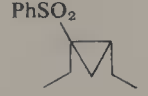
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
Pulegone	C_4	NaH, DMSO, 25° (48 hr)	 (52)	15
$(CH_3)_2C{=}C(CO_2C_2H_5)_2$	B_1	NaH, DMF, 25° (1 hr)	 (91)	136
$CH_3CH_2CH{=}C(CO_2C_2H_5)_2$	B_1	NaH, DMF, 25° (1 hr)	 (85)	136
	B	Unstated	 (80)	132
C_{11} 	B_1	NaH, THF, 0°–25° (12 hr)	 (unstated)	166–168
	B_{III}	NaH, THF, reflux	 (21)	169
	B_1	NaH, DMSO, 25°	 (72)	159

	B_1	NaH, DMSO		(50)	159
$RC_6H_4COCH{=}C(CH_3)_2$					
R = 3-Cl	B_1	NaH, DMSO, 25° (3–4 hr)	R = 3-Cl	(unstated)	170
R = 4-Cl	B_1	NaH, DMSO, 25° (3–4 hr)	R = 4-Cl	(unstated)	170
R = H	B_1	NaH, DMSO, 25° (3–4 hr)	R = H	(unstated)	170
	B_1	NaH, DMSO		(unstated)	34
$2\text{-}CH_3SC_6H_4CH{=}CHCO_2CH_3$	B_1	NaH, DMSO, 50° (2.5 hr)		(10)	171
	B	DMSO, 50°–60°		(>80)	172
Ethyl cinnamate	B_1	NaH, DMSO, 25°–30° (30 min), 55–60° (1 hr)		(31)	154
	B	NaH, DMSO, 25° (1 hr)		(34)	136
	B	NaH, DMF, 25° (1 hr)		(42)	136
	A	$KOC(CH_3)_3$, DMSO		(54)	173
$(CH_3)_2C{=}CHCONHPh$	B_1	NaH, DMSO		(30) (45)	155

(continued)

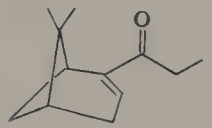
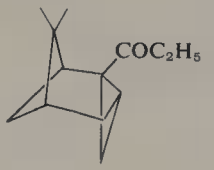
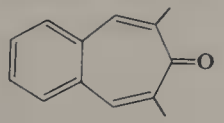
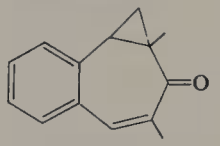
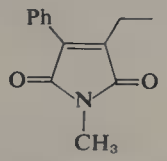
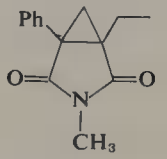
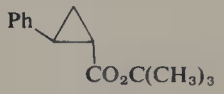
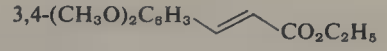
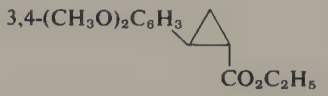
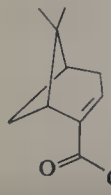
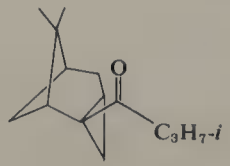
TABLE A.IV (*continued*)

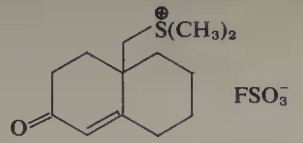
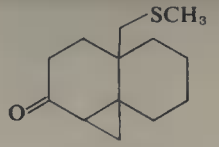
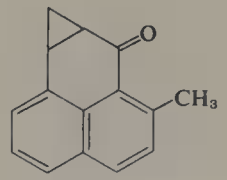
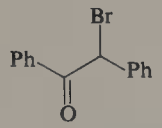
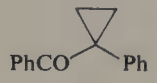
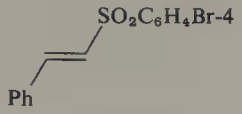
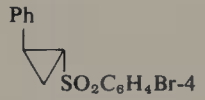
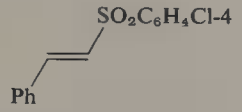
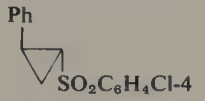
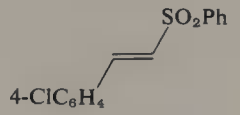
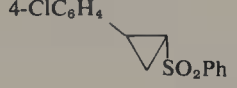
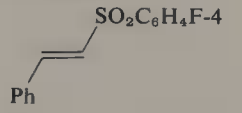
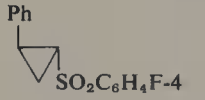
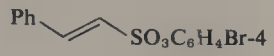
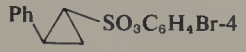
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
N,*N*-Dimethylcinnamide	B_1	NaH, DMSO, 25°–30° (30 min), 55°–60° (1 hr)	 (39)	154
 *cis* or *trans*	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (40)	174
	B_1	NaH, DMSO/THF, 25° (1 hr), 60°	 (51)	151
	B_1	NaH, DMSO, 25°	 (72)	157
$(CH_3)_2CHCH{=}C(CO_2C_2H_5)_2$	B_1	NaH, DMF, 25° (1 hr)	 (89)	136
C_{12}				
	B_1	NaH, DMSO, 25° (2 hr)	 (19)	133, 134
	A_1	$KOC(CH_3)_3$, DMSO, 25° (0.5 hr)	 (84)	175
	B_1	NaH, DMSO	 (55)	176

	B_1	NaH, DMSO/THF, 25° (1 hr), 60°	 (83)	151
	B_1	NaH, DMSO	 *cis*:*trans*, 1:19 (unstated)	177
	B_1	NaH, DMSO	 (unstated)	155, 156
	B_1	NaH, DMSO	 (13) (76)	155, 156
$RC_6H_4COCH{=}C(CH_3)_2$				
$R = 4\text{-}CH_3$	B_1	NaH, DMSO, 25° (3–4 hr)	$R = 4\text{-}CH_3$ (unstated)	170
$R = 3\text{-}CH_3O$	B_1	NaH, DMSO, 25° (3–4 hr)	$R = 3\text{-}OCH_3$ (unstated)	170
$R = 4\text{-}CH_3O$	B_1	NaH, DMSO, 25° (3–4 hr)	$R = 4\text{-}OCH_3$ (unstated)	170
	B	DMSO, 50°–60°	 (> 80)	172
	A	$KOC(CH_3)_3$, DMSO, 25° (1 hr)	 (68)	178
	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (44)	174

(*continued*)

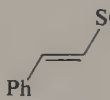
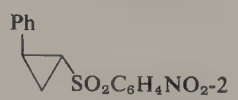
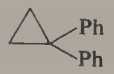
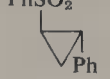
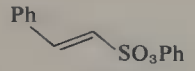
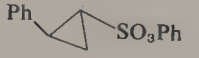
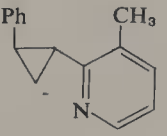
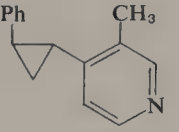
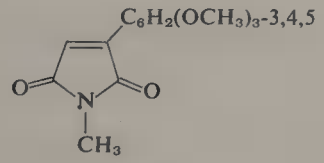
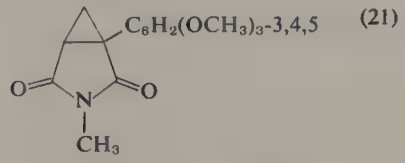
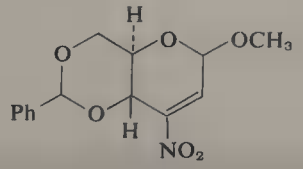
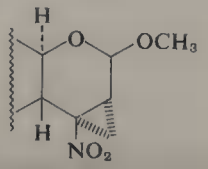
TABLE A.IV (*continued*)

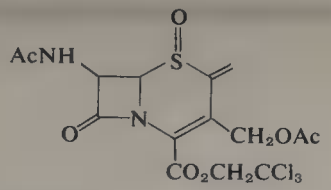
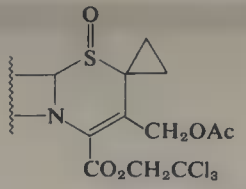
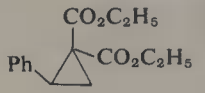
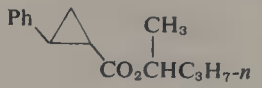
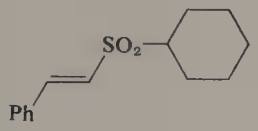
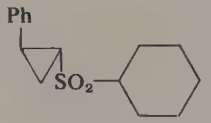
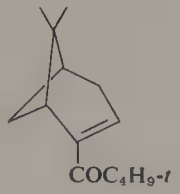
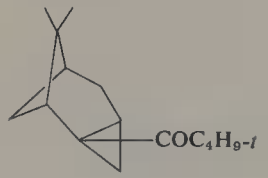
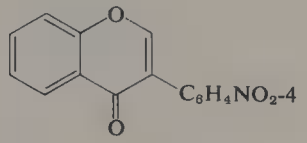
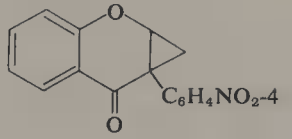
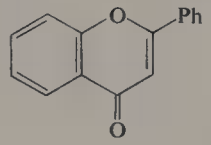
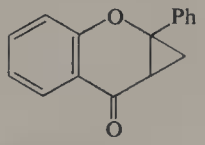
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_1	NaH, DMSO, 25° (2 hr)	 (75)	179
C_{13}				
2-ω-Styrylpyridine	A_1	*n*-C_4H_9Li, THF, 0° (1 hr), 25° (3 hr)	*trans*-1-Phenyl-2-(2′-pyridyl)-cyclopropane (70)	144a
4-ω-Styrylpyridine	A_1	*n*-C_4H_9Li, THF, 0° (1 hr), 25° (3 hr)	*trans*-1-Phenyl-2-(4′-pyridyl)-cyclopropane (81)	144a
	B_1	NaH, THF, 0°–25° (12 hr)	 (95)	167
	B_2	NaH, THF, reflux	 (81)	169
t-Butyl cinnamate	B_1	NaH, DMSO, 25°–30° (30 min), 55°–60° (1 hr)	 (65)	154
	B_1	NaH, DMSO, 25°–30° (30 min), 55°–60° (1 hr)	 (29.5)	154
	B_1	NaH, DMSO, 25° (2 hr)	 (77)	179

		$KOC(CH_3)_3$, DME, 0°–40°		(unstated)	180
C_{14} 9-Methylphenalenone	B	DMSO		(unstated)	301
	B_1	NaH, DMSO, 25° (1 hr)		(35)	133, 134
	A_3	$KOC(CH_3)_3$, DMSO, 25°		(81)	181
	A_3	$KOC(CH_3)_3$, DMSO, 25°		(46)	181
	A_3	$KOC(CH_3)_3$, DMSO, 25°		(74)	181
	A_3	$KOC(CH_3)_3$, DMSO, 25°		(67)	181
	A_1	$KOC(CH_3)_3$, DMSO, 25° (1 hr)		(60)	178

(continued)

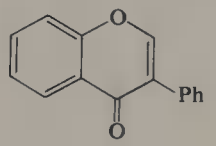
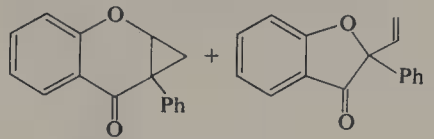
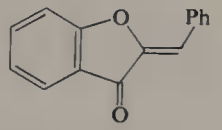
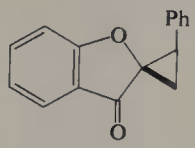
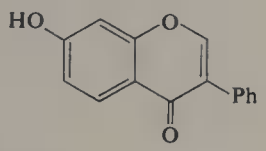
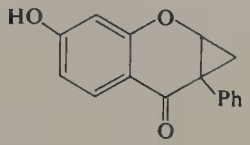
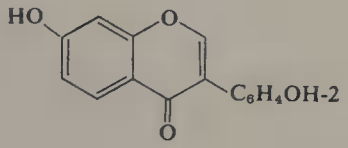
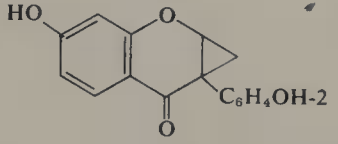
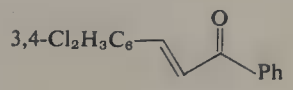
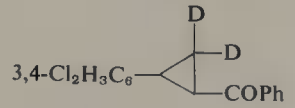
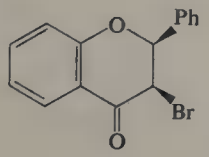
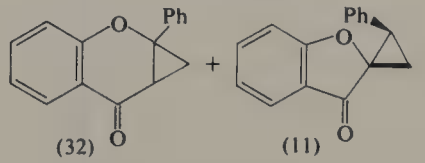
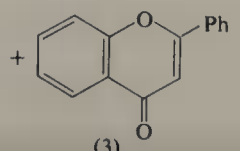
TABLE A.IV (*continued*)

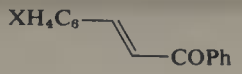
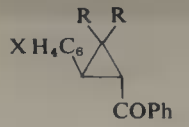
Acceptor	Ylide	Reaction conditions	Products (Yield, %)[a]	References
	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (21)	181
$Ph_2C{=}CH_2$	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0° (10 min), 25° (30–60 min)	 (61)	14
$PhCH{=}CHSO_2Ph$ *cis* or *trans*	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (87)	174
	C_4	NaH, DMSO, 25° (24 hr)	(80)	15
	A_1	$KOC(CH_3)_3$, DMSO, 25° (1 hr)	 (79)	178
3-Methyl-2-ω-styrylpyridine	A_1	*n*-C_4H_9Li, THF, 0° (1 hr), 25° (3 hr)	 (58)	144a
3-Methyl-4-ω-styrylpyridine	A_1	*n*-C_4H_9Li, THF, 0° (1 hr), 25° (3 hr)	 (91)	144a
	B_2	NaH, THF	 (21)	169
	B_2	NaH, DMSO, 25° (1 hr)	 (75)	182

	C_1	NaH, DMF, 0° (1 hr)	 (64)	183
Diethyl benzylidenemalonate	B_2	NaH, DMF, 25° (1 hr)	 (76)	136
	B_1	NaH, DMSO, 25°–30° (30 min), 55°–60° (1 hr)	(59.5)	154
sec-Pentyl cinnamate	B_1	NaH, DMSO, 25°–30° (30 min), 55°–60° (1 hr)	 (69)	154
	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (24)	181
	B_1	NaH, DMSO, 25° (2 hr)	 (75)	179
C_{15}				
	B_1	NaH, DMSO, 25°	 (32)	158
	B	NaH, DMSO, 25° (1–5 min)	 (unstated)	184

(*continued*)

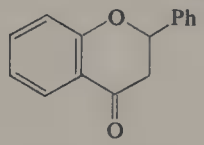
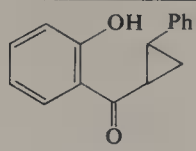
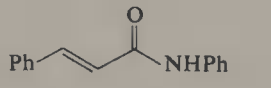
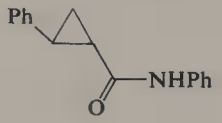
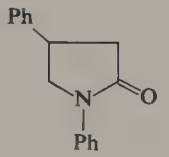
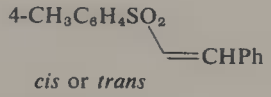
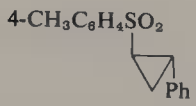
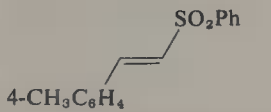
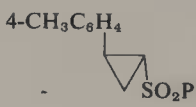
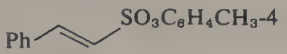
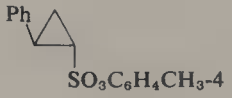
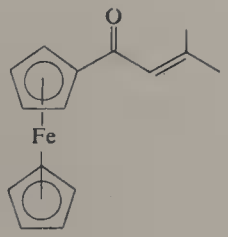
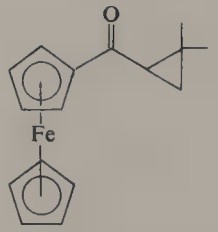
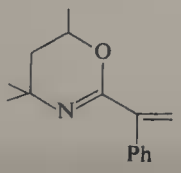
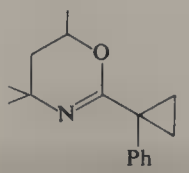
TABLE A.IV (*continued*)

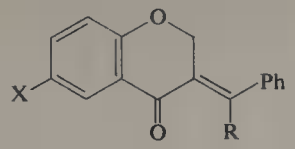
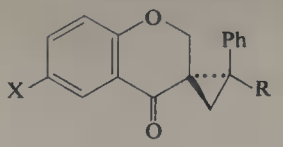
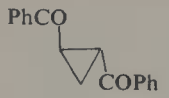
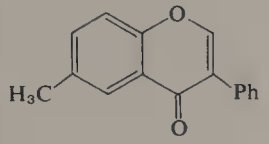
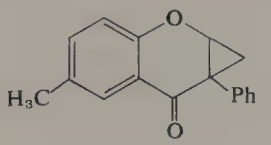
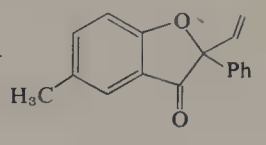
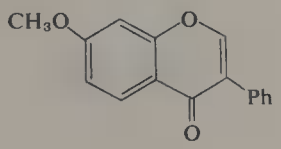
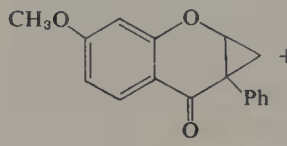
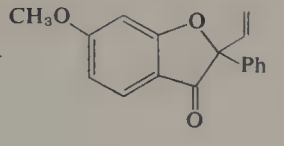
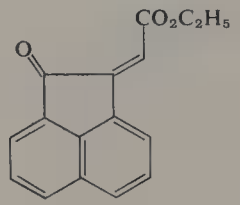
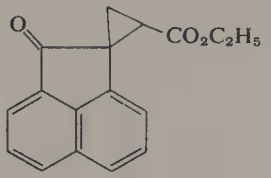
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_1	NaH, DMSO, 25°	 (60) (7)	158
	B	Unstated	 (16.9)	185
	B_1	NaH, DMSO, 25°	 (80)	158
	B_1	NaH, DMSO, 25°	 (10)	168
	B-d_8	NaH, DMSO-d_6, 30° (0.5 hr), 55°–60° (1 hr)	 (unstated)	186
	B	Unstated	 (32) (11)  (3)	184

					
X = 3-Br	B-d_6	NaH, DMSO-d_6, 30° (0.5 hr), 55°–60° (1 hr)	X = 3-Br, R = D	(unstated)	186
X = 4-Br	B_1	NaH, DMF, 25° (1 hr)	X = 4-Br, R = H	(95)	187
	B-d_6	NaH, DMSO-d_6, 30° (0.5 hr), 55°–60° (1 hr)	X = 4-Br, R = D	(unstated)	186
X = 3-Cl	B_1	NaH, DMF, 25° (1 hr)	X = 3-Cl, R = H	(50)	187
X = 4-Cl	B_1	NaH, DMF, 25° (1 hr)	X = 4-Cl, R = H	(77)	187
	B-d_6	NaH, DMSO-d_6, 30° (0.5 hr), 80° (1 hr)	X = 4-Cl, R = D	(unstated)	181
X = 4-F	B_1	NaH, DMF, 25° (1 hr)	X = 4-F, R = H	(55)	187
	B-d_6	NaH, DMSO-d_6, 30° (0.5 hr), 55°–60° (1 hr)	X = 4-F, R = D	(unstated)	186
X = 3-NO_2	B_1	NaH, DMF, 25° (1 hr)	X = 3-NO_2, R = H	(40)	187
X = 4-NO_2	B_1	NaH, DMF, 25° (1 hr)	X = 4-NO_2, R = H	(83)	187
Benzalacetophenone					
	C_2	NaH, DMSO, 25°	R = H, 35% optical yield	(94)	17
	B-d_6	NaH, DMSO-d_6, 30° (0.5 hr), 55°–60° (1 hr)	R = D	(unstated)	186
	B	NaH, DMSO, 50° (1 hr)	R = H	(94.6, 72)	188
	C_1	NaH, THF, 25° (4 hr)	R = H	(100)	33
	C_4	NaH, DMSO, 25° (4 hr)	R = H	(93)	15
	C_2	NaH, THF, 25° (overnight)	R = H, 7% optical yield	(84)	17
	C_5	NaH, DMSO, 25° (overnight)	R = H, 21% optical yield	(55)	17
	C_5	NaH, THF, 25°	R = H, 37% optical yield	(78)	17
	C_6	NaH, DMSO, 25°	R = H, 29% optical yield	(75)	17
	B_1	NaH, DMF, 25° (1 hr)	R = H	(98)	187
	B_1	NaOH, H_2O/CH_2Cl_2, $(n\text{-}C_4H_9)_4NI$, 50° (20 hr)	R = H	(86)	130

(continued)

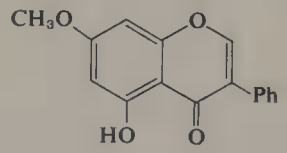
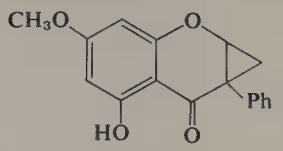
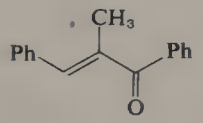
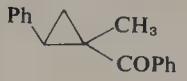
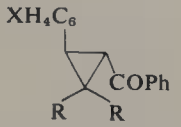
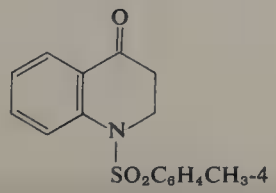
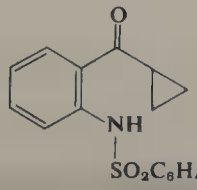
TABLE A.IV (*continued*)

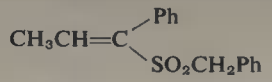
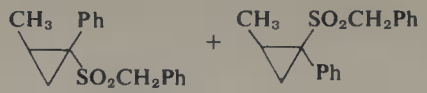
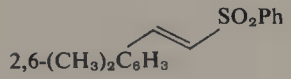
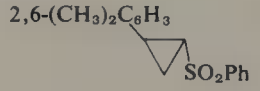
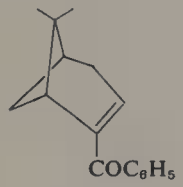
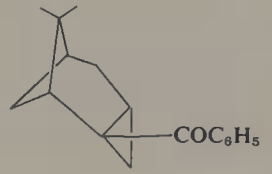
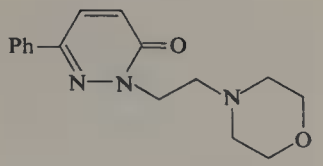
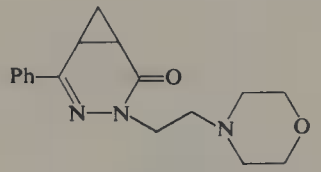
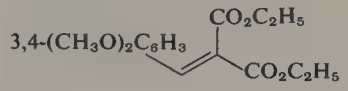
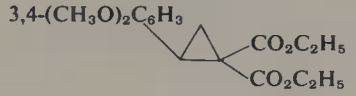
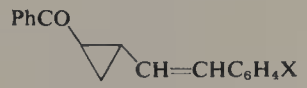
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B	Unstated	 (82)	184
	B_1	NaH, DMSO	 (20) +  (70)	155, 156
 *cis* or *trans*	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (45)	174, 181
	A_3	$KOC(CH_3)_3$, DMSO, 25°	 (68)	181
	A_1	$KOC(CH_3)_3$, DMSO, 25° (1 hr)	 (70)	178
	II	NaH, DMSO, 25° (16 hr)	 (89)	189
	C_4	NaH, DMSO, 50° (60 hr)	 (75)	15

C_{16} 				
X = Cl, R = H	B_1	NaH, DMSO, 25° (5 min)	X = Cl, R = H (48)	190
X = H, R = D	B	Unstated	X = H, R = D (43.7)	185
X = H, R = H	B	Unstated	X = H, R = H (51.4)	185
X = H, R = H	B_1	NaH, DMSO, 25° (5 min)	X = H, R = H (74)	190
trans-1,2-Dibenzoylethylene	C_1	NaH, THF, 25° (2 hr)	 (80)	33
	C_3	NaH, DMSO, 25° (12 hr)	(76) optically active	17
	C_4	NaH, DMSO, 25°	(62)	15
	B_1	NaH, DMSO, 25°	 +  (62) (5)	158
	B_1	NaH, DMSO, 25°	 +  (58) (—)	158
	B_2	NaH, THF, 25° (20 hr) 70°–80° (10 min)	 (54)	67

(*continued*)

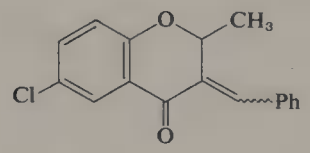
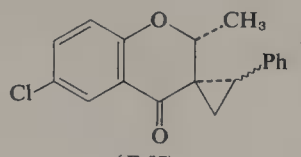
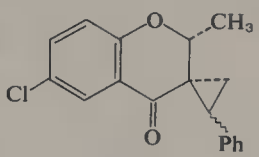
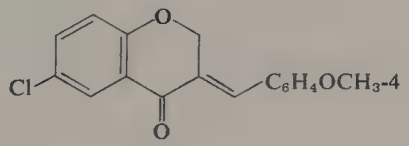
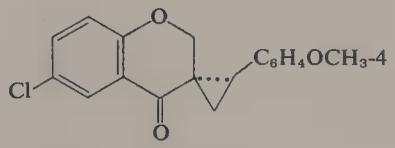
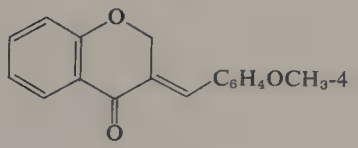
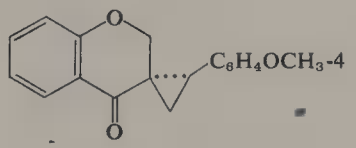
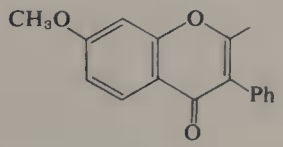
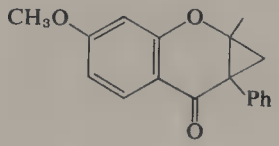
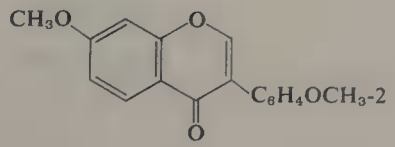
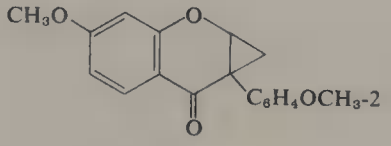
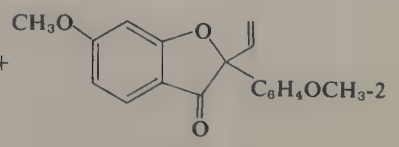
TABLE A.IV (*continued*)

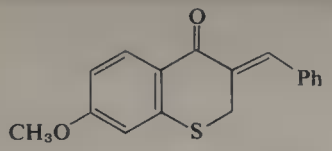
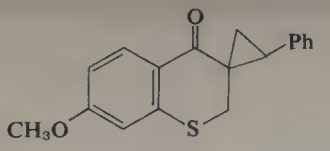
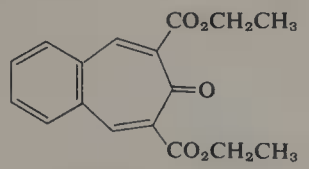
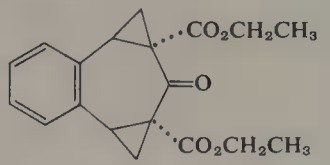
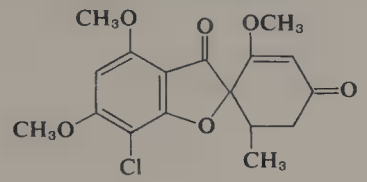
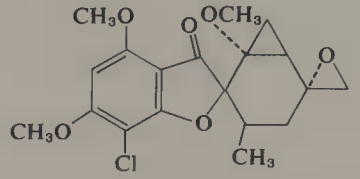
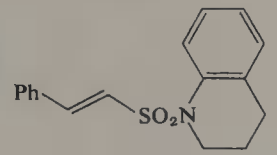
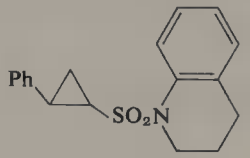
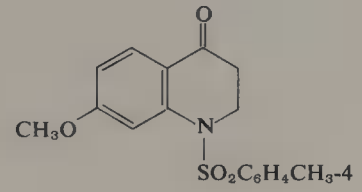
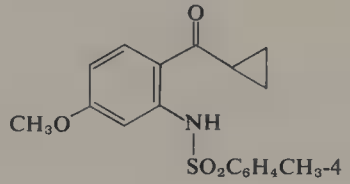
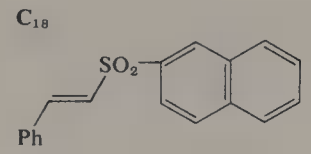
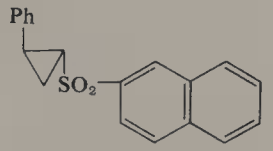
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_1	NaH, DMSO, 25°	 (69)	158
	B	NaH, DMSO	 (30)	191
				
X = 4-CH_3	B_1	NaH, DMSO, 22°–25° (0.75 hr) 50° (2 hr)	X = 4-CH_3, R = H (90)	188
		NaOH, H_2O/CH_2Cl_2, $(n\text{-}C_4H_9)_4NI$, 50° (20 hr)	X = 4-CH_3, R = H (78)	130
	B-d_6	NaH, DMSO-d_6, 30° (0.5 hr), 55°–60° (1 hr)	X = 4-CH_3, R = D (unstated)	186
X = 2-OCH_3	B	Unstated	X = 2-OCH_3, R = H (unstated)	192
X = 4-OCH_3	B_1	NaH, DMF, 25° (1 hr)	X = 4-OCH_3, R = H (65)	187
		NaOH, H_2O/CH_2Cl_2, $(n\text{-}C_4H_9)_4NI$, 50° (20 hr)	X = 4-OCH_3, R = H (74)	130
	B-d_6	NaH, DMSO-d_6, 30° (0.5 hr), 55°–60° (1 hr)	X = 4-OCH_3, R = D (unstated)	186
	A or B	Unstated	 (unstated)	23

					
cis	B	Unstated		(unstated)	193
trans	B	Unstated		(unstated)	193
	A_3	$KOC(CH_3)_3$, DMSO, 25°		(79)	181
	B_1	NaH, DMSO 25° (2 hr)		(85)	179
	B_1	NaH, DMSO		(55)	159
	B_1	NaH, DMSO, 25°–30° (30 min), 55°–60° (1 hr)		(81)	154
C_{17} $PhCO(CH{=}CH)_2C_6H_4X$					
X = 4-Br	B_1	NaH, DMF, 25° (1 hr)	X = 4-Br	(90)	187
X = 4-NO_2	B_1	NaH, DMF, 25° (1 hr)	X = 4-NO_2	(36)	187
X = H	B_1	NaH, DMF, 25° (1 hr)	X = H	(65)	187

(*continued*)

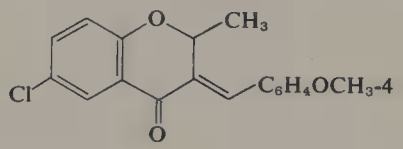
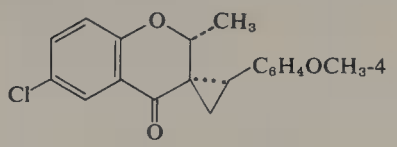
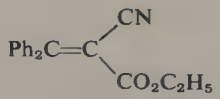
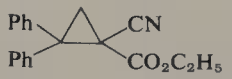
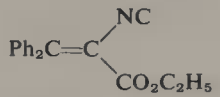
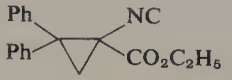
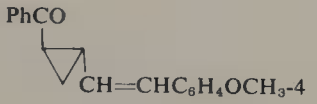
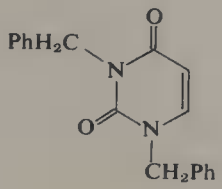
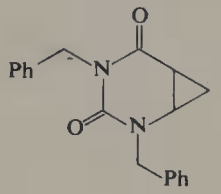
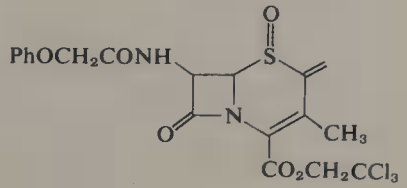
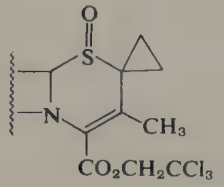
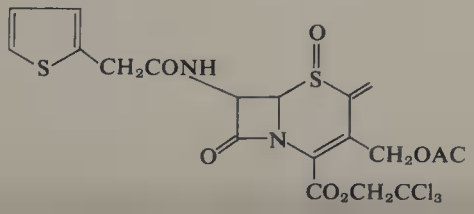
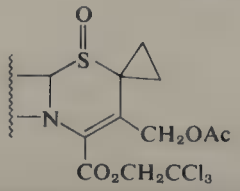
TABLE A.IV (*continued*)

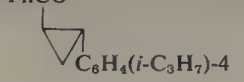
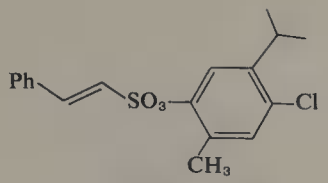
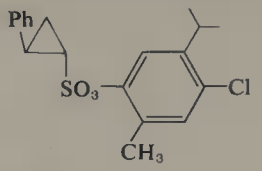
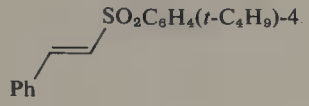
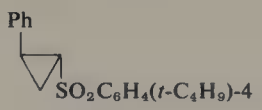
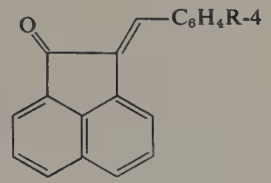
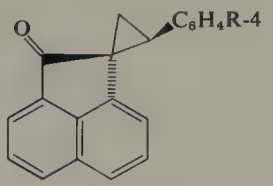
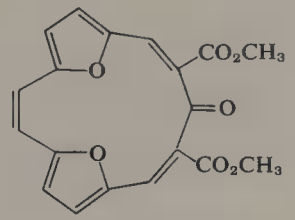
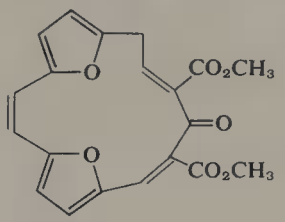
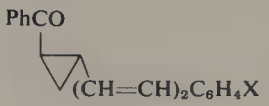
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_1	NaH, DMSO, 25° (5 min)	 (*E* 57) (*Z* 5) +  (*E* 10) (*Z* 5)	190
	B_1	NaH, DMSO, 25° (5 min)	 (61)	190
	B_1	NaH, DMSO, 25° (5 min)	 (57)	190
	B_1	NaH, DMSO, 25°	 (50)	158
	B_1	NaH, DMSO, 25°	 (74) +  (4)	158

	B	NaH, DMSO, 50°–60°		(unstated)	172
	B_1	NaH, THF, 0°–25° (12 hr)		(50)	167
	B	NaH, DMSO, 25° (1 hr)		(unstated)	59
	A_1	$KOC(CH_3)_3$, DMSO, 25° (1 hr)		(75)	178
	A or B	Unstated		(unstated)	23
C_{18} 	A_3	$KOC(CH_3)_3$, DMSO, 25°		(84)	181

(*continued*)

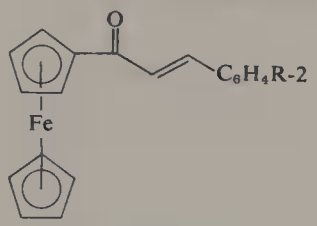
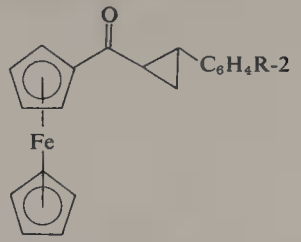
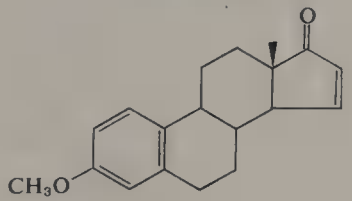
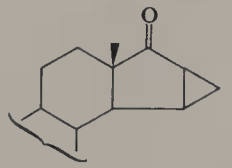
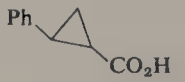
TABLE A.IV (*continued*)

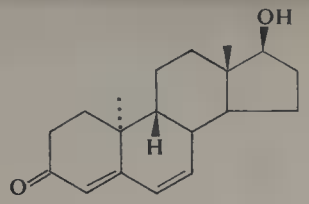
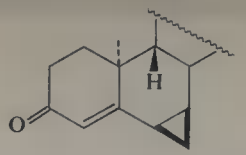
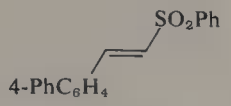
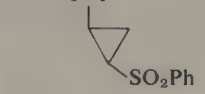
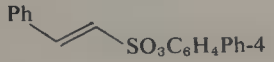
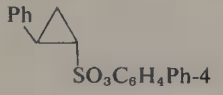
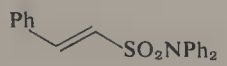
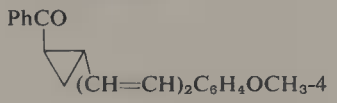
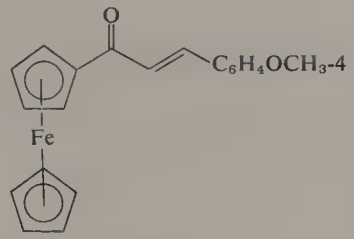
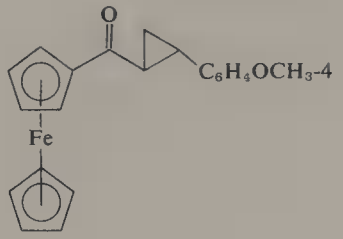
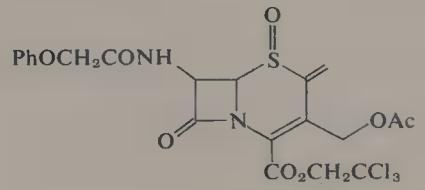
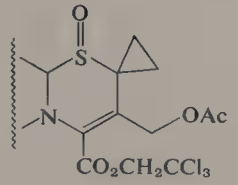
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_1	NaH, DMSO, 25° (5 min)	 (9)	190
	B_1	NaH, DMSO	 (80)	194
	B_1	NaH, DMSO/THF, 25° (1 hr), 60°	 (75)	151
$PhCO(CH{=}CH)_2C_6H_4OCH_3$-4	B_1	NaH, DMF, 25° (1 hr)	 (35)	187
	B_2	NaH, THF, reflux (24 hr)	 (60)	137
	C_1	NaH, DMF, 0° (1 hr)	 (80)	183
	C_1	NaH, DMF, 0° (1 hr)	 (72–88)	183

$PhCOCH{=}CHC_6H_4(i\text{-}C_3H_7)\text{-}4$	B_1	NaH, DMF, 25° (1 hr)		(50)	187
	A	$KOC(CH_3)_3$, DMSO, 25° (1 hr)		(45)	178
	A_3	$KOC(CH_3)_3$, DMSO, 25°		(55)	181
C_{19}					
					
R = Cl	B	NaH, THF, 0°, then 25° (2 hr)	R = Cl	(93)	67
R = H	B	NaH, THF, 0°, then 25° (2 hr)	R = H	(74)	67
	B	DMSO, 25°		(100)	187a
$PhCO(CH{=}CH)_3C_6H_4X$					
X = 4-Br	B_1	NaH, DMF, 25° (1 hr)	X = 4-Br	(81)	187
X = H	B_1	NaH, DMF, 25° (1 hr)	X = H	(55)	187

(continued)

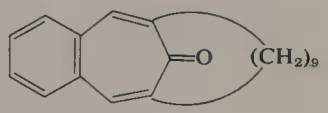
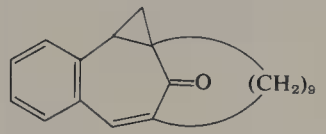
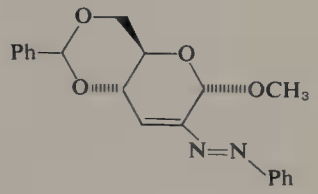
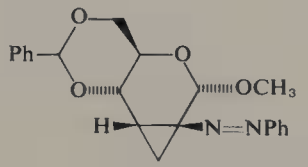
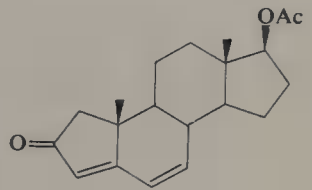
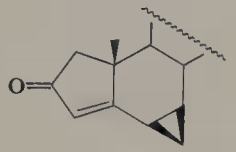
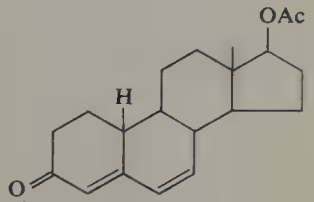
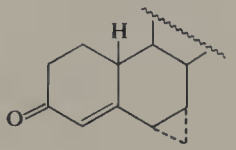
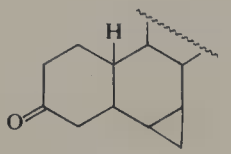
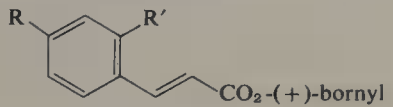
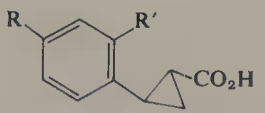
TABLE A. IV (*continued*)

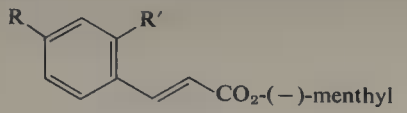
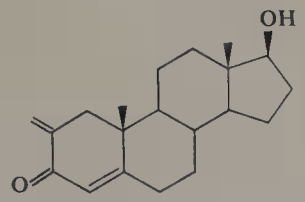
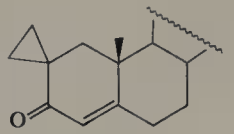
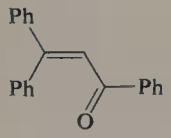
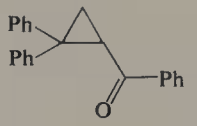
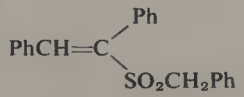
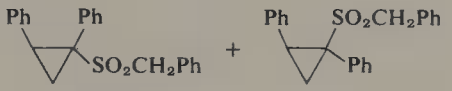
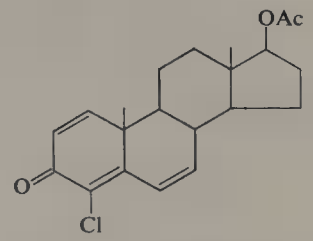
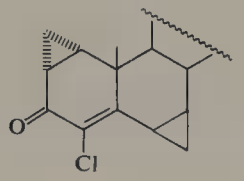
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
				
$R = NO_2$	B	NaH, DMSO, 25° (16 hr)	$R = NO_2$ (86)	189
$R = H$	B	NaH, DMSO, 25° (16 hr)	$R = H$ (90)	189
	B	NaH, DMSO, 25° (2 hr)	 (71)	195
(+)-Bornyl cinnamate	B_1	NaH, DMSO, 25° (1 hr), 50° (0.5 hr)	 (35–41)	196
	B_1	$KOC(CH_3)_3$, DMSO, 25° (1 hr), 50° (0.5 hr)	(70)	196
	B_1	NaH, THF, 25° (1 hr), 50° (1 hr)	(12)	196
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0°, 45° (1 hr)	(12)	196
(−)-Menthyl cinnamate	B_1	NaH, DMSO, 25° (1 hr), 50° (0.5 hr)	 (42–49)	196
	B_1	$KOC(CH_3)_3$, DMSO, 25° (1 hr), 50° (0.5 hr)	(58)	196
	B_1	NaH, THF, 25° (1 hr), 50° (1 hr)	(13–20)	196
	A_1	$NaCH_2\overset{O}{\overset{\|}{S}}CH_3$, DMSO/THF, 0°, 40° (1 hr)	(17)	196

	B_1	DMSO, 3 days		(unstated)	197
C_{20}					
	A_3	$KOC(CH_3)_3$, DMSO, 25°		(63)	181
	A_1	$KOC(CH_3)_3$, DMSO, 25° (1 hr)		(72)	178
	A_1	$KOC(CH_3)_3$, DMSO, 25° (1 hr)		(88)	178
$PhCO(CH{=}CH)_3C_6H_4OCH_3$-4	B_1	NaH, DMF, 25° (1 hr)		(44)	187
	B	NaH, DMSO, 25° (16 hr)		(84)	189
	C_1	NaH, DMF, 0° (1 hr)		(85)	183

(*continued*)

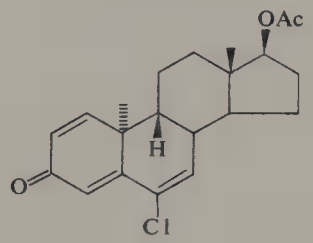
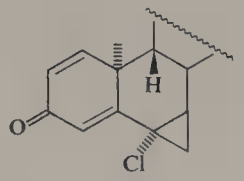
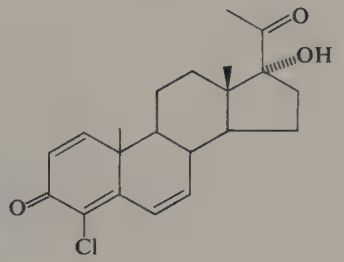
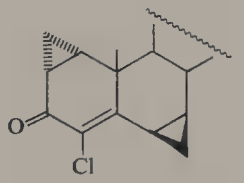
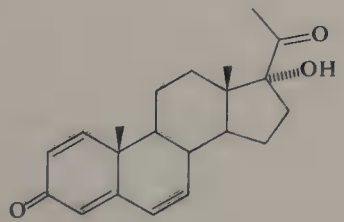
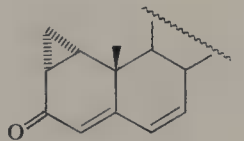
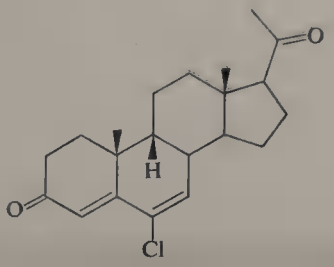
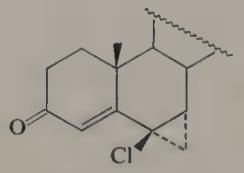
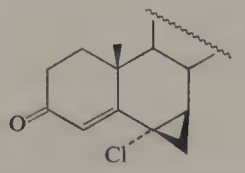
TABLE A.IV (*continued*)

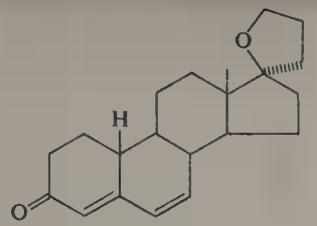
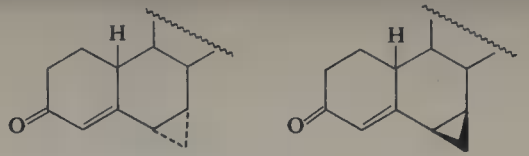
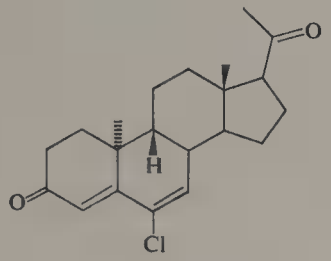
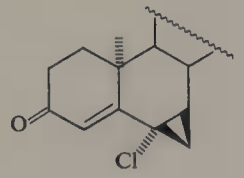
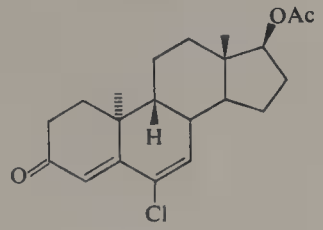
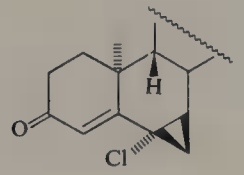
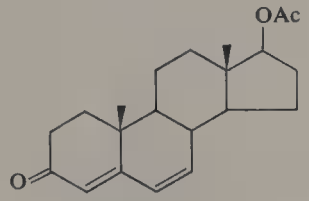
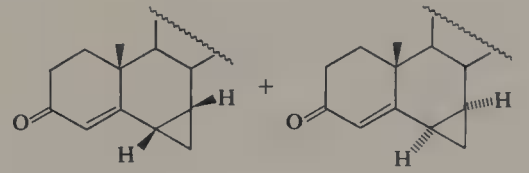
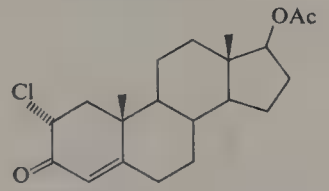
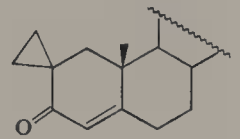
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_2	Unstated	 (50)	198
	B	NaH, DMSO, 25° (10 min)	 (60)	199
	B_1	NaH, DMSO, 25° (3 days)	 (57)	200
	B	DMSO	 9 :  1	200a
			 3–4% optical yield	
$R = OCH_3$, $R' = H$	B	NaH, DMSO, 25° (1 hr), 50° (0.5 hr)	$R = OCH_3$, $R' = H$ (13–63)	196
$R = H$, $R' = OCH_3$	B	NaH, DMSO, 25° (1 hr), 50° (0.5 hr)	$R = H$, $R' = OCH_3$ (50–57)	196

	B	NaH, DMSO, 25° (1 hr), 50° (0.5 hr)	R = OCH_3, R′ = H	(41–57)	196
	B	NaH, DMSO, 25° (1 hr), 50° (0.5 hr)	R = H, R′ = OCH_3	(18–20)	196
	B_1	NaH, DMSO, 25° (5 hr)		(100)	201
C_{21} 	B_1	NaH, DMSO		(40)	34
					
cis	B	NaH, DMSO, 25° (1 hr)	1 : 1	(86)	193
trans	B	NaH, DMSO, 25° (1 hr)	1.1 : 1	(97)	193
	B	NaH, DMSO, 25° (2 hr)		(30)	202

(*continued*)

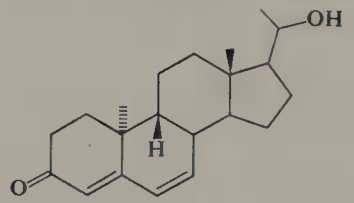
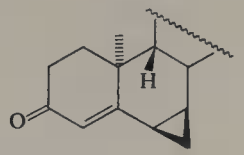
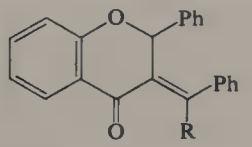
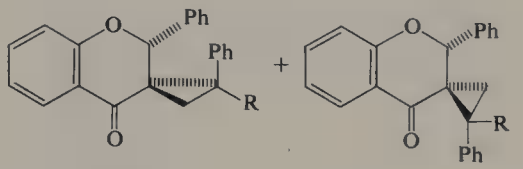
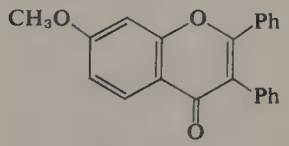
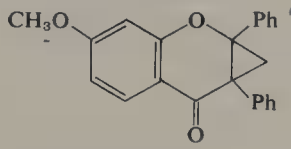
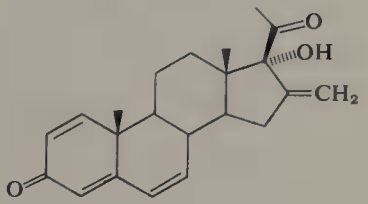
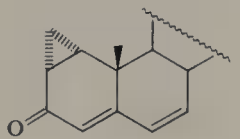
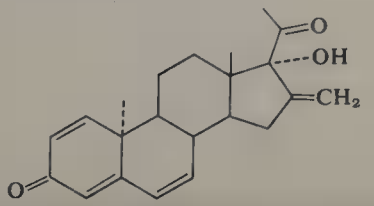
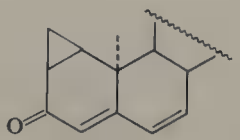
TABLE A.IV (*continued*)

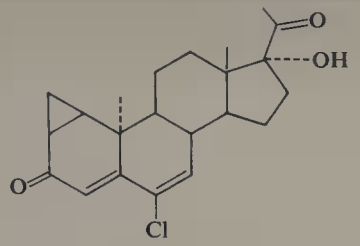
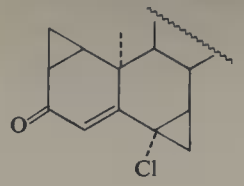
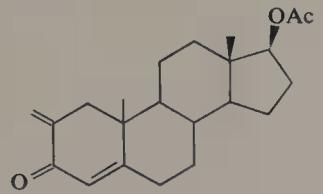
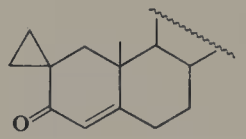
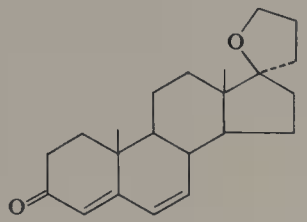
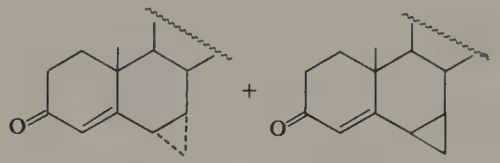
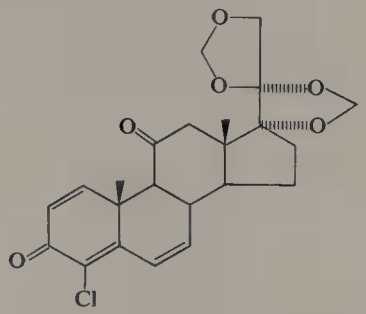
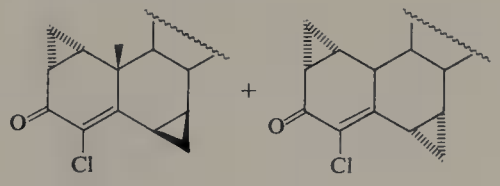
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B	DMSO (3 days)	 (unstated)	197
	B	NaH, DMSO, 25° (2 hr)	 (72)	202
	B_1	NaH, DMSO, 25° (3 hr)	 (34)	203
	B	DMSO (3 days)	 +  2 : 1 (unstated)	197

		DMSO	 9 : 1	200a
	B	DMSO (3 days)		(unstated) 197
		DMSO (3 days)		(unstated) 197
	B	NaH, DMSO, 25° (2–3 days)	 1.2 : 1	204
	B_1	NaH, DMSO/THF, 25° (1 hr)		(13) 134

(continued)

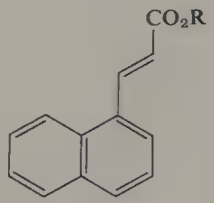
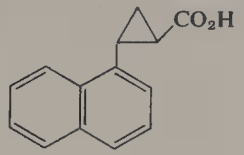
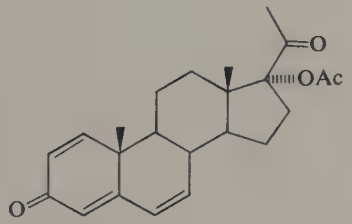
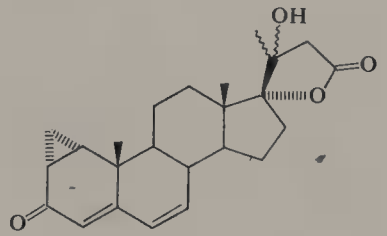
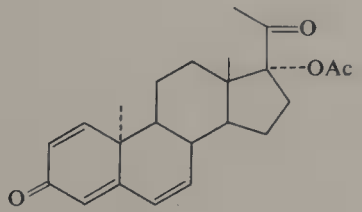
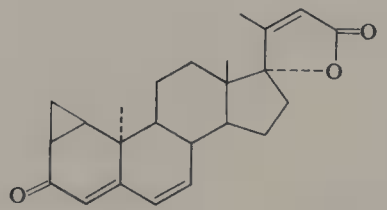
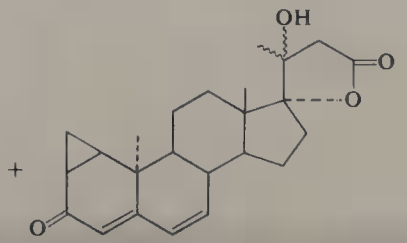
TABLE A.IV (*continued*)

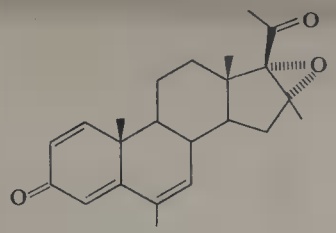
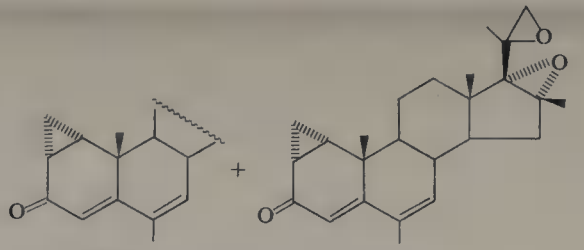
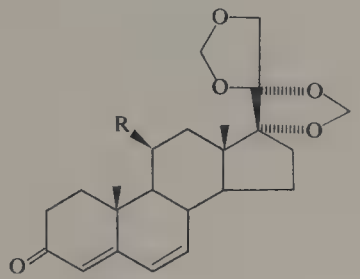
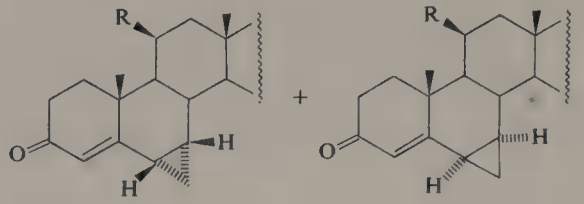
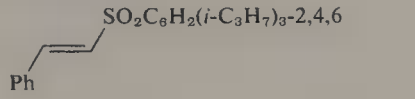
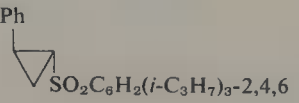
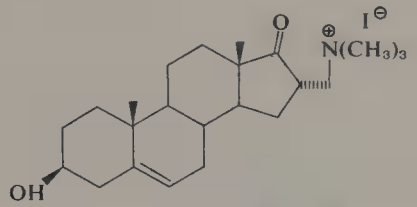
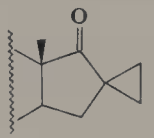
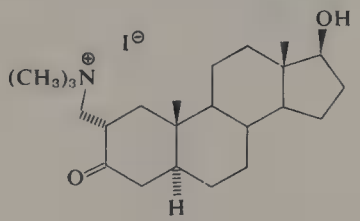
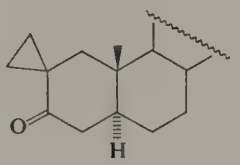
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B	DMSO (3 days)	 (unstated)	197
C_{22} 				
R = D	B	Unstated	R = D (49.6) (8.2)	185
R = H	B	Unstated	R = H (57.2) (4.7)	185
R = H	B_1	NaH, DMSO, 25° (5 min)	R = H (51 + isomer) (27 + isomer)	190
	B_1	NaH, DMSO, 25° (2 hr)	 (72)	158
	B_1	NaH, DMSO, 25° (3 hr)	 (71)	205
	B_1	Na, DMSO/THF, 22° (25 hr)	 (52)	206

	B_1	NaH, DMSO/THF, 25° (1.75 hr)		(63)	207
	B_1	NaH, DMSO, 25° (5 hr)		(100)	201
	B	DMSO	 2 : 3		200a
C_{23} 	B	NaH, DMSO, 25° (2 hr)	 4 : 1	(33)	202

(*continued*)

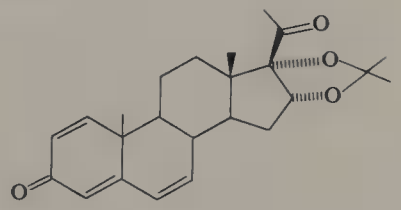
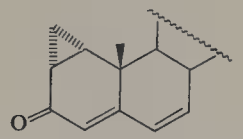
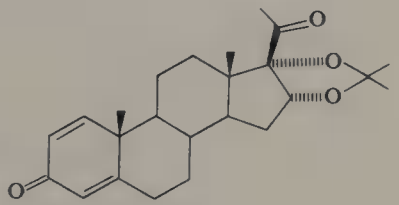
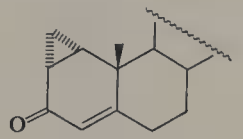
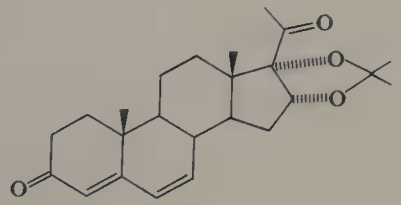
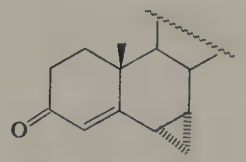
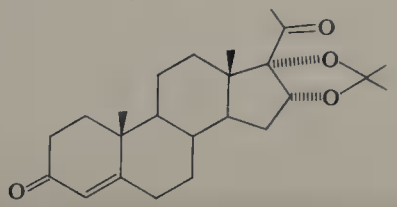
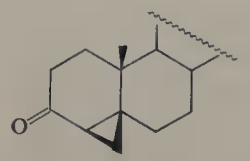
TABLE A.IV (*continued*)

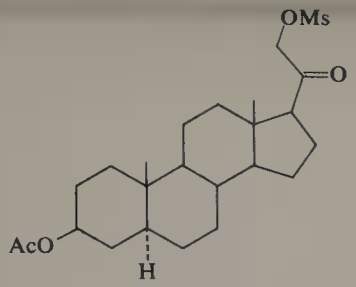
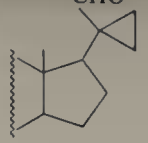
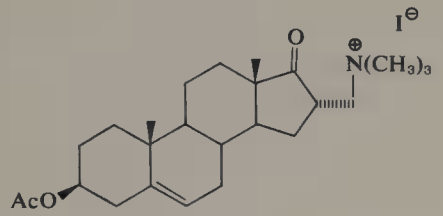
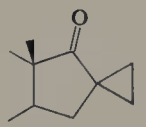
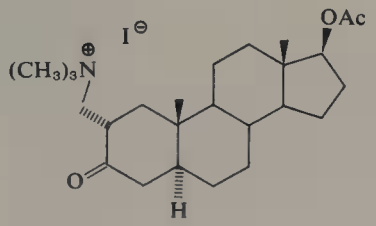
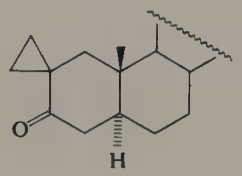
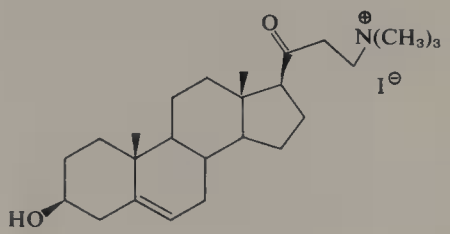
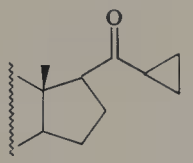
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]		References
					
R = (+)-bornyl	B	NaH, DMSO, 25° (1 hr), 50° (0.5 hr)		(33–60)	196
R = (−)-menthyl	B	NaH, DMSO, 25° (1 hr), 50° (0.5 hr)	3–4% optical yield	(26–33)	196
	B_1	NaH, DMSO, 25° (17 hr)		(64)	203
	B_1	NaH, DMSO/THF, 25° (3 hr)			207
					

	B_1	NaH, DMSO, 25° (5 hr)	 (86) (−)		205
					
R = H	B	NaH, DMSO, 25°, 2–3 days	R = H (57)	(43)	204
R = OH	B	NaH, DMSO, 25°, 2–3 days	R = OH (only)		204
	A_3	$KOC(CH_3)_3$, DMSO, 25°		(72)	181
	B_1	NaH, DMSO, 25°		(62)	201
	B_1	NaH, DMSO, 25°		(34)	201

(*continued*)

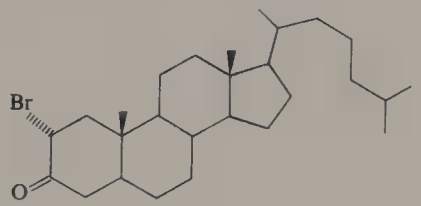
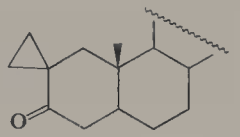
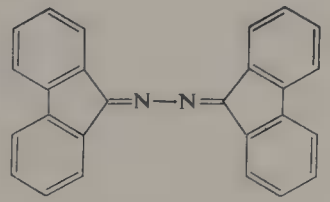
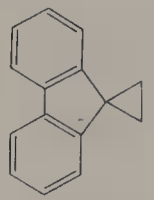
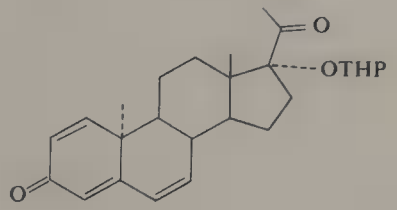
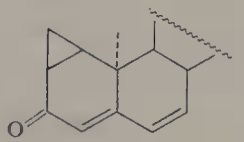
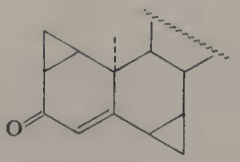
TABLE A.IV (*continued*)

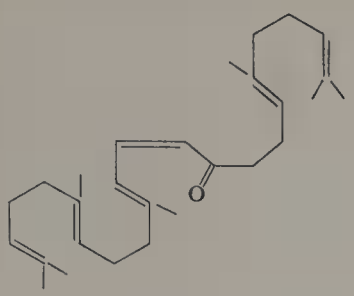
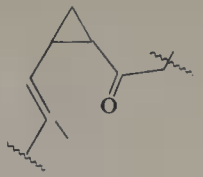
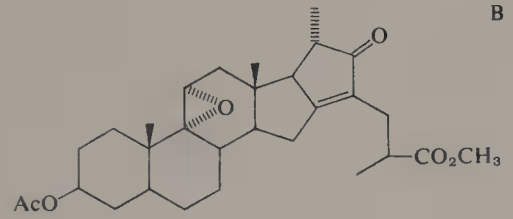
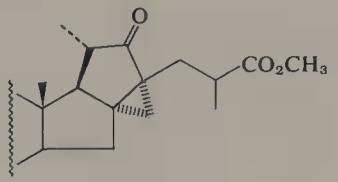
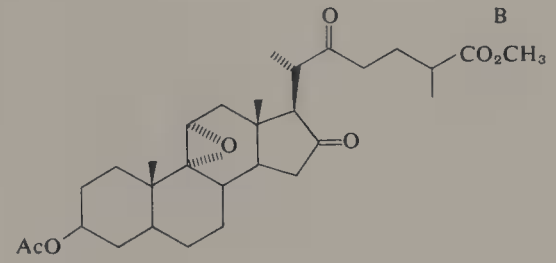
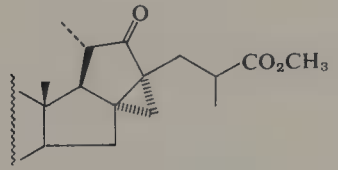
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
C_{24} 	B_1	NaH, DMSO, 25° (12 hr)		(50–60)	208
	B_1	NaH, DMSO, 25° (12 hr)		(25)	208
	B_1	NaH, DMSO, 25° (12 hr)		(18)	208
	B_1	NaH, DMSO, 25° (12 hr)		(40)	208

	B_1	NaOH, DMSO, 25° (1 hr)		(26)	209
	B_1	NaH, DMSO, 25°		(62)	201
	B_1	NaH, DMSO, 25°		(34)	201
C_{25} 	B_1	NaH, DMSO, 25°		(31)	201

(continued)

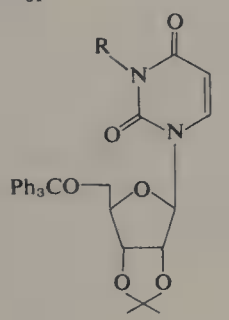
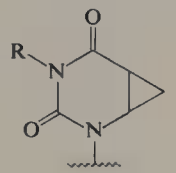
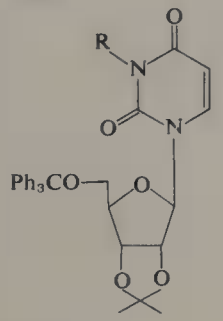
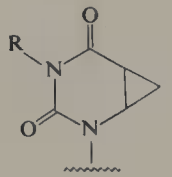
TABLE A.IV (*continued*)

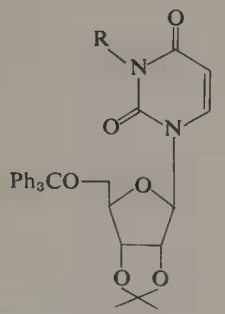
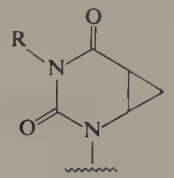
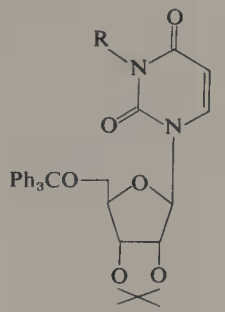
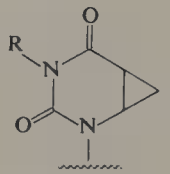
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
	B_1	NaH, DMSO, THF, 25° (1 hr)	 (15)	134
C_{26} 	B	Unstated	 (70)	210
	B_1 (1 equivalent)	NaH, DMSO/THF, 25° (24 hr)	 (unstated)	207
	B_1 (excess)	NaH, DMSO/THF, 25° (36 hr)	 (unstated)	207

C_{28}  *cis*:*trans*, 23:1	B_1	NaH, DMSO	 *trans*:*cis*, 19:1	(unstated)	211
C_{30} 	B	NaH, DMSO/THF, 40° (3 hr)		(24)	212
	B	NaH, DMSO/THF, 40° (3 hr)		(13)	212

(*continued*)

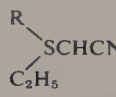
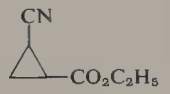
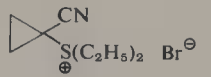
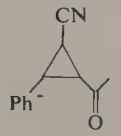
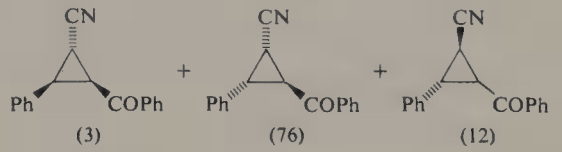
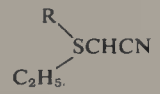
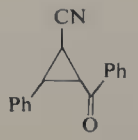
TABLE A.IV (*continued*)

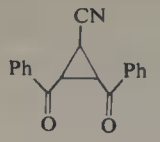
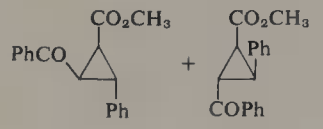
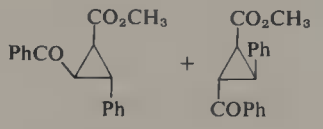
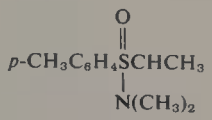
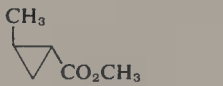
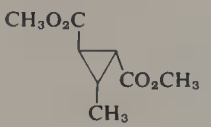
Acceptor	Ylide	Reaction conditions	Products (Yields, %)[a]	References
C_{31}  R = H	B_2	NaH, THF, reflux	 R = H (35)	137
C_{32}  R = CH_3	B_2	NaH, THF, reflux	 R = CH_3 (80)	137

C_{37}  $R = (CH_3)_3CCOCH_2$	B_2	NaH, THF, reflux	 $R = (CH_3)_2CCOCH_2$ (20) $R = H + R = CH_3$ (31)		137
C_{44}  $R = Ph_2CH$	B_2	NaH, THF, reflux (6 hr)	 $R = Ph_2CH$ (50)		213

[a] When the products obtained from various reaction conditions are the same, the structural formulas are not repeated. Only the yields (%) are given.

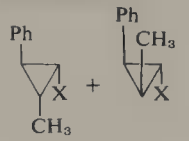
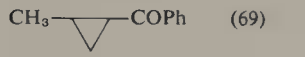
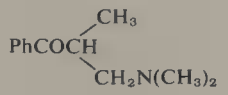
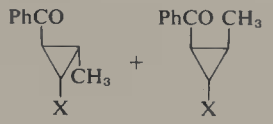
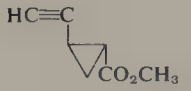
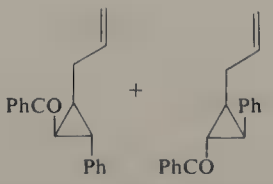
TABLE A.V
Cyclopropanations with Substituted Ylides

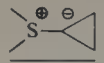
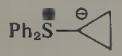
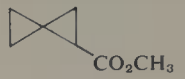
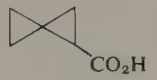
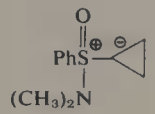
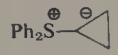
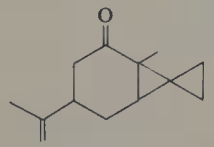
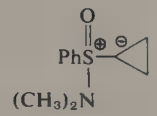
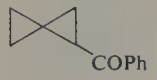
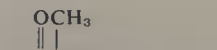
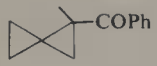
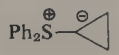
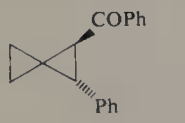
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
				
 R = CH_3, C_2H_5, Ph	Ethyl acrylate	Unstated	 (unstated)	214
	$CH_2{=}CH\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	Unstated	 (unstated)	214
	$PhCH{=}C(CN)_2$	Unstated	 (unstated)	214
	Benzalacetone	Unstated	 (unstated)	214
	$PhCH{=}C(CO_2C_2H_5)_2$	Unstated	 (unstated)	214
$(CH_3)_2SCHCN$	Benzalacetophenone	*n*-C_4H_9Li, THF, −78° (15 min), 25° (16 hr)	 (3) (76) (12)	215
	Benzalacetophenone	Unstated	 (unstated)	214

$R = CH_3, C_2H_5, Ph$	Dibenzolyethylene	Unstated	 (unstated)	214
$\diagdown SCHCO_2^{\ominus}$				
$(CH_3)_2SCHCO_2^{\ominus}$	Benzalacetophenone	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO, 25°	 1 : 1 (59)	98
$Ph_2SCHCO_2^{\ominus}$	Benzalacetophenone	$NaCH_2\overset{\overset{O}{\|}}{S}CH_3$, DMSO, 25°	 1.5 : 1 (89)	98
$\diagdown SCHCH_3$				
 optically active	Methyl acrylate	NaH, DMSO, 25°	 (74) 43% optically active	17
	Dimethyl fumarate	NaH, DMF, 25° (5 hr)	 (72)	97
	Dimethyl maleate	NaH, DMF, 25° (5 hr)	(66)	97

(continued)

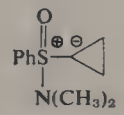
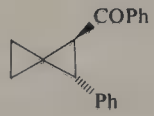
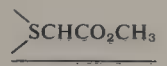
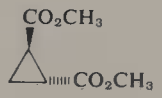
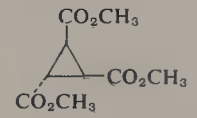
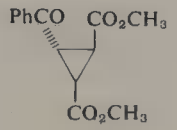
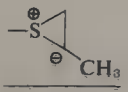
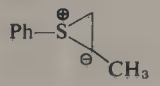
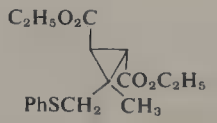
TABLE A.V (*continued*)

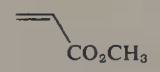
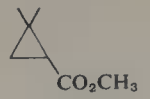
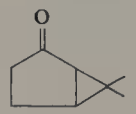
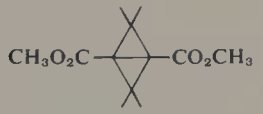
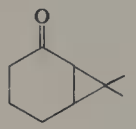
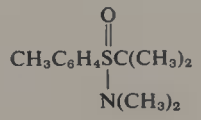
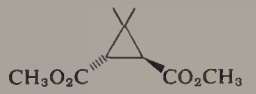
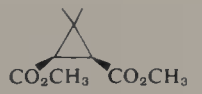
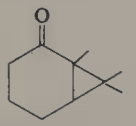
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
				
	Cinnamonitrile	NaH, DMF, 0° (2 days), 25° (1 day)	9 : 1 X = CN (73)	97
	Methyl cinnamate	NaH, DMF, 25° (100 hr)	3 : 2 X = CO_2CH_3 (86)	97
	$PhCOCH_2CH_2N(CH_3)_2$	*n*-C_4H_9Li, DMSO, 25° (22 hr)	 (69)	97
				
		n-C_4H_9Li, DMSO, 25° (21 hr)	1 : 1 X = H (74)	97
	Benzalacetophenone	NaH, DMF, 0° (16 hr), 25° (1 hr)	X = Ph (85)	97
	trans-1,2-Dibenzoylethylene	NaH, DMF, 25° (30 min)	1 : 1 X = PhCO (93)	97
				
	Methyl acrylate	NaH, THF, 0°–5° (30 min), 20°–25° (3 hr)	 (6)	216
				
$Ph_2SCHCH{=}CH_2$	Benzalacetophenone	*n*-C_4H_9Li, THF, −78° (30 min), 25° (1 hr)	 1 : 2.5 (53)	99

					
	Methyl acrylate	$NaCH_2SCH_3$, DME/DMSO, −40°		(41)	217
		KOH (1 equivalent), DMSO, 25°		(83)	217
		KOH (5 equivalents), DMSO, 25°		(89)	217
	Mesityl oxide	NaH, DMSO, 25°		(61)	97
	Carvone	$NaCH_2SCH_3$, DME/DMSO, −40°		(67)	217
		KOH, DMSO, 25°		(75)	217
	$PhCOCH_2CH_2N(CH_3)_2$	NaH, DMSO, 25°		(85)	97
optically active		NaH, DMSO, 25° (20 hr)	Optically active	(41)	97
		NaH, DMSO, 25° (40 hr)		(57)	97
optically active		NaH, DMSO, 25° (40 hr)	Optically active	(41)	97
	Benzalacetophenone	$NaCH_2SCH_3$, DME/DMSO, −40°		(55)	217
		KOH, DMSO, 25°		(79)	217

(continued)

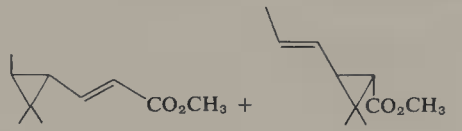
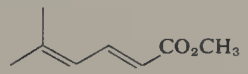
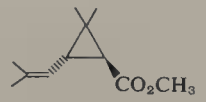
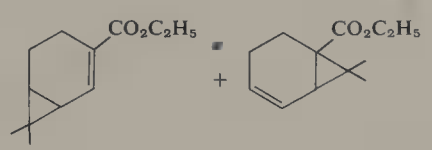
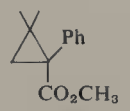
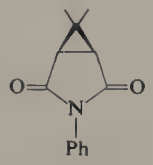
TABLE A.V (*continued*)

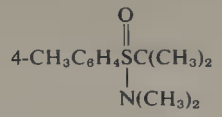
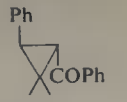
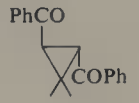
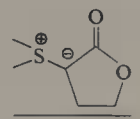
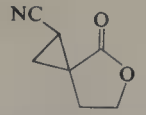
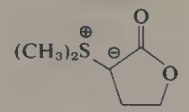
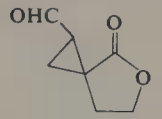
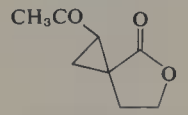
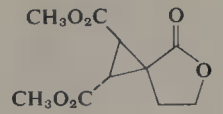
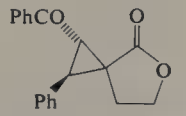
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
	Benzalacetophenone	NaH, DMSO, 25° (15 min)	 (95)	97
optically active	Benzalacetophenone	NaH, DMSO, 25° (15 min)	Optically active (89)	97
				
$(CH_3)_2SCHCO_2CH_3$	Methyl acrylate	DMSO	 (44)	218
	$(CH_3)_2S{=}CHCO_2CH_3$	Unstated	 (unstated)	123
	Dimethyl maleate	DMSO, THF, reflux (17 hr)	(54)	218
			(71)	123
	Dimethyl fumarate	DMSO	(45)	218
	ω-Bromoacetophenone	THF, 25°	 (50)	218a
				
	Diethyl fumarate	NaH, diglyme, 180°	 (61)	219
	Diethyl maleate	NaH, diglyme, 180°	(67)	219

$\diagdown SC(CH_3)_2$					
$Ph_2S{=}C(CH_3)_2$		$LiN(i\text{-}C_3H_7)_2$, DME/hexane, −80°		(71)	109
	Cyclopentenone	$LiN(i\text{-}C_3H_7)_2$, DME/hexane, −80°		(48)	220
	Dimethyl acetylenedicarboxylate	$LiN(i\text{-}C_3H_7)_2$, DME/hexane, −80°		(16)	109
	Cyclohex-2-enone	$LiN(i\text{-}C_3H_7)_2$, DME/hexane, −80°		(74)	109
	Dimethyl fumarate	$LiN(i\text{-}C_3H_7)_2$, DME/hexane, −80°		(82)	109
	Dimethyl fumarate	NaH, DMF, 25° (3 hr)		(75)	97
$Ph_2SC(CH_3)_2$	Dimethyl maleate	$LiN(i\text{-}C_3H_7)_2$, DME/hexane, −80°	 +  (9) (66)		109
	2-Methylcyclohex-2-enone	$LiN(i\text{-}C_3H_7)_2$, DME/hexane, −80°		(86)	109

(continued)

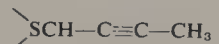
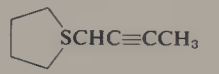
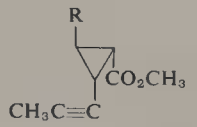
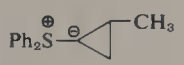
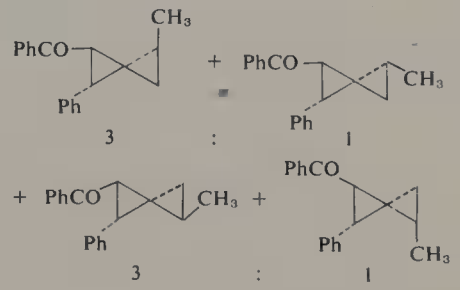
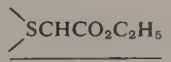
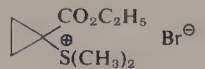
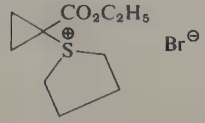
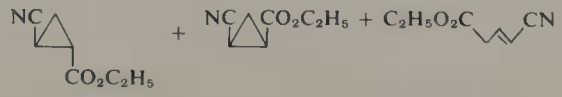
TABLE A.V (*continued*)

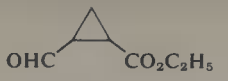
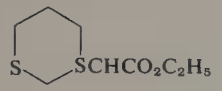
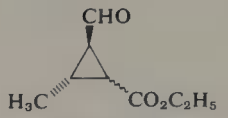
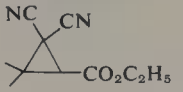
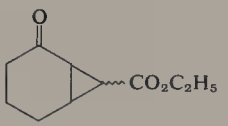
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
				
	Methyl sorbate	$LiN(i\text{-}C_3H_7)_2$, DME, −78°, 40° (10 hr), 25° (overnight)	4 : 1	97
		$(CH_3)_3CLi$, THF	4 : 1	97
		$(CH_3)_3CLi$, THP	3.5 : 1	97
		$LiN(i\text{-}C_3H_7)_2$, DME/hexane, −80°	 (72)	109
				
	Ethyl cyclohexa-1,3-dien-1-carboxylate	$LiN(i\text{-}C_3H_7)_2$, DME, −40° (10 hr), 25° (overnight)	4 : 1 (70)	97
		$LiN(i\text{-}C_3H_7)_2$, THF, −50° (2.5 hr), 25° (8 hr)	1 : 2 (unstated)	97
	Methyl 2-phenylacrylate	$LiN(i\text{-}C_3H_7)_2$, DME/hexane, −80°	 (90.5)	221
	N-Phenylmaleimide	$LiN(i\text{-}C_3H_7)_2$, DME/hexane	 (84)	109

	Benzalacetophenone	NaH, DMF, 25° (10 min)	 (51–67)	97
	trans-1,2-Dibenzoylethylene	NaH, DMF, 25° (10 min)	 (85–88)	97
	Acrylonitrile	NaH, THF, −20° (1 hr), 25° (8 hr)	 (84)	115
	Acrolein	NaH, THF, 25° (3 hr)	 (28)	115
	Methyl vinyl ketone	DMF, 25° (7 hr)	 (22)	115
	Dimethyl fumarate	NaH, THF, 25° (3 hr)	 (56)	115
	Diethyl maleate	CH_3CN, −20° (1 hr), 25° (3 hr)	(80)	115
	Benzalacetophenone	NaH, THF, 25° (6 hr)	 (88)	115

(*continued*)

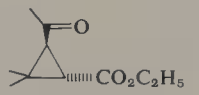
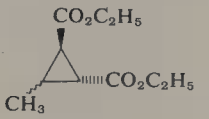
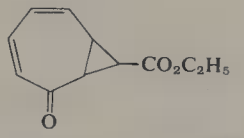
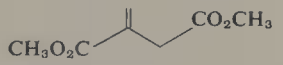
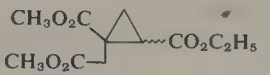
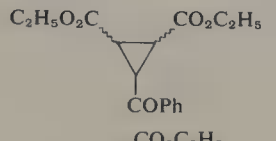
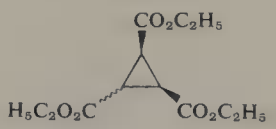
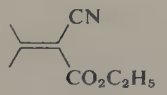
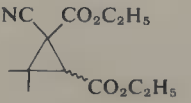
TABLE A.V (*continued*)

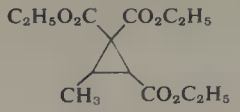
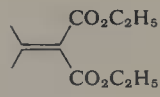
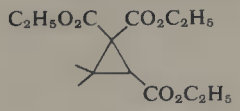
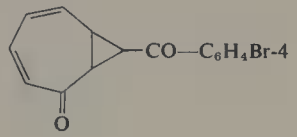
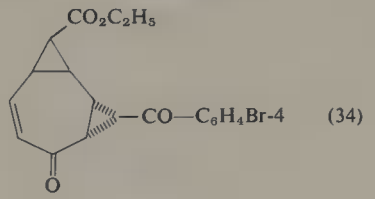
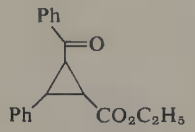
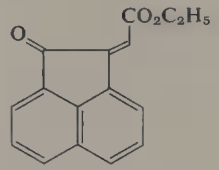
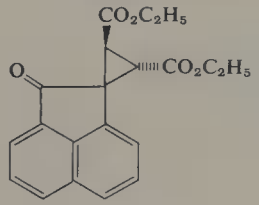
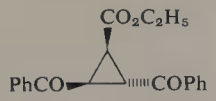
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
				
				
	Methyl acrylate	NaH, THF, 0° (30 min), 25° (3 hr)	R = H (57)	216
	Methyl crotonate	NaH, THF, 0° (30 min), 25° (3 hr)	R = CH_3 (33)	216
				
	Benzalacetophenone	KOH, DMSO, 25° (1 hr)	 (79)	217
				
$(CH_3)_2SCHCO_2C_2H_5$	$CH_2{=}CH\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	C_2H_5OH, 25°	 (77)	222
	$CH_2{=}CH\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	C_2H_5OH, 25°	 (52)	222
$(CH_3)_2SCHCO_2C_2H_5$	Acrylonitrile	CH_2Cl_2, reflux (0.5 hr), 25° (18 hr)	 (70)	223

	Acrolein	Acetone, reflux (0.3 hr)	 *trans*:*cis*, 4.9 : 1	(63)	223, 224
	Acrolein	Unstated	(unstated)		225
$(CH_3)_2SCHCO_2C_2H_5$	Crotonaldehyde	Acetone, reflux (0.3 hr)	 *trans*:*cis*, 4.5:1	(50)	223
	2-Methylacrolein	PhH, reflux (1 hr)	 *trans*:*cis*, 2.1:1	(86)	223
	Methyl vinyl ketone	CH_2Cl_2, reflux (2.5 hr)	 *trans*:*cis*, 49:1	(87)	223
	Ethyl acrylate	CH_2Cl_2, reflux (18 hr)	 *trans*:*cis*, 32:1	(84)	223
	Methyl methacrylate	CH_2Cl_2, reflux (18 hr)	 *trans*:*cis*, 10:1	(69)	223
		CH_2Cl_2, reflux (18 hr)		(85)	223
	Cyclohexenone	PhH, reflux (18 hr)	 *anti*:*syn*, 2:1	(71)	223

(*continued*)

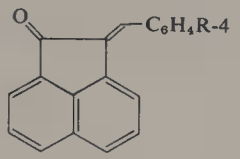
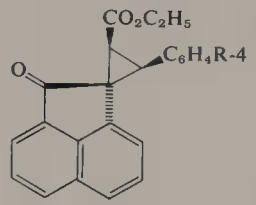
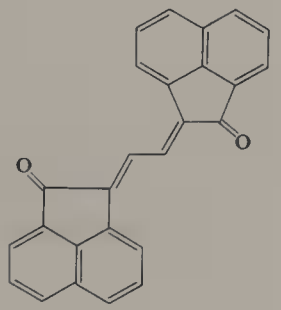
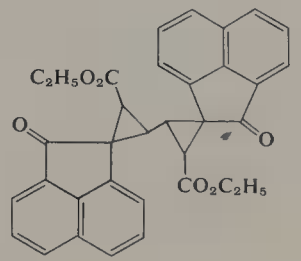
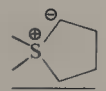
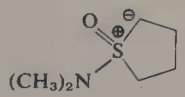
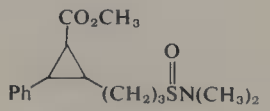
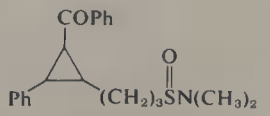
TABLE A.V (*continued*)

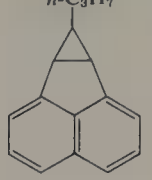
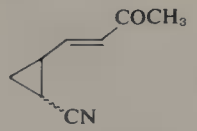
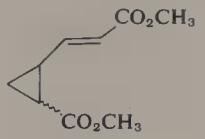
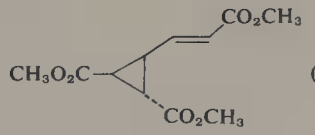
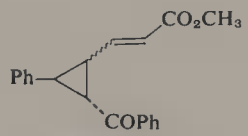
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
	4-Methyl-3-penten-2-one	PhH, reflux (18 hr)	 (75)	223
	Ethyl crotonate	CH_2Cl_2, reflux (18 hr)	 (71) *trans*:*cis*, 1.3:1	223
	Tropone	THF (4–6 hr)	 (75)	223
		PhH, reflux (18 hr)	 (89)	223
	ω-Bromoacetophenone	THF, 25°	 (90)	218a
	Diethyl fumarate	PhH, reflux (2 hr)	 *trans*:*cis*, 100:0 (91)	223
	Diethyl maleate	CH_2Cl_2, reflux (3 hr)	*trans*:*cis*, 2:1 (79)	223
		CH_2Cl_2, reflux (18 hr)	 (91)	223

	Diethyl ethylidenemalonate	CH_2Cl_2, reflux (18 hr)		(90)	223
		PhH, reflux (18 hr)		(65)	223
		PhH, reflux		(34)	226
$Ph_2SCHCO_2C_2H_5$	Benzalacetophenone	THF, 25° (5 hr), reflux (5 hr)		(20)	227
$(CH_3)_2SCHCO_2C_2H_5$		NaH, THF, 25° (3.5 hr)		(88)	67
	trans	NaH, THF, 25° (3.5 hr)		(90)	67
	trans- or *cis*-1,2-Dibenzoylethylene	THF, 25° (1.5), reflux (20 min)		(5)	227

(*continued*)

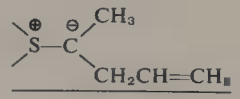
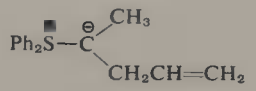
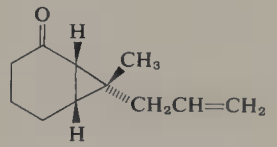
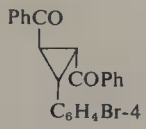
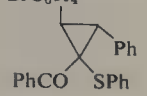
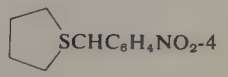
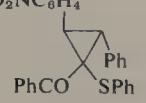
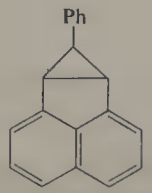
TABLE A.V (*continued*)

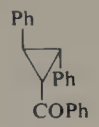
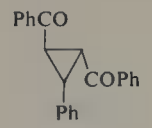
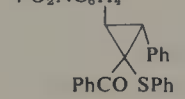
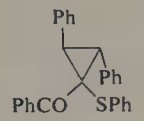
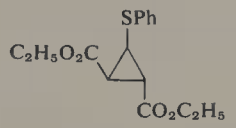
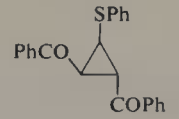
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
				
	R = Cl, R = H, or R = CH_3	NaH, THF, 25° (1 hr), 70°–80° (30 min)	R = Cl, (77), R = H, (62), or R = CH_3 (57)	67
		NaH, THF, 25° (3 hr), 70°–80° (1 hr)	 (57)	67
				
	Methyl cinnamate	NaH, DMSO, 25°	 (64)	116
	Benzalacetophenone	NaH, DMSO, 25°	 (unstated)	116

$\diagdown$SCHC$_3$H$_7$-*n*					
PhSCHC$_3$H$_7$-*n*	Acenaphthylene	*n*-C$_4$H$_9$Li, THF, −70°		(60)	117
$\diagdown$SCHCH=CHCO$_2$CH$_3$					
(CH$_3$)$_2$SCHCH=CHCO$_2$CH$_3$	Acrylonitrile	NaH, *t*-C$_4$H$_9$OH, THF, 20° (16 hr)		(20)	227a
	Methyl acrylate	NaH, *t*-C$_4$H$_9$OH, THF, 20° (16 hr)	 *trans*:*cis* 97:3	(50)	227a
	Dimethyl fumarate	NaH, *t*-C$_4$H$_9$OH, THF, 20° (16 hr)		(57)	227a
	Dimethyl maleate	NaH, *t*-C$_4$H$_9$OH, THF, 20° (16 hr)		(60)	227a
	Benzalacetophenone	NaH, *t*-C$_4$H$_9$OH, THF, 20° (16 hr)	 *trans*:*cis* 55:45	(50)	227a

(continued)

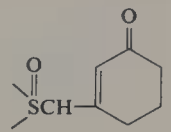
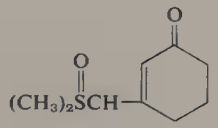
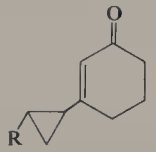
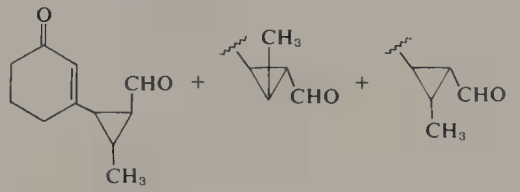
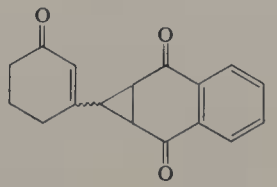
TABLE A.V (*continued*)

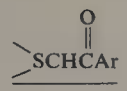
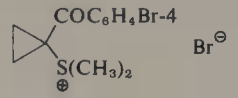
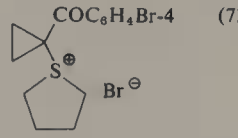
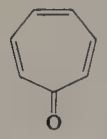
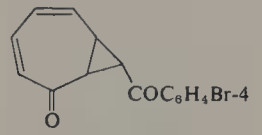
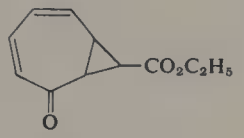
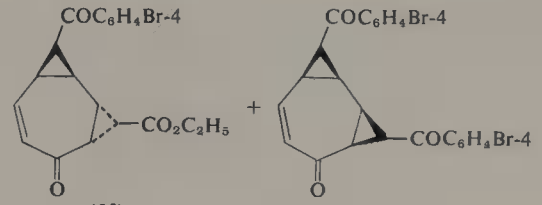
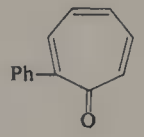
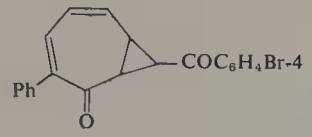
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
				
	Cyclohexenone	$LiN(i\text{-}C_3H_7)_2$, DME		228
				
	*trans*-1,2-Dibenzoylethylene	$KOC(CH_3)_3$, THF, 25° (20 min)	 (91)	229
	2-Phenylthio-*trans*-benzalacetophenone	$KOC(CH_3)_3$, THF, 25° (20 min)	 (81)	229
	2-Phenylthio-*trans*-benzalacetophenone	$KOC(CH_3)_3$, THF, 25° (20 min)	 (89)	229
Ph_2SCHPh	Acenaphthylene	$n\text{-}C_4H_9Li$, THF, −50°	 (43)	117

	trans-Benzalacetophenone	$KOC(CH_3)_3$, THF, 25° (20 min)		(82)	229
	trans-1,2-Dibenzoylethylene	$KOC(CH_3)_3$, THF, 25° (20 min)		(81)	229
	2-Phenylthio-*trans*-benzal-4′-nitroacetophenone	$KOC(CH_3)_3$, THF, 25° (20 min)		(78)	229
	2-Phenylthio-*trans*-benzalacetophenone	$KOC(CH_3)_3$, THF, 25° (20 min)		(91)	229
					
$(CH_3)_2SCHSPh$	Diethyl fumarate	*n*-C_4H_9Li, THF, −20° (1 hr)		(51)	225
	trans-1,2-Dibenzoylethylene	*n*-C_4H_9Li, THF, −20° (1 hr)		(27)	225, 230
	cis-1,2-Dibenzoylethylene	*n*-C_4H_9Li, THF, −20° (1 hr)		(53)	225

(*continued*)

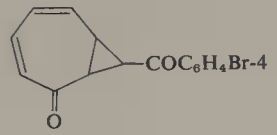
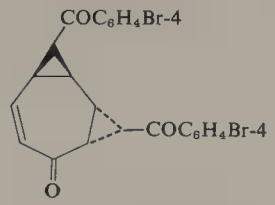
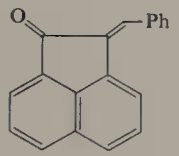
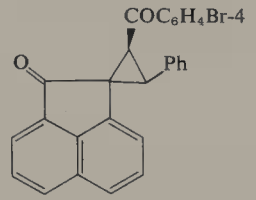
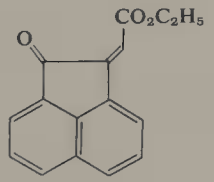
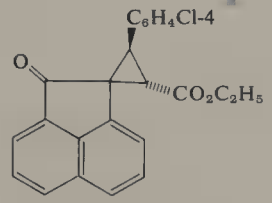
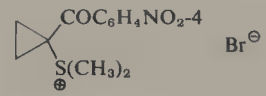
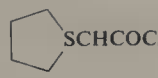
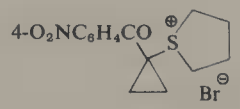
TABLE A.V (*continued*)

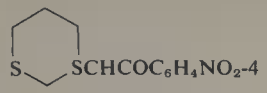
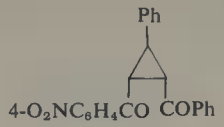
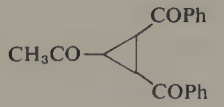
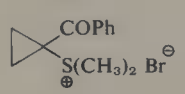
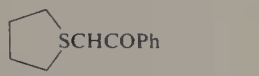
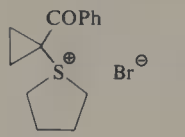
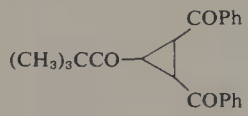
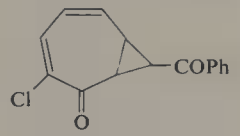
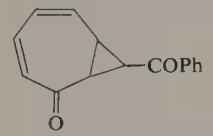
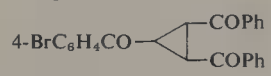
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
				
				
	Nitroethylene	Acetone, 25° (4 hr)	R = NO_2 (55)	231
	Acrylonitrile	Acetone, 56° (20 hr)	R = CN (50)	231
	Acrolein	Acetonitrile, 25° (5 hr)	R = CHO (85–90)	231
	Methyl vinyl ketone	Acetonitrile, 56° (4 hr)	R = $COCH_3$ (87)	231
		Acetonitrile, 110°	R = $COCH_3$ (92)	232
	Crotonaldehyde	Acetonitrile, 56° (8 hr)		231
			5 : 3 : 2 (87)	
	1,4-Naphthoquinone	Acetonitrile, 110°	 (47)	232

				
$(CH_3)_2SCHCOC_6H_4Br\text{-}4$	$CH_2{=}CH\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	C_2H_5OH, 25°	 (73)	222
	$CH_2{=}CH\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	C_2H_5OH, 25°	 (73)	222
$(CH_3)_2SCHCOC_6H_4Br\text{-}4$		THF, 25° (4–6 hr)	 (57)	226
		PhH, reflux (7 hr)	 (55) (21)	226
		THF, 25° (4–5 hr)	 (30)	226

(continued)

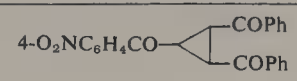
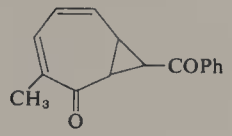
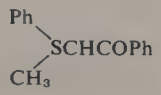
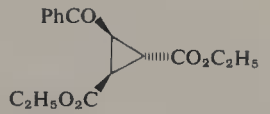
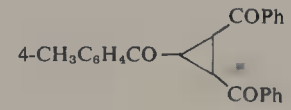
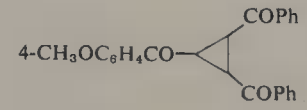
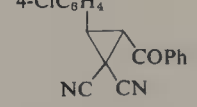
TABLE A.V (*continued*)

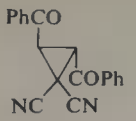
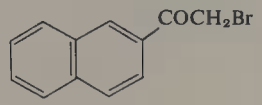
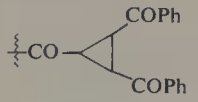
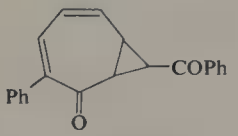
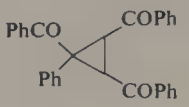
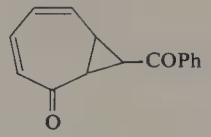
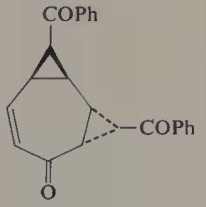
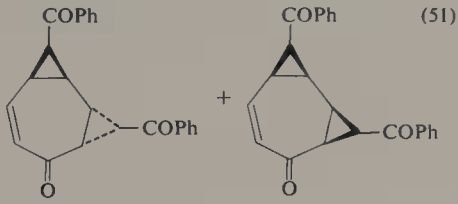
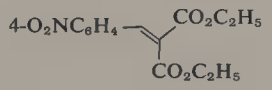
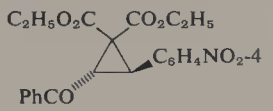
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]		References
		THF, reflux		(63)	226
		NaH, THF, 25° (12 hr), 70°–80° (30 min)		(81)	67
$(CH_3)_2S{=}CHCOC_6H_4Cl\text{-}4$		NaH, THF, 25° (3 hr), 70°–80° (30 min)		(57)	67
$(CH_3)_2S{=}CHCOC_6H_4NO_2\text{-}4$	$CH_2{=}CHS(CH_3)_2\ Br^{\ominus}$	C_2H_5OH, 25°		(58)	222
	$CH_2{=}CHS(CH_3)_2\ Br^{\ominus}$	C_2H_5OH		(unstated)	222

	Benzalacetophenone	Unstated		(unstated)	225
$(CH_3)_2SCHCOPh$	Bromoacetone	THF, 25° (6–12 hr)		(65)	218a, 233
	Chloroacetone	THF, 25° (6–12 hr)		(22)	218a, 233
	$CH_2{=}CH\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	C_2H_5OH, 25°		(33)	222
	$CH_2{=}CH\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	C_2H_5OH, 25°		(68)	222
$(CH_3)_2SCHCOPh$	$(CH_3)_3CCOCH_2Br$	THF, 25° (6–12 hr)		(87)	218a, 233
	2-Chlorotropone	THF, 50°–60° (4–6 hr)		(56)	226
	Tropone	THF, 50°–60° (4–6 hr)		(55)	226
	$4\text{-}BrC_6H_4COCH_2Br$	THF, 25° (6–12 hr)		(68)	218a, 233

(continued)

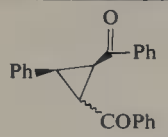
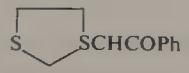
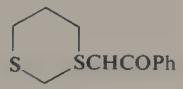
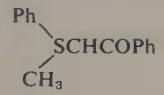
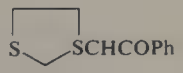
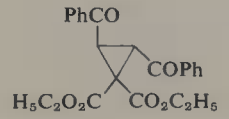
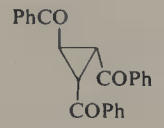
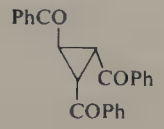
TABLE A.V (*continued*)

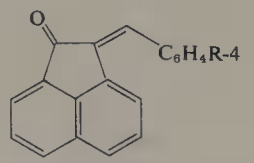
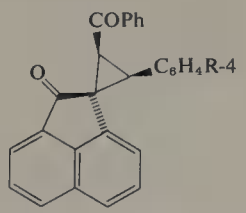
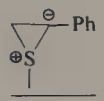
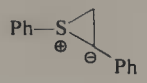
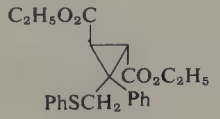
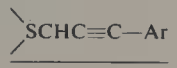
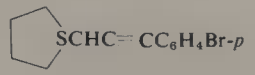
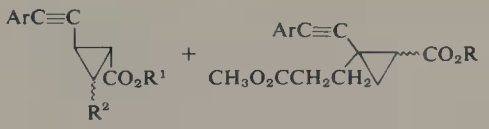
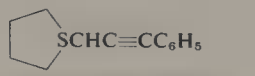
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
	$4\text{-}O_2NC_6H_4COCH_2Br$	THF, 25° (6–12 hr)	 (85)	218a, 233
	2-Methyltropone	THF, 50°–60° (4–6 hr)	 (80)	226
	Diethyl maleate	THF, reflux (30 hr)	 (50)	230
	Diethyl fumarate	THF, reflux (30 hr)	(70)	
$(CH_3)_2SCHCOPh$	$4\text{-}CH_3C_6H_4COCH_2Br$	THF, 25° (6–12 hr)	 (70)	218a, 233
	$4\text{-}CH_3OC_6H_4COCH_2Br$	THF, 25° (6–12 hr)	 (80)	218a, 233
	$4\text{-}ClC_6H_4CH{=}C(CN)_2$	C_2H_5OH, 25°	 (78)	234
	$PhCOCHS(CH_3)_2$	THF	 (47)	123
	$PhCOCHS(CH_3)_2$	$Fe(CO)_5$, THF, reflux	(20)	235
	$PhCOCH_2\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	THF	(100)	123

	$PhCOCH{=}C(CN)_2$	Unstated		(unstated)	236
$(CH_3)_2SCHCOPh$		THF, 25° (6–12 hr)		(84)	218a, 233
	2-Phenyltropone	THF, 50°–60° (4–6 hr)		(62)	226
	$PhCOCHBrPh$	THF, 25° (6–12 hr)		(15)	218a, 233
		THF, 50°–60° (4–6 hr)		(90)	226
		PhH, reflux		(51)	226
		C_2H_5OH, 25°		(36.5)	234

(continued)

TABLE A.V (*continued*)

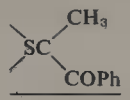
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
	trans-Benzalacetophenone	PhH, 25°	 (66) *trans*	237
	*trans*-Benzalacetophenone	Unstated	(unstated)	235
	*trans*-Benzalacetophenone	Unstated	*cis* (unstated)	225
	*trans*-Benzalacetophenone	$CHCl_3$, reflux (6 hr)	*trans* (77)	230
	$PhCOCH{=}C(CO_2C_2H_5)_2$	Unstated	 (unstated)	236
	cis-1,2-Dibenzoylethylene	Unstated	 (unstated)	236
$(CH_3)_2SCHCOPh$	*trans*-1,2-Dibenzoylethylene	PhH, 25°	 (98)	237

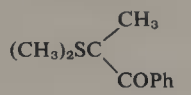
	trans-1,2-Dibenzoylethylene	C_2H_5OH, 25° (30 min)	(87)		230
	cis-1,2-Dibenzoylethylene	C_2H_5OH, 25° (30 min)	(83)		230
	 R = H or R = Cl	NaH, THF, 25° (12 hr), 70°–80° (30 min)	 R = H (82) or R = Cl (55)		67
					
	Diethyl maleate	NaH, diglyme, 180°		(72)	219
					
			 **1** **2**		
	Methyl acrylate	NaH, THF, 0° (30 min), 25° (3 hr)	Ar = C_6H_4 Br-*p*, R^1 = CH_3, R^2 = H; **1**	(56)	216
	Methyl cinnamate	NaH, THF, 0° (30 min), 25° (3 hr)	Ar = C_6H_4 Br-*p*, R^1 = CH_3, R^2 = Ph; **1**	(5)	216
$(CH_3)_2SCHC{\equiv}CC_6H_5$	Methyl acrylate	NaH, THF, 0° (30 min), 25° (3 hr)	Ar = C_6H_5, R^1 = CH_3, R^2 = H; **1** (36), **2**	(11)	216, 238
	Methyl acrylate	NaH, THF, 0° (30 min), 25° (3 hr)	Ar = C_6H_5, R^1 = CH_3, R^2 = H; **1**	(75)	216

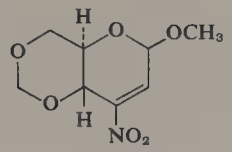
(continued)

TABLE A.V (*continued*)

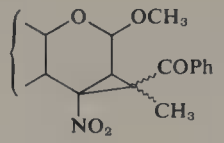
Ylide	Acceptor	Reaction conditions	Products (Yields, %)[a]	References
	Ethyl acrylate	NaH, THF, 0° (30 min), 25° (3 hr)	Ar = C_6H_5, R^1 = C_2H_5, R^2 = H; **1** (55)	216
	Methyl crotonate	NaH, THF, 0° (30 min), 25° (3 hr)	Ar = C_6H_5, R^1 = R^2 = CH_3; **1** (11)	216
	Methyl fumarate	NaH, THF, 0° (30 min), 25° (3 hr)	Ar = C_6H_5, R^1 = CH_3, R^2 = CO_2CH_3; **1** (19)	216
	Methyl maleate	NaH, THF, 0° (30 min), 25° (3 hr)	(25)	216
	Ethyl 3-methyl-crotonate	NaH, THF, 0° (30 min), 25° (3 hr)	PhC≡C, $CO_2C_2H_5$, H_3C, CH_3 (trace)	216
$\diagdown$SCHCOAr$\diagup$				
$(CH_3)_2SCHCOC_6H_4CH_3$-4	Bromoacetone	THF, 25° (6–12 hr)	CH_3CO, $COC_6H_4CH_3$-4, $COC_6H_4CH_3$-4 (56)	218a, 233
	PhCOCHBrPh	THF, 25° (6–12 hr)	PhCO, Ph, $COC_6H_4CH_3$-4, $COC_6H_4CH_3$-4 (15)	218a, 233
	trans-Benzalacetophenone	unstated	Ph, *p*-$CH_3C_6H_4CO$, COPh (unstated)	225
$(CH_3)_2SCHCOC_6H_4OCH_3$-4	Bromoacetone	THF, 25° (6–12 hr)	RCO, $COC_6H_4OCH_3$-4, $COC_6H_4OCH_3$-4; R = CH_3 (48)	218a, 233
	Bromoacetophenone	THF, 25° (6–12 hr)	R = Ph (50)	218a, 233





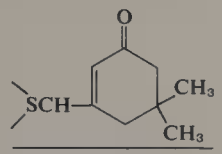


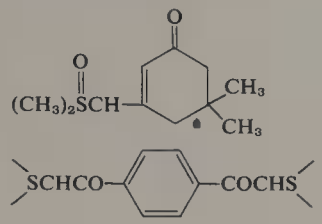
THF, 25°



(71)

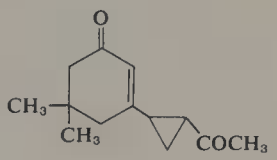
182





Methyl vinyl ketone

110°



(62)

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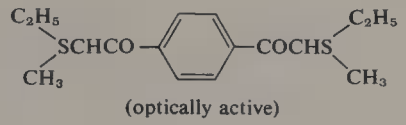
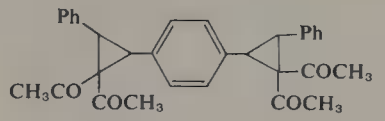


(optically active)

$PhCH{=}C(COCH_3)_2$

DMSO, 25° (2 days)



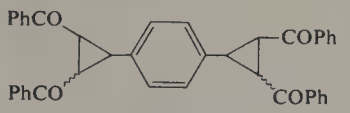
optically active

(41)

238a

trans-1,2-Dibenzoylethylene

DMSO, 25° (2 days)



optically active

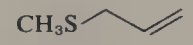
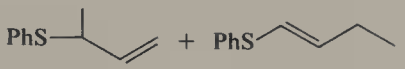
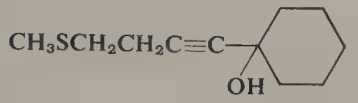
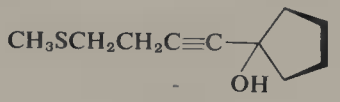
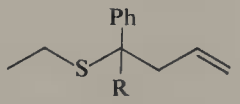
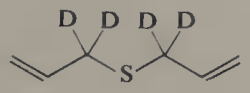
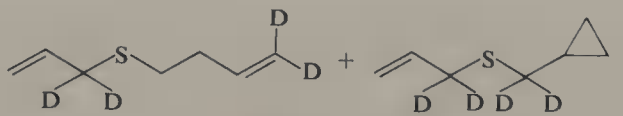
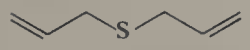
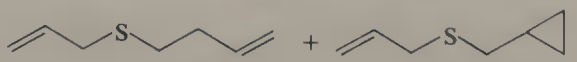
(42)

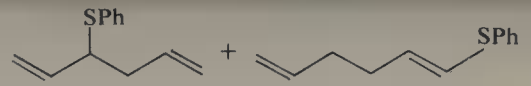
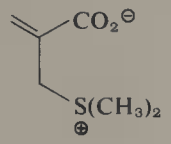
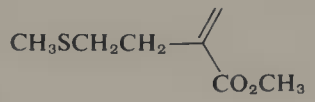
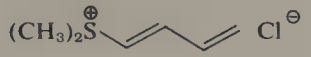
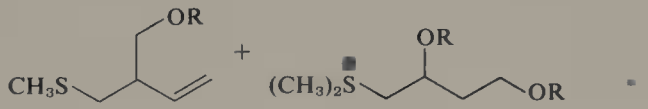
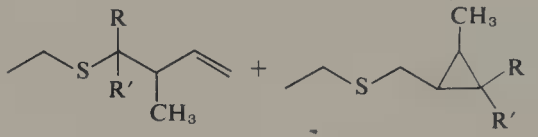
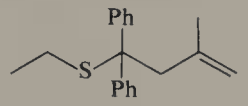
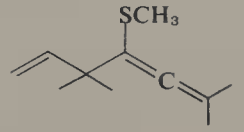
238a

[a] When the products obtained under various reaction conditions are the same, the structural formulas are not repeated. Only the yields (%) are given.

TABLE A.VI

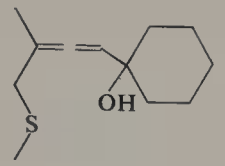
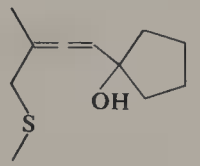
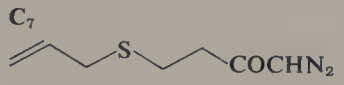
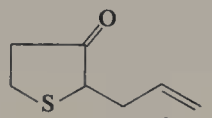
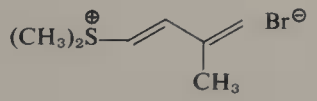
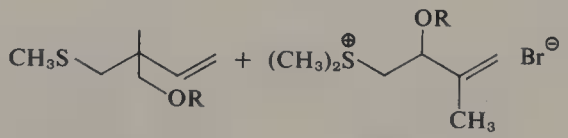
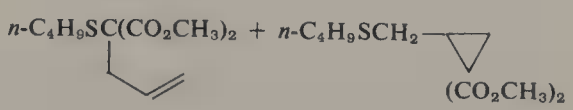
Rearrangements: [2,3]Sigmatropic

Precursor	Reaction conditions	Products (Yields, %)[a]	References
C_2			
Dimethyl sulfide	$PhCHN_2$, *hν*	2-Methylthiomethyltoluene (20)	239
	Ph_2CN_2, *hν*	2-$CH_3SCH_2C_6H_4CH_2Ph$ (10)	239
C_4			
	Benzyne	 (31)	240
C_5			
	NaH, THF, cyclohexanone	 (53)	241
	NaH, THF, cyclopentanone	 (53)	241
Allyl ethyl sulfide			
	$PhCHN_2$, $CuSO_4$, 110°	R = H (49)	239
	$PhCHN_2$, *hν*	R = H (31)	239
	Ph_2CN_2, $CuSO_4$, 110°	R = Ph (38)	239
	Ph_2CN_2, *hν*	R = Ph (26)	239
C_6			
	CH_2N_2, CuCl, pentane	 (unstated)	242
	CH_2N_2, CuCl, pentane	 (30–35) 4.9 : 1	242

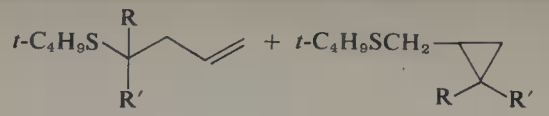
	Benzyne	 9 : 1	(unstated)		243
	$NaCH_2SCH_3$, DMSO, THF, $-17°$ (40 min), dimethylsulfate, 25° (2 hr)		(50)		215
					
	$NaOCH_3$, CH_3OH, 25° (17 hr)	$R = CH_3$	(76)	(3)	244
	$NaOC_2H_5$, C_2H_5OH, 25° (13 hr)	$R = C_2H_5$	(80)	(—)	244
Crotyl ethyl sulfide					
	$N_2C(CO_2CH_3)_2$, $h\nu$	$R = R' = CO_2CH_3$	(53)	(7)	245
	$N_2C(CO_2CH_3)_2$, $h\nu$, Ph_2CO	$R = R' = CO_2CH_3$	(31)	(19)	245
	$PhCHN_2$, $CuSO_4$, 110°	R = Ph, R′ = H	(45)	(0)	239
	$PhCHN_2$, $h\nu$	R = Ph, R′ = H	(30)	(0)	239
	Ph_2CN_2, $CuSO_4$, 110°	R = R′ = Ph	(26)	(0)	239
	Ph_2CN_2, $h\nu$	R = R′ = Ph	(38)	(0)	239
2-Methallyl ethyl sulfide	Ph_2CN_2, $CuSO_4$, 110°		(43)		239
	Ph_2CN_2, $h\nu$		(21)		239
3-Methyl-2-butenyl methyl sulfide	$HC{\equiv}CC(CH_3)_2Cl$, n-C_4H_9Li, ether, 20°		(35–56)		245a

(continued)

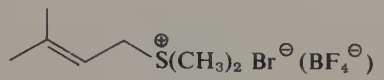
TABLE A.VI (*continued*)

Precursor	Reaction conditions	Products (Yields, %)[a]	References
$CH_3—C\equiv C—CH_2\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	NaH, THF, cyclohexanone	 (40)	241
	NaH, THF, cyclopentanone	 (17)	241
	$CuSO_4$, dioxane, reflux	 (78)	246
			
	$NaOCH_3$, CH_3OH, 25° (3 hr)	$R = CH_3$ (59) (8)	244
	$NaOC_2H_5$, C_2H_5OH, 25° (15 min)	$R = C_2H_5$ (73) (21)	244
Allyl *n*-butyl sulfide			
	$N_2C(CO_2CH_3)_2$, $h\nu$	(57) (11)	247
	$N_2C(CO_2CH_3)_2$, $h\nu$, benzophenone	(28) (55)	247
	$N_2C(CO_2CH_3)_2$, Δ, $CuSO_4$	(93) (0)	247

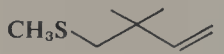
Allyl *t*-butyl sulfide



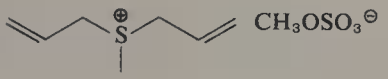
$N_2C(CO_2CH_3)_2$, *hν*	R = R′ = CO_2CH_3	(34)	(14)	247
$N_2C(CO_2CH_3)_2$, *hν*, benzophenone	R = R′ = CO_2CH_3	(–)	(50)	247
$N_2C(CO_2CH_3)_2$, $CuSO_4$, 110°	R = R′ = CO_2CH_3	(13)	(0)	247
$PhCHN_2$, $CuSO_4$, 110°	R = Ph, R′ = H	(54)	(0)	239
$PhCHN_2$, *hν*	R = Ph, R′ = H	(29)	(6)	239
Ph_2CN_2, $CuSO_4$, 110°	R = R′ = Ph	(14)	(16)	239
Ph_2CN_2, *hν*	R = R′ = Ph	(22)	(3)	239



n-C_4H_9Li, THF, −78°

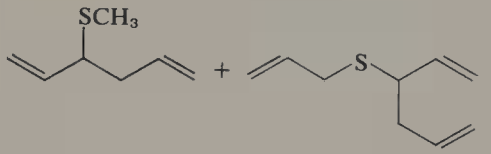


(84) 249, 249

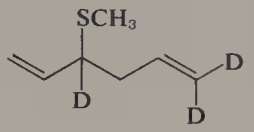


n-C_4H_9Li, THF, −78°

(20) 99

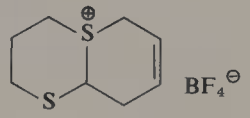


NaOH, H_2O 9.4 : 1 (50) 250

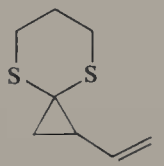


NaOD, D_2O (45–50) 250

C_8



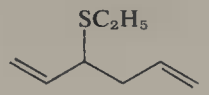
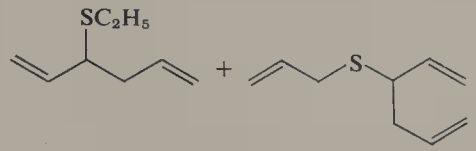
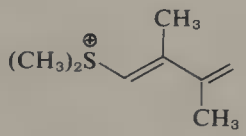
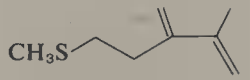
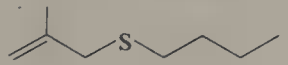
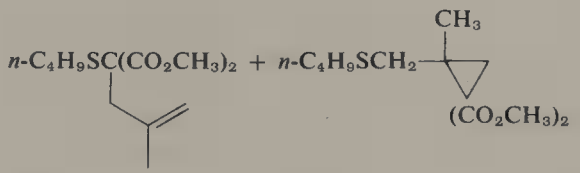
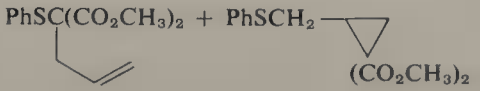
n-C_4H_9Li, THF, −78° (20 min), 25° (25 min)

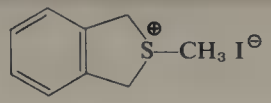
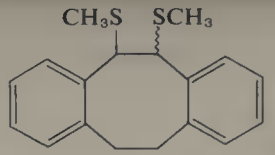
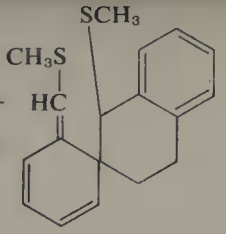
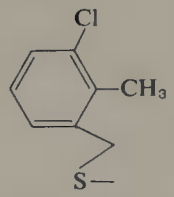
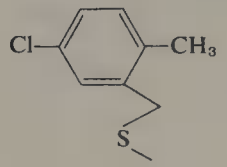


(87) 251

(*continued*)

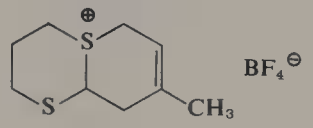
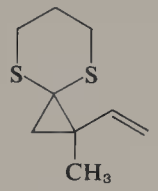
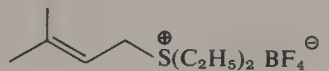
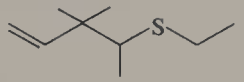
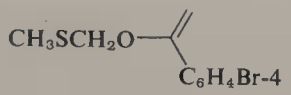
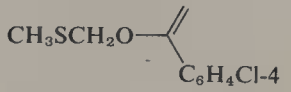
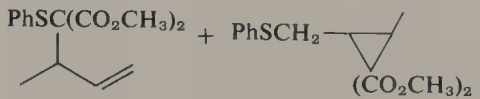
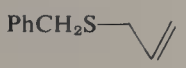
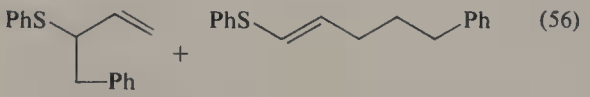
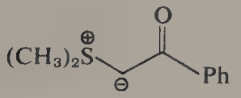
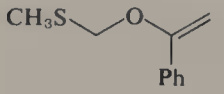
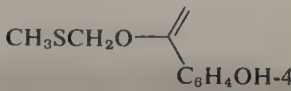
TABLE A.VI (*continued*)

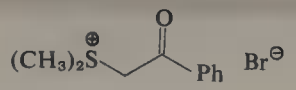
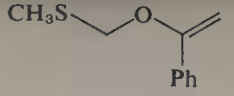
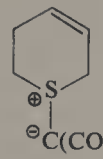
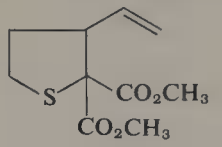
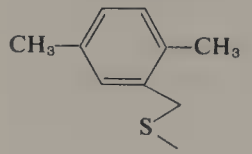
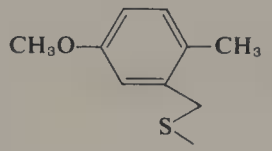
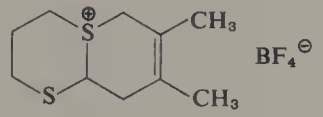
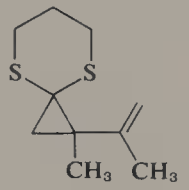
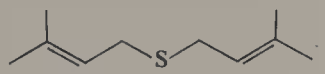
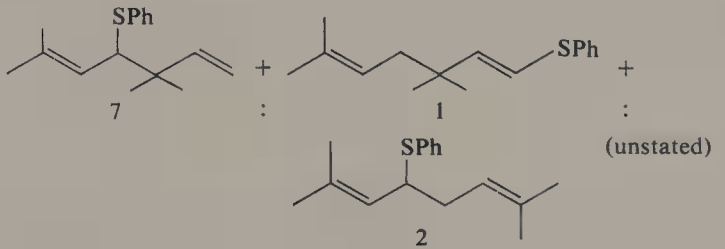
Precursor	Reaction conditions	Products (Yields, %)[a]	References
$(CH_2{=}CHCH_2)_2\overset{\oplus}{S}C_2H_5\ X^{\ominus}$			
$X = BF_4^{\ominus}$	$NaOH, H_2O, 25°$	(unstated)	252
	$NaOCH_3, CH_3OH, 25°$	(unstated)	252
	$KOC(CH_3)_3, PhH, 25°$	(unstated)	252
	NaH, THF	(90–95)	243
			
$X = CH_3OSO_3^{\ominus}$	$NaOH, H_2O$	3 : 1 (60)	250
	$NaOCH_3, CH_3OH, 25°$	 (63)	244
			
	$N_2C(CO_2CH_3)_2, h\nu$	(54) (12)	247
	$N_2C(CO_2CH_3)_2, \Delta, CuSO_4$	(100) (0)	
C_9 Allyl phenyl sulfide			
	$N_2C(CO_2CH_3)_2, h\nu$	(32) (7)	247
	$N_2C(CO_2CH_3)_2, \Delta, CuSO_4$	(90) (0)	

	PhLi, ether, 25°	 (1.4–2.2) +  (16)		253
$2\text{-}ClC_6H_4CH_2\overset{\oplus}{S}(CH_3)_2\ X^{\ominus}$				
$X = Cl^{\ominus}$	35% $NaOCH_3$, $HOCH_3$, 60°–65° (2 hr)		(64)	254
$X = ClO_4^{\ominus}$	35% $NaOCH_3$, $HOCH_3$, 60°–65° (2 hr)		(85)	254
$4\text{-}ClC_6H_4CH_2\overset{\oplus}{S}(CH_3)_2\ X^{\ominus}$				
$X = Cl^{\ominus}$	35% $NaOCH_3$, $HOCH_3$, 60°–65° (2 hr)		(70)	254
$X = ClO_4^{\ominus}$	35% $NaOCH_3$, $HOCH_3$, 60°–65° (2 hr)		(56)	254
$PhCH_2\overset{\oplus}{S}(CH_3)_2\ X^{\ominus}$				
$X = Cl$	35% $NaOCH_3$, $HOCH_3$, 60°–65° (2 hr)	$2\text{-}CH_3C_6H_4CH_2SCH_3$	(35)	254
	$KOC(CH_3)_3$, $HOC(CH_3)_3$		(unstated)	254
	NaOH, high concentration		(87)	254
$X = Br$	$NaNH_2$, liquid, NH_3		(51)	255
$X = BF_4$	Electrolysis, DMSO, 25°		(17)	6
$X = ClO_4$	$NaOCH_3$, CH_3OH, 60°–65° (2 hr)		(40)	254

(continued)

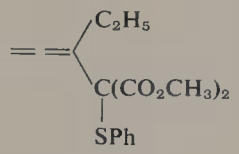
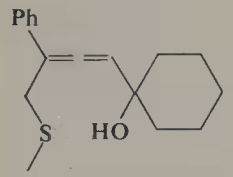
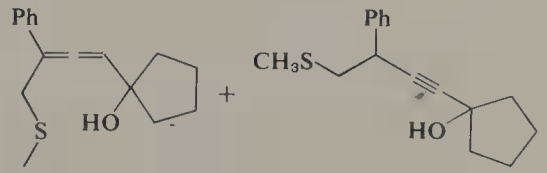
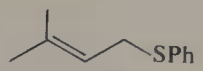
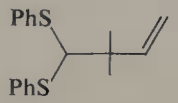
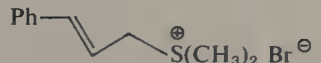
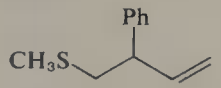
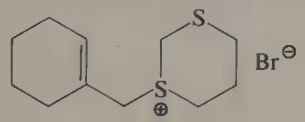
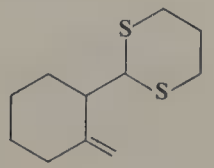
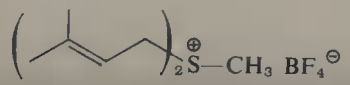
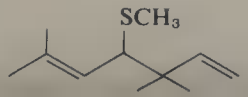
TABLE A.VI (*continued*)

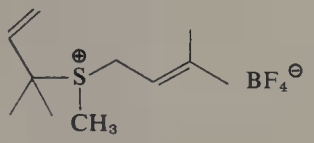
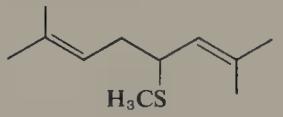
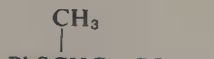
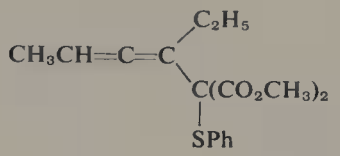
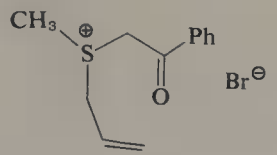
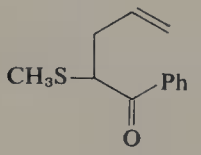
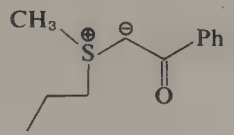
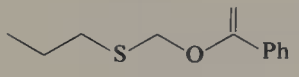
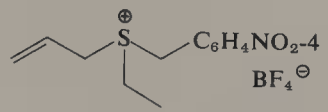
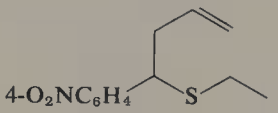
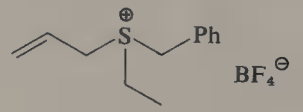
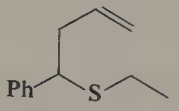
Precursor	Reaction conditions	Products (Yields, %)[a]	References
	*n*-C_4H_9Li, THF, −78° (20 min), 25° (25 min)	 (96)	251
	$KOC(CH_3)_3$, PhH, 25°	 (unstated)	252
C_{10}			
4-$BrC_6H_4COCHS(CH_3)_2$	H_2O, 100° (5 hr)	 (50)	256
4-$ClC_6H_4COCHS(CH_3)_2$	H_2O, 100° (5 hr)	 (64)	256
Crotyl phenyl sulfide			
	$N_2C(CO_2CH_3)_2$, *hν*	(47) (10)	247
	$N_2C(CO_2CH_3)_2$, $CuSO_4$, 110°	(92) (0)	247
	Benzyne	 (56)	240
	H_2O, 100° (4 hr)	 (66)	256
4-$HOC_6H_4COCHS(CH_3)_2$	H_2O, 100° (5 hr)	 (84)	256

	1 *N* KOH, 100° (5 hr)		(unstated)	256
	180°		(83)	245
4-$CH_3C_6H_4CH_2\overset{\oplus}{S}(CH_3)_2$ $X^{\ominus}$				
X = $Cl^{\ominus}$	35% $NaOCH_3$, $HOCH_3$, 60°–65° (2 hr)		(33)	254
X = $ClO_4^{\ominus}$	35% $NaOCH_3$, $HOCH_3$, 60°–65° (2 hr)		(15)	254
4-$CH_3OC_6H_4CH_2\overset{\oplus}{S}(CH_3)_2$ $X^{\ominus}$				
X = $Cl^{\ominus}$	35% $NaOCH_3$, $HOCH_3$, 60°–65° (2 hr)		(unstated)	254
X = $ClO_4^{\ominus}$	35% $NaOCH_3$, $HOCH_3$, 60°–65° (2 hr)		(3)	254
	*n*-C_4H_9Li, THF, −78° (20 min), 25° (25 min)		(93)	251
	Benzyne			243, 257

(*continued*)

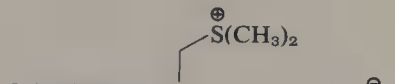
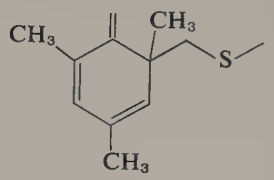
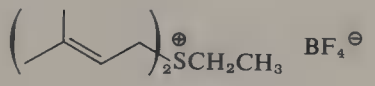
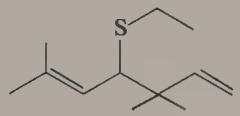
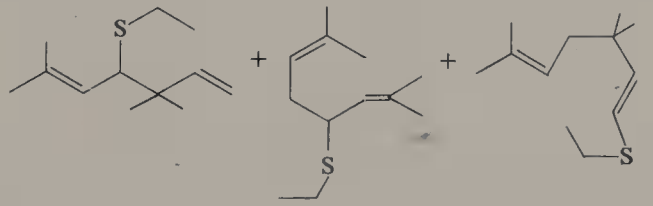
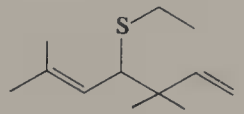
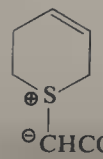
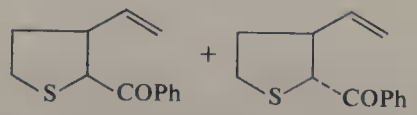
TABLE A.VI (*continued*)

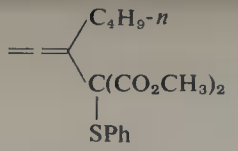
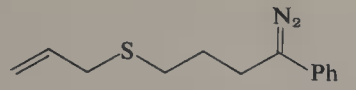
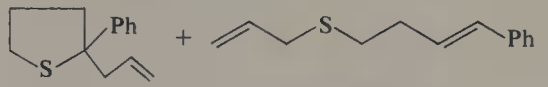
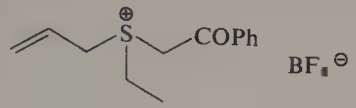
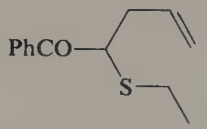
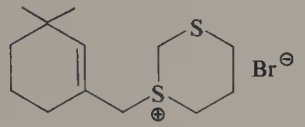
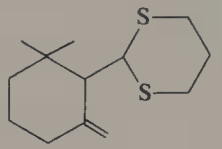
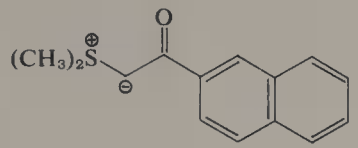
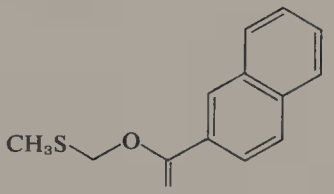
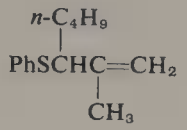
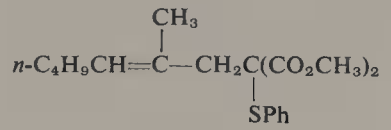
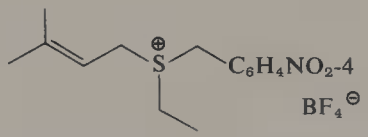
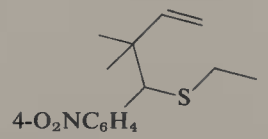
Precursor	Reaction conditions	Products (Yields, %)[a]	References
C_{11}			
$PhSCH_2C{\equiv}CC_2H_5$	$N_2C(CO_2CH_3)_2$, $CuSO_4$, 95°–100°	 (71)	257a
$PhC{\equiv}CCH_2\overset{\oplus}{S}(CH_3)_2\ Br^{\ominus}$	NaH, THF, cyclohexanone	 (43)	241
	NaH, THF, cyclopentanone		241
	$PhSCH_2Cl$, $KOC(CH_3)_3$, DME	 (80)	258
	*n*-C_4H_9Li, THF, −78°	 (78)	249
	*n*-C_4H_9Li, THF, −78°	 (80)	259
	$KOC(CH_3)_3$, −45°	 (unstated)	257

	$PhCH(CF_3)OLi$, $PhCH(CF_3)OH$/pentane, −10°	5% optical yield	(54)	260
	$PhCH(CF_3)OLi$, $[(CH_3)_2NCH_2\underset{\displaystyle CH_3O}{\underset{\vert}{C}}H]_2$/THF, −20°	12% optical yield	(48)	260
	*n*-C_4H_9Li, −70°		(unstated)	261
C_{12} 	$N_2C(CO_2CH_3)_2$, $CuSO_4$, 95°–100°		(60)	257a
	$NaOH$, H_2O		(unstated)	262
	H_2O, 100°		(40)	256
	$NaOC_2H_5$, HOC_2H_5, 25°		(unstated)	263
	$NaOC_2H_5$, HOC_2H_5, 25°		(unstated)	263

(*continued*)

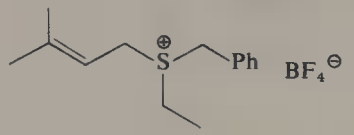
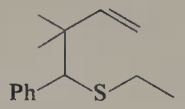
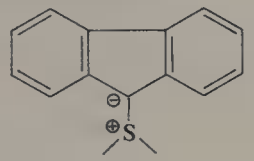
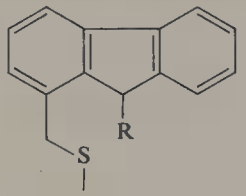
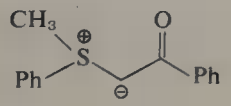
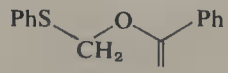
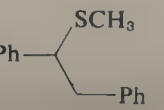
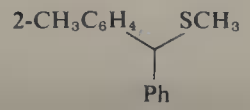
TABLE A.VI (*continued*)

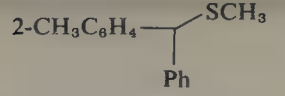
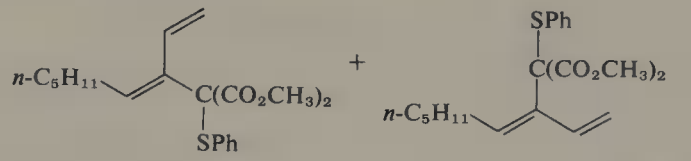
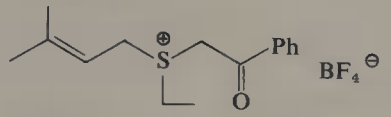
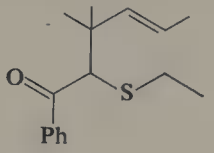
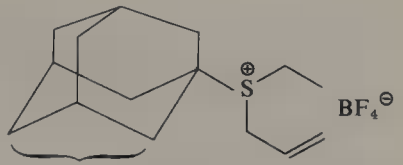
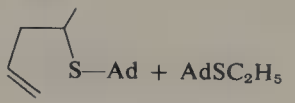
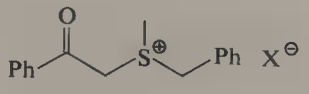
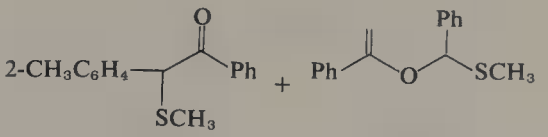
Precursor	Reaction conditions	Products (Yields, %)[a]	References
	$KOC(CH_3)_3$, $HOC(CH_3)_3$	 (90–95)	254
	NaH, THF	 (90–95)	243
		 95 : 3 : 2 (unstated)	257
			
	(Unstated), 60°		
	$NaOH$, H_2O, 25°	(95)	252
	$NaOCH_3$, $HOCH_3$, 25°	(95)	252
	$KOC(CH_3)_3$, PhH, 25°	(95)	252
C_{13}			
Benzyl phenyl sulfide	$PhSCH_2Cl$, $KOC(CH_3)_3$, DME	$2\text{-}CH_3C_6H_4CH(SPh)_2$ (70)	258
	0°	 25 : 1	264

$PhSCH_2C{\equiv}CC_4H_9$-*n*	$N_2C(CO_2CH_3)_2$, $CuSO_4$, 95°–100°		(80)	257a
	*hv*, DME, 10°	 (26) (48)		246
	K_2CO_3, C_2H_5OH, 25°		(unstated)	263
	*n*-C_4H_9Li, THF, −78°		(unstated)	259
C_{14}				
	H_2O, 100° (5 hr)		(57)	256
	$N_2C(CO_2CH_3)_2$, $CuSO_4$, 100°	 *E*:*Z*, 9:1	(unstated)	265
	K_2CO_3, C_2H_5OH, 25°		(unstated)	263

(*continued*)

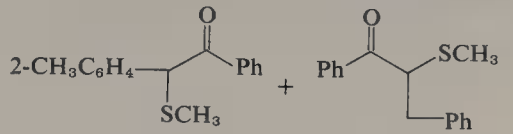
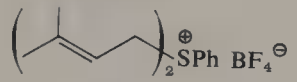
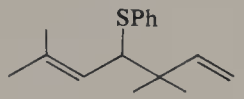
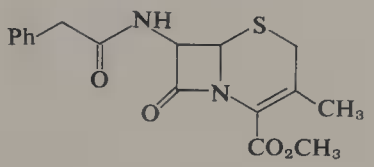
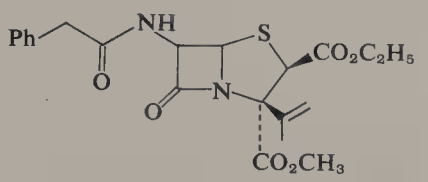
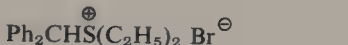
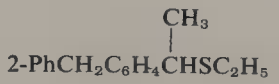
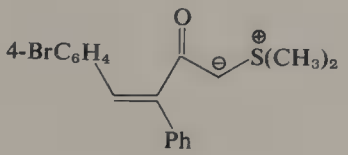
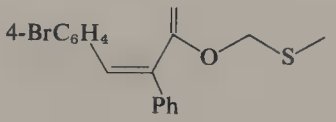
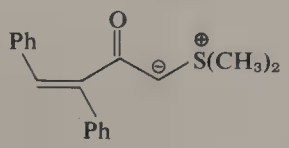
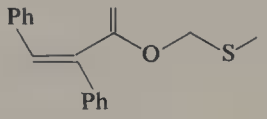
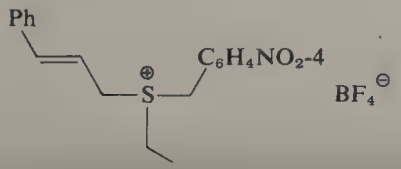
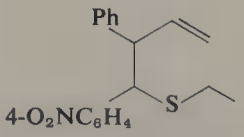
TABLE A.VI (*continued*)

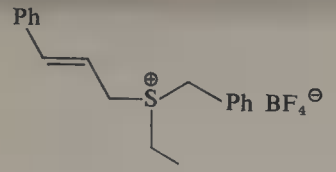
Precursor	Reaction conditions	Products (Yields, %)[a]	References
	$NaOC_2H_5$, C_2H_5OH, 25°	 (unstated)	263
C_{15} 			
	$NaOH$, C_2H_5OH	R = H (28)	126, 266, 267
	Liquid, NH_3, 25° (2 weeks)	R = H (76)	126
	CH_2Cl_2, acetaldehyde reflux	R = $CH(OH)CH_3$ (45)	126
	2,4-$Cl_2C_6H_3CHO$	R = $CH(OH)C_6H_3Cl_2$-2,4 CH_2Cl_2 (33), ether (26)	126
	4-NCC_6H_4CHO	R = $CH(OH)C_6H_4CN$-4 CH_2Cl_2 (29), ether (64)	126
	2-$O_2NC_6H_4CHO$	R = $CHOHC_6H_4NO_2$-2 CH_2Cl_2 (35), ether (34)	126
	3-$O_2NC_6H_4CHO$	R = $CH(OH)C_6H_4NO_2$-3 CH_2Cl_2 (32), ether (78)	126
	4-$O_2NC_6H_4CHO$	R = $CH(OH)C_6H_4NO_2$-4 CH_2Cl_2 (25), ether (83)	126
 $(PhCH_2)_2SCH_3\ ClO_4^{\ominus}$	H_2O, 100° (4 hr)	 (unstated)	256
	$NaOH$, H_2O	PhCH=CHPh +  + 	254

	$KOC(CH_3)_3$, $HOC(CH_3)_3$		(unstated)	254
$Ph_2\overset{\oplus}{C}HS(CH_3)_2\ BF_4^{\ominus}$	$NaNH_2$, acetone	$2\text{-}CH_3SCH_2C_6H_4CH_2Ph$	(55)	239
$PhSCH_2CH{=}C{=}CHC_5H_{11}\text{-}n$	$N_2C(CO_2CH_3)_2$, $CuSO_4$, 95°–100°		4 : 1 (66)	257a
	K_2CO_3, C_2H_5OH, 25°		(unstated)	263
 Ad	$KOC(CH_3)_3$, crown ether, PhH, 25°		(74.6) (17.4)	268
	$KOC(CH_3)_3$, $(CH_3)_3COH$, 25°		(30.8) (13.3)	268
C_{16} 				
X = Br	5% Na, CH_3OH, 60°–65° (2 hr)		(3) (78)	254
	10% Na		(48) (32)	254
	15% Na		(69) (trace)	254
	$NaOCH_3$, CH_3OH		(unstated) (unstated)	269
	NaOH, H_2O		(unstated) (unstated)	269

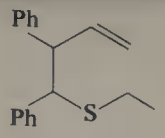
(continued)

TABLE A.VI (*continued*)

Precursor	Reaction conditions	Products (Yields, %)[a]	References
			
X = OH 	$NaOCH_3$, $HOCH_3$	(79) (5.6)	270
	$KOC(CH_3)_3$, THF, −45°	 (100)	257
	$N_2CHCO_2C_2H_5$, Cu, xylene, reflux	 (53)	271
	$NaNH_2$, acetone	 (45)	239
C_{18} 	HOC_2H_5, reflux	 (30)	272
	HOC_2H_5, reflux	 (51)	272
	$NaOC_2H_5$, HOC_2H_5, 25°	 (unstated)	263

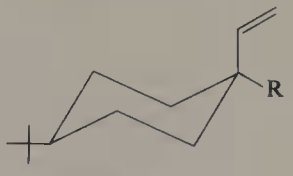


$NaOC_2H_5$, HOC_2H_5, 25°

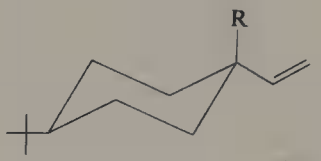


(unstated)

263



+



$PhCH_2\overset{\oplus}{N}(CH_3)_3\ \overset{\ominus}{O}H$, $CHCl_3$, H_2O, 25°, then silica gel

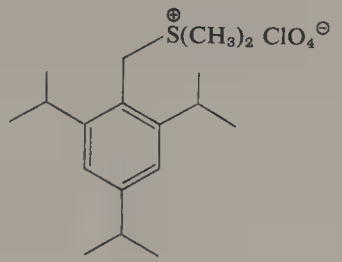
R = COSPh

32 : 1 (53) 273

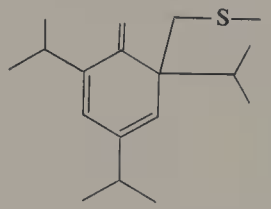
$N_2CHCO_2C_2H_5$, $(C_2H_5O)_3P$, CuCl, hexane, 25°

R = $\underset{\text{SPh}}{\text{CH}}\text{CO}_2\text{C}_2\text{H}_5$

10 : 1 (59) 273



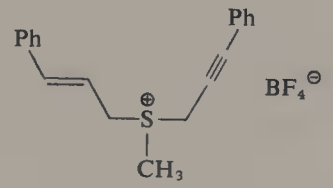
$KOC(CH_3)_3$, $HOC(CH_3)_3$



(90–95)

254

C_{19}



$NaOCH_3$, DMSO

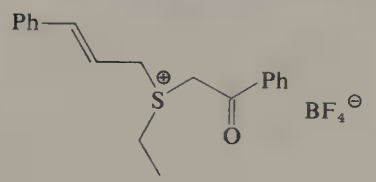
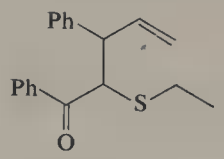
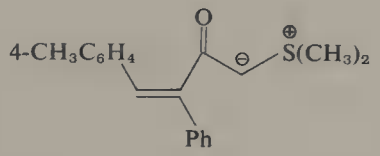
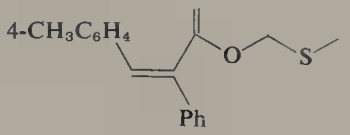
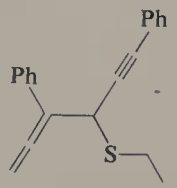
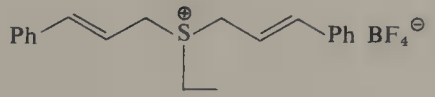
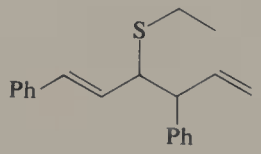
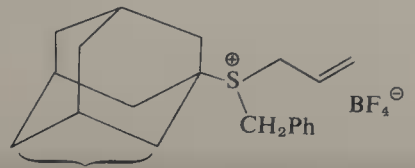
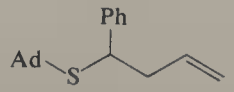
$PhC{\equiv}CCH(SCH_3)CH(Ph)CH{=}CH_2$

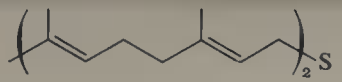
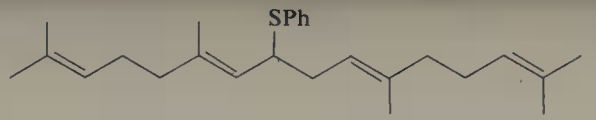
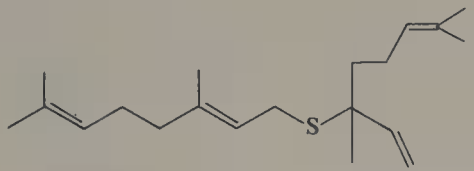
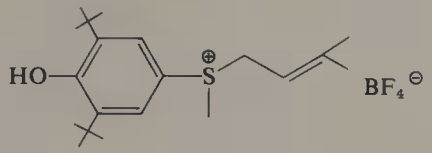
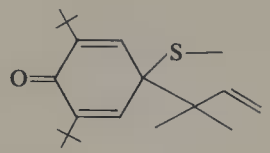
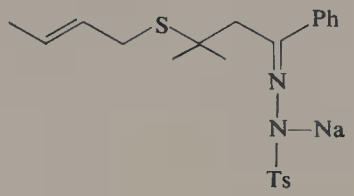
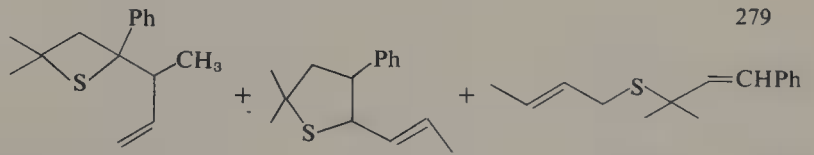
(unstated)

273a

(*continued*)

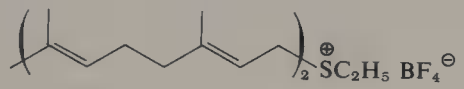
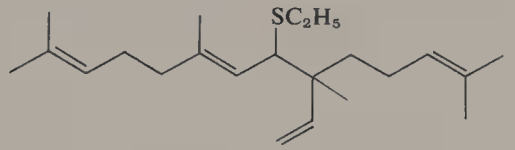
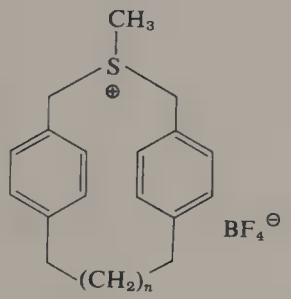
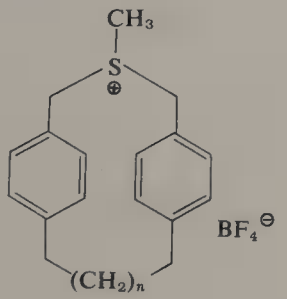
TABLE A.VI (*continued*)

Precursor	Reaction conditions	Products (Yields, %)[a]	References
	K_2CO_3, C_2H_5OH, 25°	 (unstated)	263
	HOC_2H_5, reflux	 (62)	272
C_{20}			
$(PhC{\equiv}CCH_2)_2\overset{\oplus}{S}CH_2CH_3\ BF_4^{\ominus}$	*n*-C_4H_9Li, THF, −70°	 (unstated)	274
	K_2CO_3, C_2H_5OH	 (90–95)	243
	$NaOH$, H_2O, 25°	(unstated)	252
	$NaOCH_3$, $HOCH_3$	(unstated)	252
	$KOC(CH_3)_3$, PhH	(unstated)	252
	$KOC(CH_3)_3$, $HOC(CH_3)_3$, 25°	 (29)	275

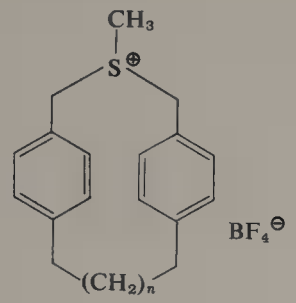
	Benzyne	 3 : 7	(unstated)	276
	Benzyne	19 : 1	(unstated)	276
	*n*-C_4H_9Li, −40°		(unstated)	277
C_{21} $(PhCH_2)_3\overset{\oplus}{S}\ ClO_4^{\ominus}$	KOH, $HOCH_3$, reflux (2 hr)	2-$CH_3C_6H_4$ CHPh SCH_2Ph	(80)	278
C_{22} 	*hν*, monoglyme, 10°	 1 : 1.3 : 1.6 diastereomers (56:44)	(69)	279

(*continued*)

TABLE A.VI (*continued*)

Precursor	Reaction conditions	Products (Yields, %)[a]		References
	$KOC(CH_3)_3$, PhH		(unstated)	280
C_{23}  $n = 8$	See Table A.VII			281
C_{24}  $n = 9$	See Table A.VII			281

C_{25}

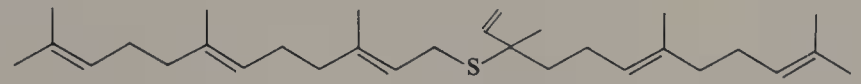


$n = 10$

See Table A.VII

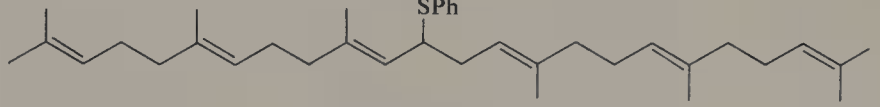
281

C_{30}



Benzyne

282

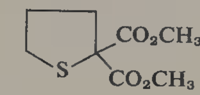
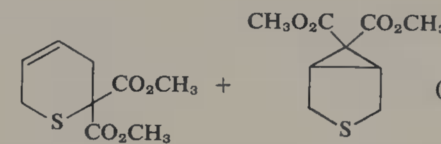
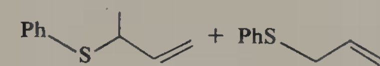
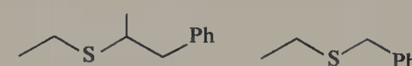
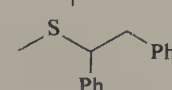
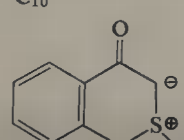
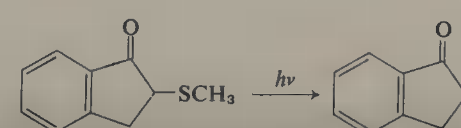


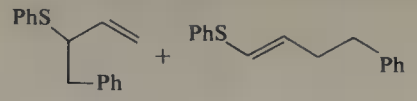
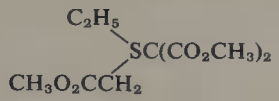
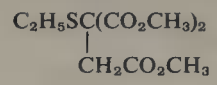
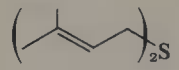
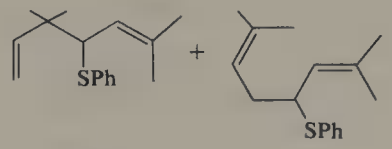
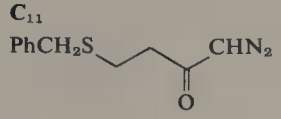
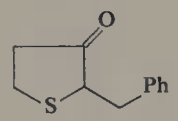
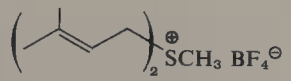
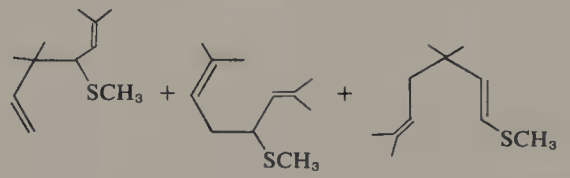
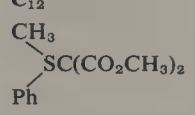
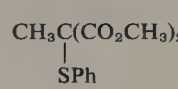
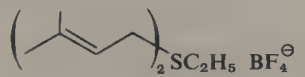
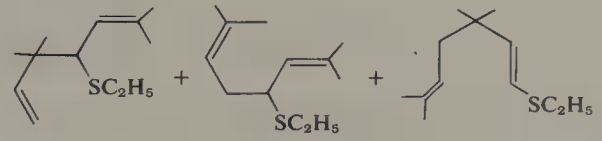
(unstated)

299

[a] When the products obtained under various reaction conditions are the same, the structural formulas are not repeated. Only the yields (%) are given.

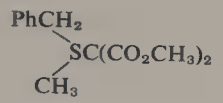
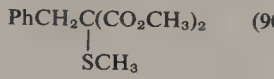
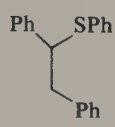
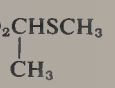
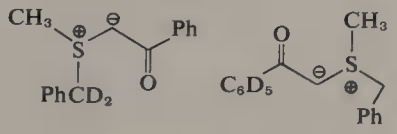
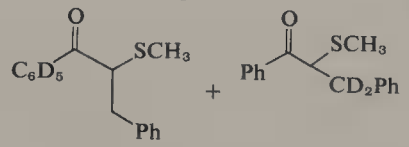
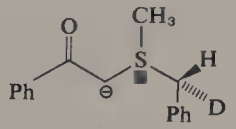
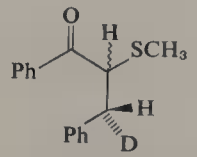
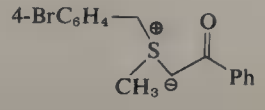
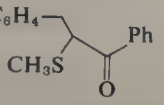
TABLE A.VII
Rearrangements: 1,2-Shift or Stevens Type

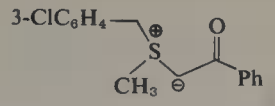
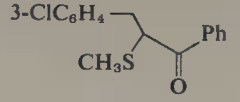
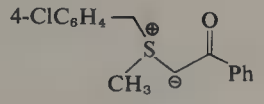
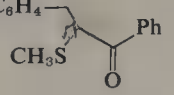
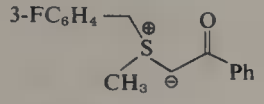
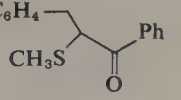
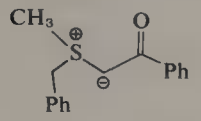
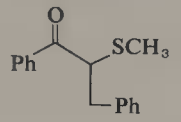
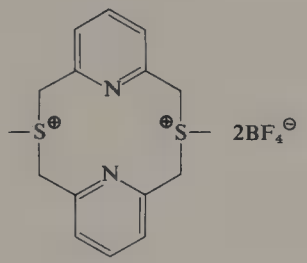
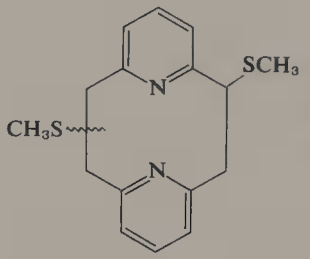
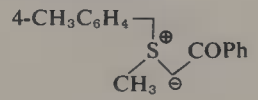
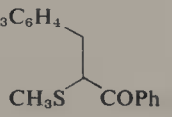
Precursor	Reaction conditions	Products (Yields, %)[a]	References
C_3			
Thietan	$N_2C(CO_2CH_3)_2$, $CuSO_4$, 110°	 (26)	283
C_4			
2,5-Dihydrothiophene	$N_2C(CO_2CH_3)_2$, $h\nu$, 25°	 (unstated)	245
Allyl methyl sulfide	Benzyne	 (31)	240
Diethyl sulfide	$PhCHN_2$, $h\nu$, 25°	 (35) (4)	239
C_7			
$(CH_3)_2SC(CO_2CH_3)_2$	> 155° (20 hr)	$CH_3C(CO_2CH_3)_2$ with SCH_3 (16)	283
C_8			
Benzyl methyl sulfide	Benzyne	 (14)	240
	$PhCHN_2$, $h\nu$, 25°	 (20)	239
C_{10}			
	$h\nu$, $CHCl_3$ or CH_3OH	 (45)	284

Allyl benzyl sulfide	Benzyne		(56)	240
	160°		(43)	283
	Benzyne, 65°			257
		(69) (12)		
C_{11} 	$CuSO_4$, dioxane, reflux		(51)	246
				
	$KOC(CH_3)_3$	95 : 3 : 2	(unstated)	257
	$KOC(CH_3)_3$, 65°	(74) (11) (5)		257
	$KOC(CH_3)_3$, −45°	(99) (0.3) (0.3)		257
C_{12} 	> 155° (20 hr)		(10)	283
	$KOC(CH_3)_3$			257
		95 : 3 : 2	(unstated)	

(continued)

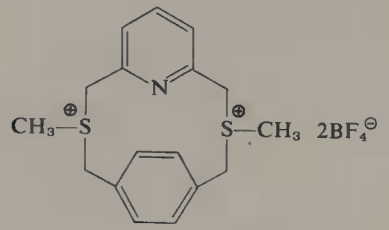
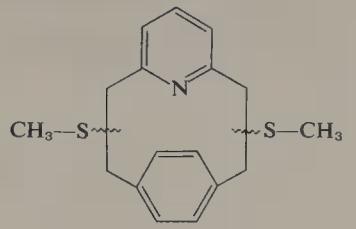
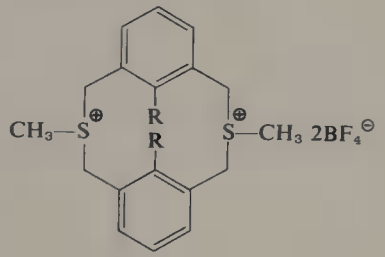
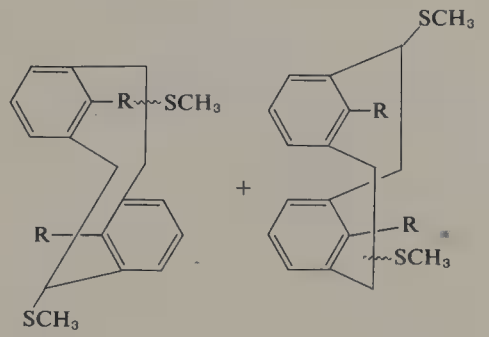
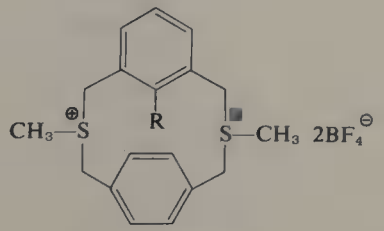
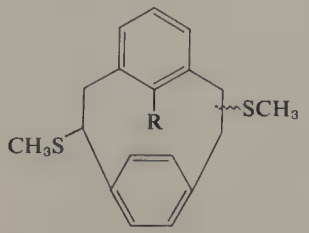
TABLE A.VII (*continued*)

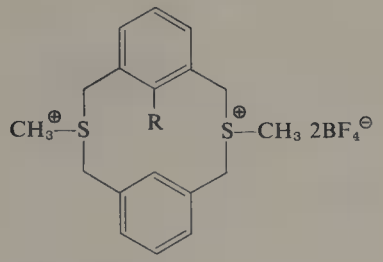
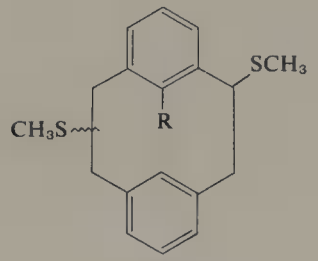
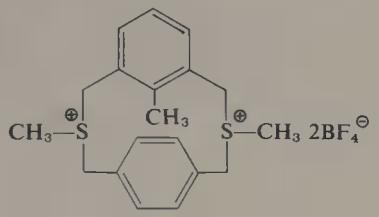
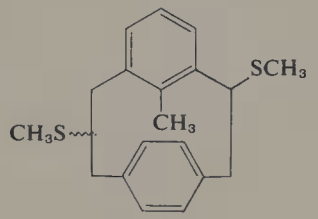
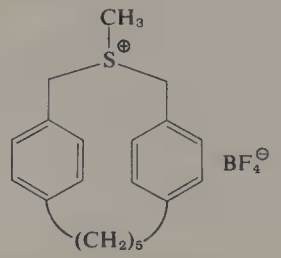
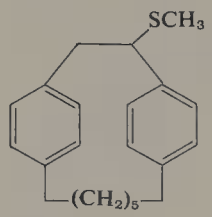
Precursor	Reaction conditions	Products (Yields, %)[a]	References
C_{13}			
	200° (5 hr)	 (90)	283
C_{14}			
$(PhCH_2)_2S$	Benzyne, 190° (600 sec)	 (unstated)	284
	Benzyne	(20)	240
C_{15}			
$C_{12}H_{25}SO_2CHS(CH_3)_2$		$C_{12}H_{25}SO_2CH_2SCH_3$ + 	
	PhH, 80° (4 hr)	1 : 1 (60)	286
	hν, PhH, 25°	1 : 1 (37)	286
C_{16}			
	Toluene, 110° (5 min)	 only 18 ± 6% crossover (unstated)	287
	Toluene, 110° (5 min)	 36 ± 15% retention	287
	THF, acetone, PhH, $CHCl_3$, or DMF, Δ	 (unstated)	269

	THF, acetone, PhH, $CHCl_3$, or DMF, Δ		(unstated)		269
	THF, acetone, PhH, $CHCl_3$, or DMF, Δ		(unstated)		269
	THF, acetone, PhH, $CHCl_3$, or DMF, Δ		(unstated)		269
	Toluene, 110° (5 min)		(45)		287
	$CHCl_3$, 90°		(unstated)		288
	H_2O, 100° (4 hr)		(unstated)		256
	THF, acetone, PhH, $CHCl_3$, or DMF, Δ		(unstated)		269
	$KOC(CH_3)_3$, THF		(42)		289
C_{17}					
	THF, acetone, PhH, $CHCl_3$, or DMF, Δ		(unstated)		269

(continued)

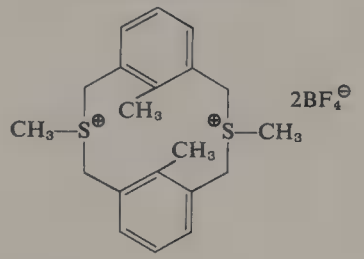
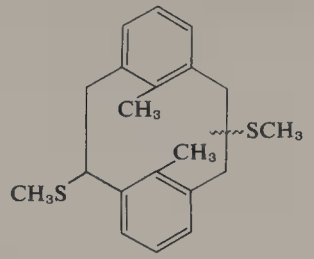
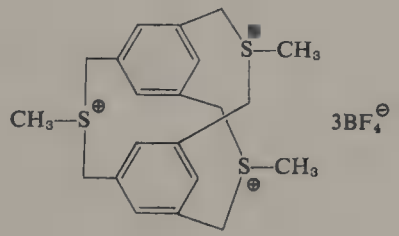
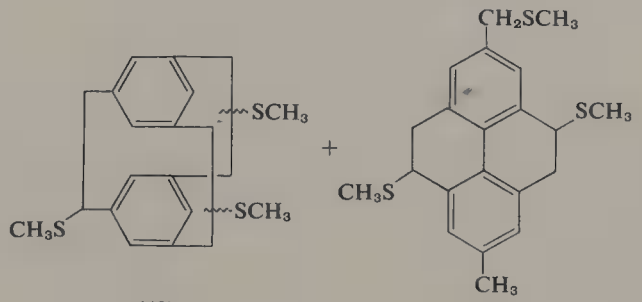
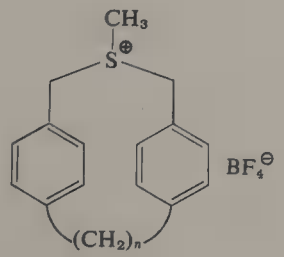
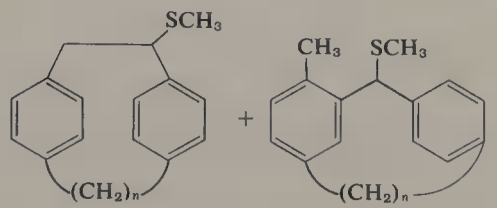
TABLE A.VII (*continued*)

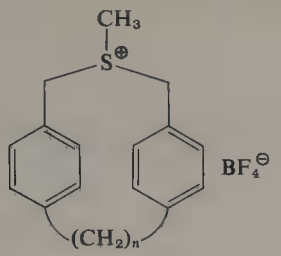
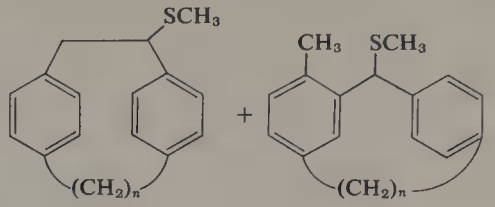
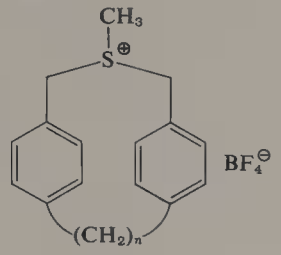
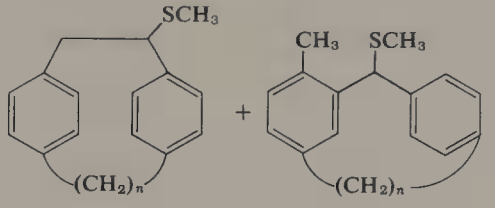
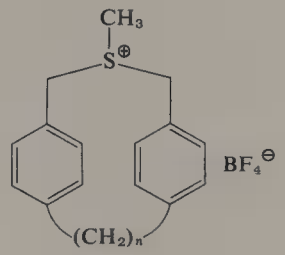
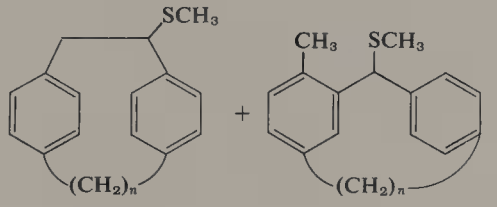
Precursor	Reaction conditions	Products (Yields, %)[a]	References
	$KOC(CH_3)_3$, THF, 25° (25 min)	 (26)	294
C_{18}			
			
R = F	$KOC(CH_3)_3$, THF, 25° (9 hr)	R = F (47)	290
R = H	$KOC(CH_3)_3$, THF, 25° (10 min)	R = H (100)	291
			
R = F	$KOC(CH_3)_3$, THF, 25° (overnight)	(52)	299
R = H	NaH, DMSO	(67)	292
R = H	IRA-400, THF, 25° (8 hr)	(45)	299

C_{19}			
$Ph_2CHS^{\oplus}(i\text{-}C_3H_7)_2\ Br^{\ominus}$	$NaNH_2$, PhH	$i\text{-}C_3H_7SC(Ph)_2C_3H_7\text{-}i$ (22) + $i\text{-}C_3H_7SCHPh_2$ (23)	239
			
R = CH_3	$KOC(CH_3)_3$, THF, 25° (5 hr)	(31)	293
R = CN	IRA-400 ($^-$OH), THF, reflux (2 hr)	(77)	299
	$KOC(CH_3)_3$, THF, 25° (overnight)	 (31)	293
C_{20}			
	NaH, DMSO	 (unstated)	281

(*continued*)

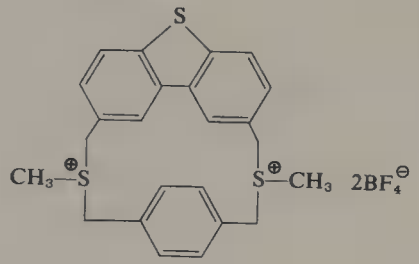
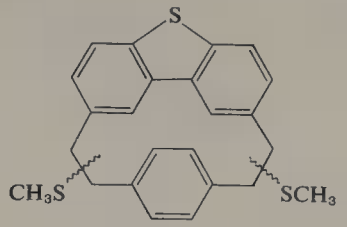
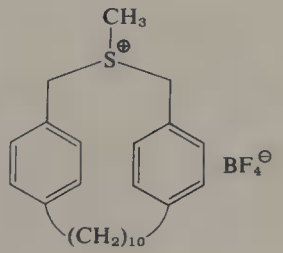
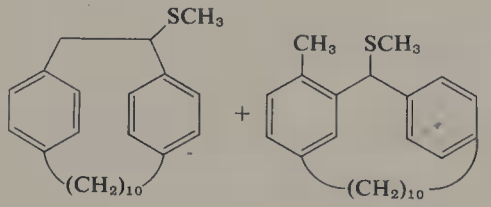
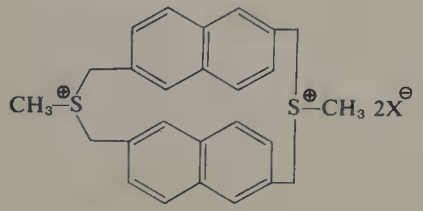
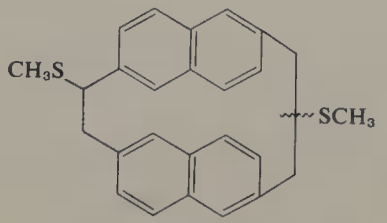
TABLE A.VII (*continued*)

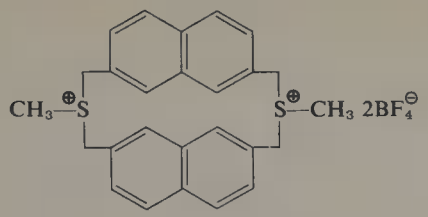
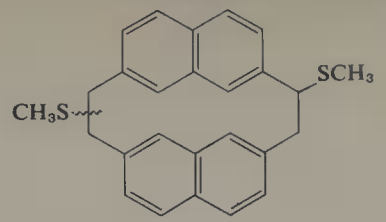
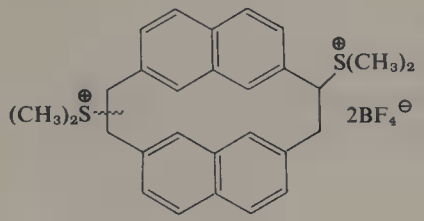
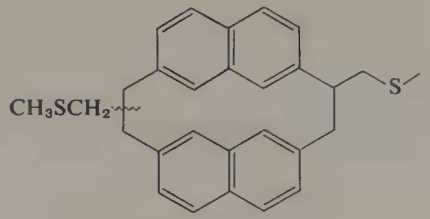
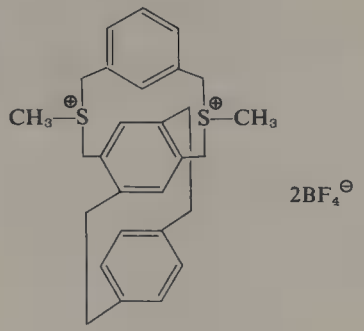
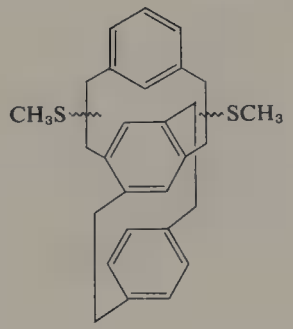
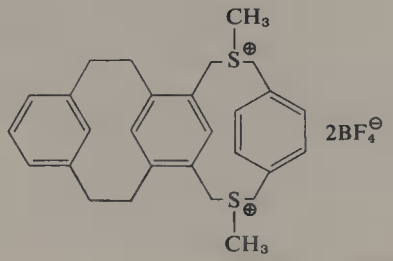
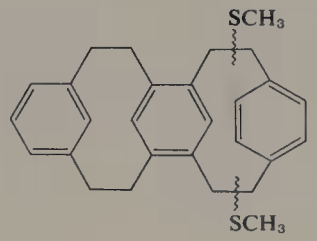
Precursor	Reaction conditions	Products (Yields, %)[a]	References
			
anti	NaH, THF, 25°	(100)	292
anti	$KOC(CH_3)_3$, THF, 25° (5 min)	(94)	292
syn	NaH, THF, 25° (9 hr)	(100)	292
C_{21}			
	NaH ,THF, 25° (24 hr)	 (42) (12)	295
		 (unstated) (0)	
$n = 6$	NaH, DMSO	$n = 6$	281

C_{22}  $n = 7$	NaH, DMSO	 (unstated) (0) $n = 7$		281
C_{23}  $n = 8$	NaH, DMSO	 (unstated) (8) $n = 8$		281
C_{24}  $n = 9$	NaH, DMSO	 (unstated) (55) $n = 9$		281

(*continued*)

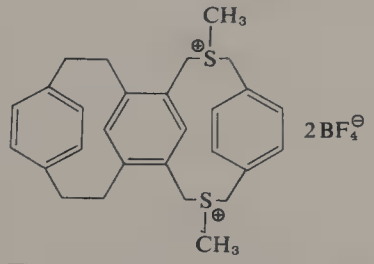
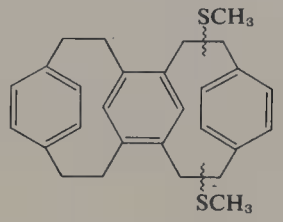
TABLE A.VII (*continued*)

Precursor	Reaction conditions	Products (Yields, %)[a]		References
	$KOC(CH_3)_3$, THF		(22)	296
C_{25} 	NaH, DMSO		(unstated)	281
C_{26}  $X = BF_4^{\ominus}$ $X = CH_3OSO_3^{\ominus}$	NaH, THF, reflux (12 hr) $KOC(CH_3)_3$, $HOC(CH_3)_3$/THF, 25°(15 hr)		(46) (53)	297 297

	NaH, THF		(90)	298
C_{28}				
	NaH, THF		(53)	298
	$KOC(CH_3)_3$		(6.8)[b]	300
	$KOC(CH_3)_3$		(19)[b]	300

(*continued*)

TABLE A.VII (*continued*)

Precursor	Reaction conditions	Products (Yields, %)[a]	References
	$KOC(CH_3)_3$	 (6.8)[b]	300

[a] When the products obtained under various reaction conditions are the same, the structural formulas are not repeated. Only the yields (%) are given.
[b] Yield given is for further transformation product.

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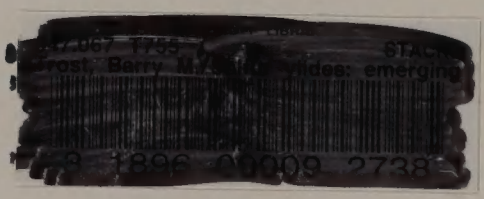

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