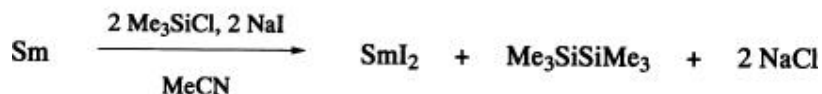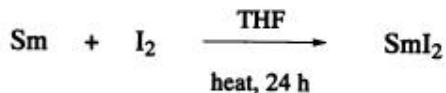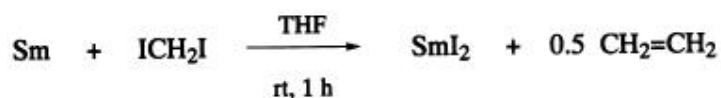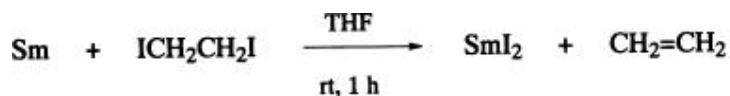# Reductions with Samarium(II) Iodide

Gary A. Molander, University of Colorado at Boulder, Boulder, Colorado

1. Introduction

Reducing agents (along with complementary oxidants) constitute the most fundamental class of reagents available to synthetic chemists for the conversion of organic substrates to desirable organic products. As a consequence of their central importance, the search for novel reducing agents remains the focus of intense exploration. Especially valued are those reagents that not only transform a board range of diverse functional groups, but do so with a high degree of selectivity. Since the early 1980s, samarium(II) iodide (SmI_2) has been increasingly recognized as a reducing agent capable of meeting the intensifying demands of synthetic organic chemistry. Although the compound itself has been known for many years, (1, 2) it was not until Kagan and co-workers developed a convenient synthesis of SmI_2 and outlined its general reactivity with common organic functional groups (3) that SmI_2 became of general interest and importance to synthetic organic chemists.

Samarium(II) iodide is a powerful one-electron reducing agent that can be prepared in moderate concentrations (0.1 M) in tetrahydrofuran (THF) by one of several different reactions from samarium metal. (3-8)

$$Sm \ + \ ICH_2CH_2I \ \xrightarrow[\text{rt, 1 h}]{\text{THF}} \ SmI_2 \ + \ CH_2{=}CH_2$$

$$Sm \ + \ ICH_2I \ \xrightarrow[\text{rt, 1 h}]{\text{THF}} \ SmI_2 \ + \ 0.5 \ CH_2{=}CH_2$$

$$Sm \ + \ I_2 \ \xrightarrow[\text{heat, 24 h}]{\text{THF}} \ SmI_2$$

$$Sm \ \xrightarrow[\text{MeCN}]{2 \ Me_3SiCl, \ 2 \ NaI} \ SmI_2 \ + \ Me_3SiSiMe_3 \ + \ 2 \ NaCl$$

Deep blue solutions of SmI_2 are generated in virtually quantitative yields by these procedures, but the preparations using diiodomethane or diiodoethane as the oxidants would appear to be the easiest and most reliable methods. The reducing agent can be stored as a solution in THF for reasonably long periods of time, particularly when it is stabilized by a small amount of samarium metal.

Alternatively, the solvent may be removed, providing $SmI_2(THF)_n$ powder. For synthetic purposes, SmI_2 is typically generated and utilized in situ, although THF solutions of SmI_2 are commercially available.

The reduction potential of Sm^{+2}/Sm^{+3} as measured in water is −1.55 V. ([9]) However, the reduction potential as well as the ability of SmI_2 to promote the reduction of diverse organic substrates varies widely according to the solvent and the presence of various additives.

Kagan's pioneering studies on the reaction of SmI_2 with organic substrates not only provided a general outline for its reactivity, ([3]) but also inspired an extraordinary number of subsequent studies with important ramifications for selective organic synthesis. As a consequence of these extensive studies, SmI_2 has emerged as one of the more useful reducing agents in synthetic organic chemistry. The complementary reactivity of SmI_2 as compared to the vast inventory of other available reducing agents constitutes one reason for its appeal. Another attraction of SmI_2 is its ready accessibility, either from commercial sources or by in situ preparation via one of the convenient methods outlined above. The high chemoselectivity exhibited by SmI_2 and the ability to change its reactivity (selectivity) rather dramatically based upon solvent effects further enhance its attractiveness. Finally, SmI_2 is easily handled by standard techniques for the manipulation of air-sensitive materials.

As testimony to its increasing importance, several review articles have appeared that focus on the utility of SmI_2 both as a reducing agent and as a reductive coupling agent in selective organic synthesis. ([10-22]) This review outlines some of the practical aspects of reactions employing SmI_2, but is strictly limited to functional group reductions. Thus those reactions promoted by SmI_2 that result in the formation of new carbon–carbon bonds are not included. The chapter is organized according to the type of organic functional groups involved, and topics covered include the reduction of organic halides, sulfonates, ([3], [23-30]) and sulfones, ([31-33]) reductive elimination/fragmentation processes; ([26-28], [31], [33-39]) reduction of aldehydes and ketones; ([3], [6], [25], [40-45]) reduction of carboxylic acids and their derivatives; ([42], [46-48]) reduction of conjugated carbonyl substrates; ([3], [47], [49-52]) reductive cleavage of α -heterosubstituted carbonyl substrates; ([7], [29], [49], [53-72]) reduction of cyclopropyl ketones; ([61], [73], [74]) various deoxygenation reactions; ([3], [41], [49], [75-78]) reduction of nitrogenbased functional groups, ([42], [46], [49], [79-84]) and finally an outline of the reduction of miscellaneous functional groups ([25], [85-91]) that cannot be appropriately assigned to the general classifications outlined above. In covering these topics, the literature has been surveyed through 1992.

2. Mechanism and Stereochemistry

Because SmI_2 is a one-electron reducing agent, the transformations carried out with it are single-electron transfer processes with mechanisms similar to those established with other one-electron reducing systems (including other low-valent metals and metal complexes, dissolving metal reductions, and electro-chemical methods). For example, reduction of organic halides, reductive elimination processes, reductions of aldehydes and ketones, reductions of conjugated carbonyl systems, and reductions of α-heterosubstituted carbonyl substrates undoubtedly follow along the lines of traditional mechanistic interpretations for such substrates, although there are some caveats that will be discussed in greater detail.

There are several attractive features of SmI_2 that render its use advantageous over many other similar reducing agents. The first is that samarium ions are excellent Lewis acids. Thus in reactions with polarized functional groups, complexation with either Sm(II) or Sm(III) can greatly facilitate electron transfer by lowering the energy of the lowest unoccupied molecular orbital of the substrate. Additionally, samarium(III) ions produced upon electron transfer can enhance the leaving group ability of those functional groups with which it can complex, again facilitating intermediate steps in mechanistic schemes involving displacement of a leaving group. Finally, although they are considered rather powerful reducing agents, samarium(II) species are reasonably stable in alcohols, in water, and, apparently, even in acidic and basic aqueous solutions. Consequently, for reaction processes that generate reactive intermediates requiring immediate quenching upon generation, the use of SmI_2 in the presence of protic solvent additives provides a means to produce these species and protonate them before they can react via unproductive pathways.

2.1. Reduction of Organic Halides, Sulfonates, and Sulfones

Early studies on the reduction of alkyl halides to the corresponding alkanes by SmI_2 suggested that organosamariums were not involved as intermediates, but that radical processes were uniquely responsible for the observed products. (3, 26) However, these results appear to have been a consequence of the solvent used. Organosamariums now appear to be well-established intermediates in the conversion of many alkyl halides to alkanes, particularly when hexamethylphosphoric triamide (HMPA) is used as a cosolvent.

In these initial studies, most alkyl halide reductions with SmI_2 were performed in THF solvent heated at reflux. (3) Quenching the reaction mixtures with D_2O afforded nondeuterated alkanes, leading to the conclusion that organosamariums were not involved as intermediates and that the alkane products arose as a result of hydrogen atom abstraction from THF by alkyl
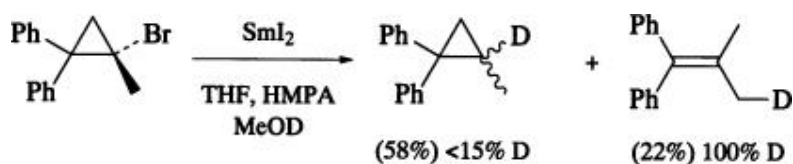
radicals. (3, 26)

Subsequent studies with various alkyl halide substrates performed in THF/HMPA provided a growing body of evidence that organosamariums are frequently generated as intermediates from alkyl halide precursors. (24, 41, 73, 92) The addition of HMPA to SmI_2 affords a much more powerful reducing system, allowing reactions to be carried out under considerably milder conditions. (24, 41) Consequently, when SmI_2 reductions of 2-bromoadamantane are carried out at room temperature in the presence of D_2O , the adamantane recovered is deuterated to the extent of 80%. (24) This is in stark contrast to the results obtained when the reactions are carried out in boiling THF. Prompted by the accumulating results and apparent discrepancies, a mechanistic study was undertaken to provide further clarification of the mechanism of alkyl halide reductions. (93-95) These investigations provided convincing evidence that organosamariums are indeed intermediates in such reductions, and suggested that the lack of deuterium incorporation in the initial study was a result of decomposition of the organometallic formed at the relatively high temperatures required for reductions carried out in the absence of HMPA. (92)

The mechanism for SmI_2 reductions of primary and secondary alkyl halides in THF/HMPA is now reasonably clear. Dissociative electron transfer (96) from SmI_2 to the alkyl halide initiates the process, generating a primary or secondary alkyl radical. Rapid reduction of this radical ($k = 10^6$ M^{-1} s^{-1}) (94) provides an organosamarium intermediate that can be protonated, affording the alkane.

$$RX \xrightarrow[-X^-]{SmI_2} \left[R \bullet \right] \xrightarrow{SmI_2} RSmI_2 \xrightarrow{H^+} RH$$
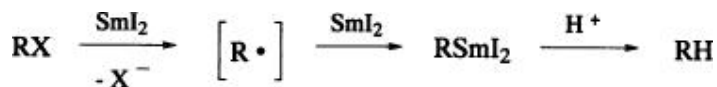
With the exception of substrates possessing special structural features, there is a loss of stereochemical integrity during reductions of chiral organic halides. Along these lines, the reduction of cyclopropyl halides by SmI_2 not only provides interesting insight into reductions of this special class of alkyl halides, but also into the properties of SmI_2 and organosamarium species as well. (92) Thus treatment of enantiomerically pure 1-bromo-1-methyl-2,2-diphenylcyclopropane with SmI_2 in THF/HMPA followed by a MeOD quench provides a 58% yield of racemic 1-methyl-2,2-diphenylcyclopropane in which no more than 15% deuterium has been incorporated. An independent synthesis of the presumed organosamarium intermediate reveals that this species reacts slowly with THF, and slowly racemizes as well.

Ph--Br (cyclopropane, Ph, Ph) → SmI$_2$, THF, HMPA, MeOD → Ph--D (cyclopropane, Ph) + Ph, Ph C=C(CH$_3$)--D

(58%) <15% D   (22%) 100% D

On the other hand, enantiomerically pure 1-fluoro-1-iodo-2,2-diphenylcyclopropane reacts with SmI$_2$ in THF/HMPA to provide 55% of 1-fluoro-2,2-diphenylcyclopropane with 95% retention of configuration. (92) Fluoro-substituted cyclopropyl radicals have greater configurational stability than simple alkyl-substituted cyclopropyl radicals. The configurational lifetime is thus long enough that reaction with SmI$_2$ can occur prior to inversion, providing racemic product. Consequently, stereochemical fidelity is maintained in conversion of the iodide to the organosamarium intermediate. This intermediate organosamarium itself must exhibit high configurational stability as evidenced by the high degree of stereospecificity of the overall process. A minor byproduct of the reaction (18%) is 1,1-diphenylallene, presumably formed as a result of carbene formation from the intermediate organosamarium species by an α -elimination process.

Ph--I, F (cyclopropane, Ph, Ph) → SmI$_2$, THF, HMPA, MeOH → Ph--H, F (cyclopropane, Ph) + Ph, Ph C=C=CH$_2$

(55%) 95% retention   (18%)
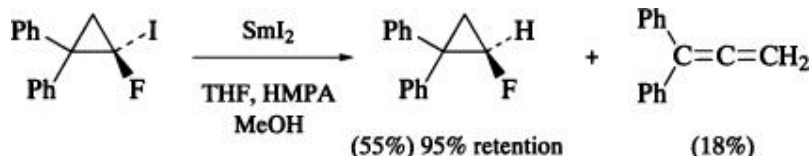
Finally, nonracemic 1-bromo-1-methoxymethyl-2,2-diphenylcyclopropane affords a 50% yield of racemic reduced product upon reaction with SmI$_2$ followed by protonation of the reaction mixture with methanol. (92) In addition, a 16% yield of 1-methylene-2,2-diphenylcyclopropane is generated as a result of β elimination of the intermediate organosamarium species.

Ph--Br, --OMe (cyclopropane, Ph, Ph) → SmI$_2$, THF, HMPA, MeOH → Ph--H, --OMe (cyclopropane, Ph) + Ph (cyclopropane, Ph, methylene)

(50%)   (16%)
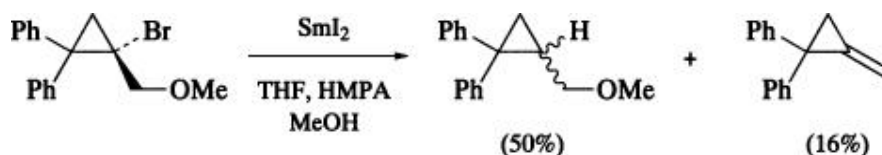
The mechanism of reduction of tertiary alkyl halides is a matter of some

contention. Simple reduction of such substrates with samarium(II) iodide in THF/HMPA followed by a D_2O quench provides no deuterium incorporation in the alkane product. (24, 41, 93) The implication is that the tertiary radicals formed by reduction of the tertiary halides are not reduced rapidly enough by SmI_2 to prevent radical–radical and/or radical–solvent reactions. However, studies have surfaced in which tertiary organosamariums may be intermediates formed from the corresponding halide. (27, 73, 92) Consequently, the issue of whether tertiary organosamariums can or cannot be formed by reduction of tertiary halides at this point remains unresolved.

Samarium(II) iodide can be utilized to reduce aryl halides and alkenyl halides in THF/HMPA, but it does so without the intermediacy of organosamariums. Thus both aryl radicals and alkenyl radicals undergo rapid hydrogen atom abstraction (from the solvent) or other relatively facile processes before they can be reduced to the corresponding organosamariums. (24, 93-95, 97, 98)
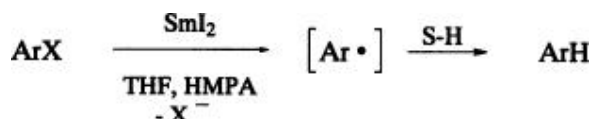
One apparent exception to this general phenomenon may be seen in the reduction of 1,1-dibromoalkenes, wherein the intermediacy of an alkenylsamarium species has been postulated. In this case, it is likely that the second electron transfer is facilitated because the anion thus formed is electronically stabilized by the remaining bromide.
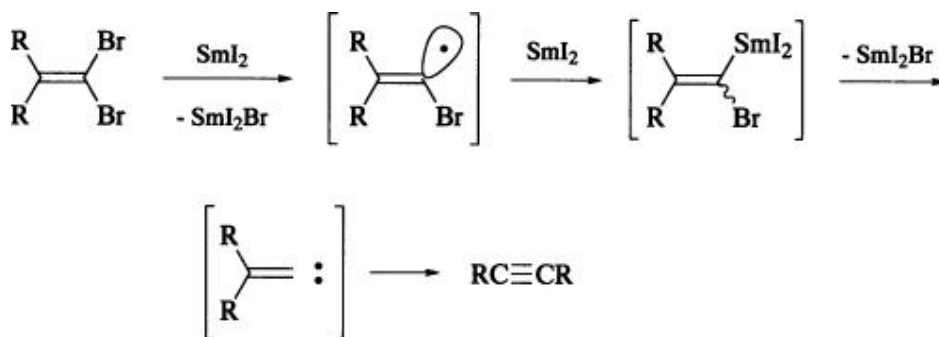
Allylic and benzylic halides are rapidly reduced by SmI_2, but the major products are homocoupled dimers. Although it was originally suggested that these products arise from coupling of the respective radicals, (3, 26) more recent evidence suggests that the bibenzyl and 1,5-hexadiene products are

generated by reaction of intermediate organosamariums with the benzylic or allylic halide precursors, respectively. (94)

Although alkyl tosylates are reduced by SmI_2 to the corresponding alkanes, (3) experimental evidence suggests that the tosylates are first converted to iodoalkanes, and that the iodides are reduced to the hydrocarbons. (26) Thus addition of sodium iodide to SmI_2-promoted reductions of alkyl tosylates enhances the rate of reduction, and, even in the absence of sodium iodide, alkyl iodides are detected among the products of reaction between SmI_2 and alkyl tosylates.

The reduction of sulfones undoubtedly follows along the same lines as those of alkyl halides. (37) Single-electron transfer from SmI_2 to the sulfone provides a radical anion, which dissociates to the alkyl radical and the sulfinate anion. (99) Reduction of the alkyl radical provides an organosamarium intermediate, which is protonated to provide the alkane. Alkenyl sulfones presumably generate alkenyl radicals, which are quenched by hydrogen abstraction from the solvent before they can be reduced further to the organosamarium species.

$$RSO_2Ar \xrightarrow{SmI_2} \left[RSO_2Ar \right]^{-\bullet} \xrightarrow{-ArSO_2^-} \left[R\bullet \right] \xrightarrow{SmI_2} \left[RSmI_2 \right] \xrightarrow{H^+} RH$$
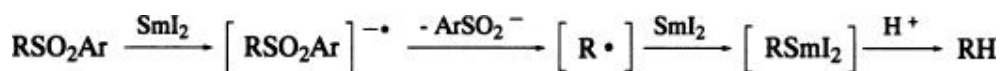
2.2. Reductive Elimination/Fragmentation Reactions

A variety of appropriately functionalized 1,2-disubstituted alkanes undergo elimination reactions by initial formation of the organosamarium followed by rapid β elimination.
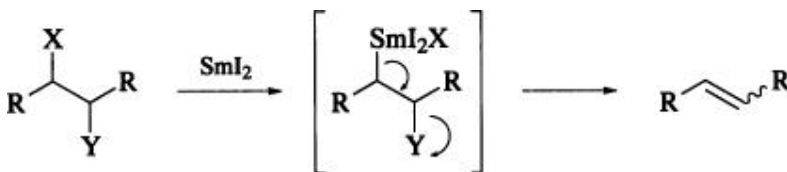
X = halide, SO_2Ar

Y = OH, OR, O_2CR, SO_2Ar

This reductive elimination process has been utilized as a mechanistic probe for intermediate organosamariums, (18, 73, 92) as a means to deprotect protected alcohols and amines, (35, 36) and also as a synthesis of alkenes. (26-28, 31, 33-37) As expected, there appears to be little difference in the rate

of reaction or yields obtained in elimination of diastereomeric cyclic substrates wherein the two substituents to be eliminated are either *cis* or *trans* to one another. (33) Acyclic substrates generally provide diastereomeric mixtures of olefinic products. However, in the reductive fragmentation of cyclic β-halogeno tetrahydrofurans, high levels of selectivity for the *E* isomer have been achieved regardless of the stereochemistry of the starting material. (34) This is in contrast to the same process carried out with sodium metal, which provides different mixtures of *E* and *Z* olefinic isomers depending on the stereochemistry of the starting material.

Cl · · · SmI₂ / THF, heat · · · HO · · · R
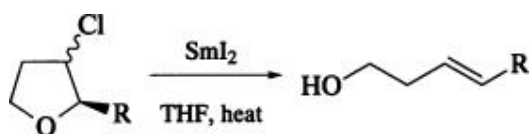
Interestingly, the analogous cleavage of cyclic β-halo tetrahydropyrans with SmI₂ is less useful than that of its sodium-promoted counterpart. The SmI₂-promoted reactions provide mixtures of *E* and *Z* olefin products that appear to arise from a common intermediate from diastereomeric halide precursors. (34)

Cl · · · SmI₂ / THF, heat · · · HO · · · + · · · HO · · · 3 : 1

Cl · · · SmI₂ / THF, heat · · · HO · · · + · · · HO · · · 3 : 1
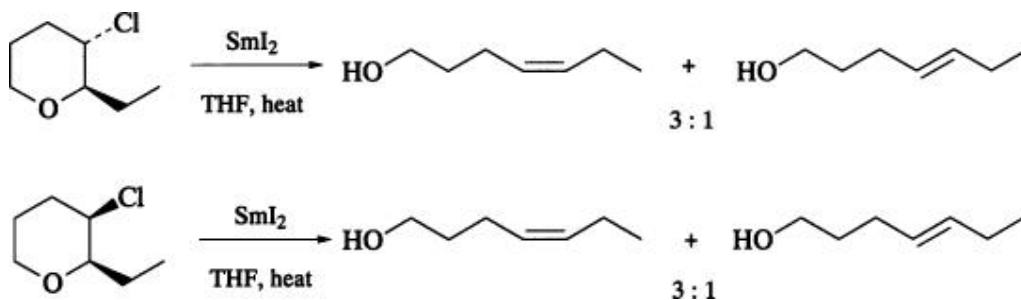
In general these 1,2-reductive elimination processes are reasonably straight-forward, proceeding without interference from other mechanistic pathways. However, one particular substitution pattern has been discovered in which reactions of the intermediate radical species intervene in the desired process, providing unexpected products. (37) Thus in the attempted reductive elimination of β-hydroxy imidazoyl sulfones the initial radical formed upon single electron transfer from SmI₂ to the sulfone forms a homoallylic radical that undergoes 3-*exo* ring closure, forming a benzylically stabilized cyclopropylcarbinyl radical. This radical can fragment, forming an isomeric

homoallylic radical that is stabilized by the adjacent hydroxy group. Hydrogen atom abstraction from the solvent affords the observed product of the reaction.
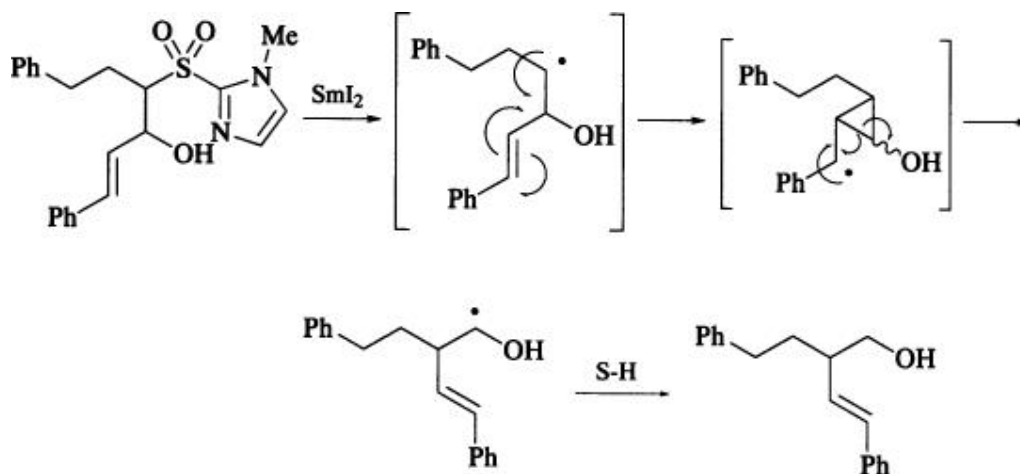
Diverse fragmentation reactions resulting in the cleavage of carbon–carbon bonds with concomitant formation of enolates can be promoted by SmI$_2$. As in the β -elimination processes, the fragmentation reactions appear to transpire via intermediate organosamariums, and some of these would appear to involve the generation of tertiary organosamariums. (27, 38, 39)
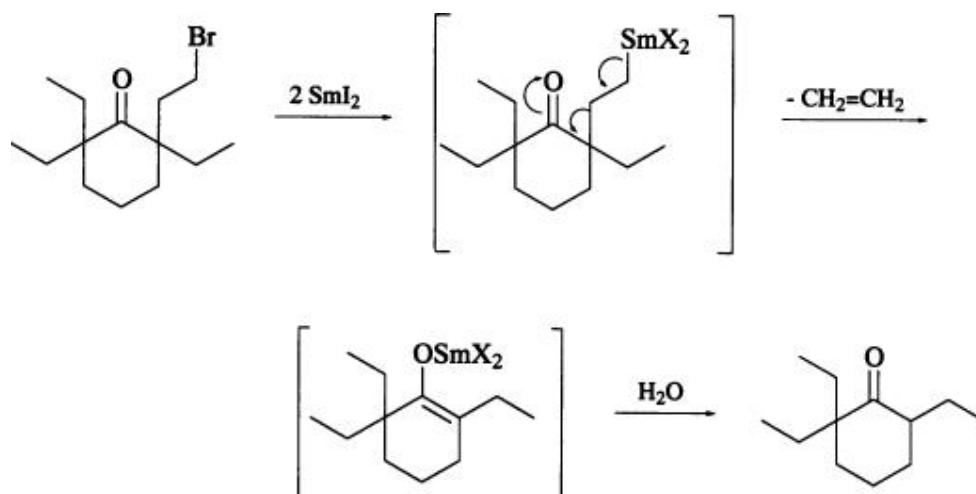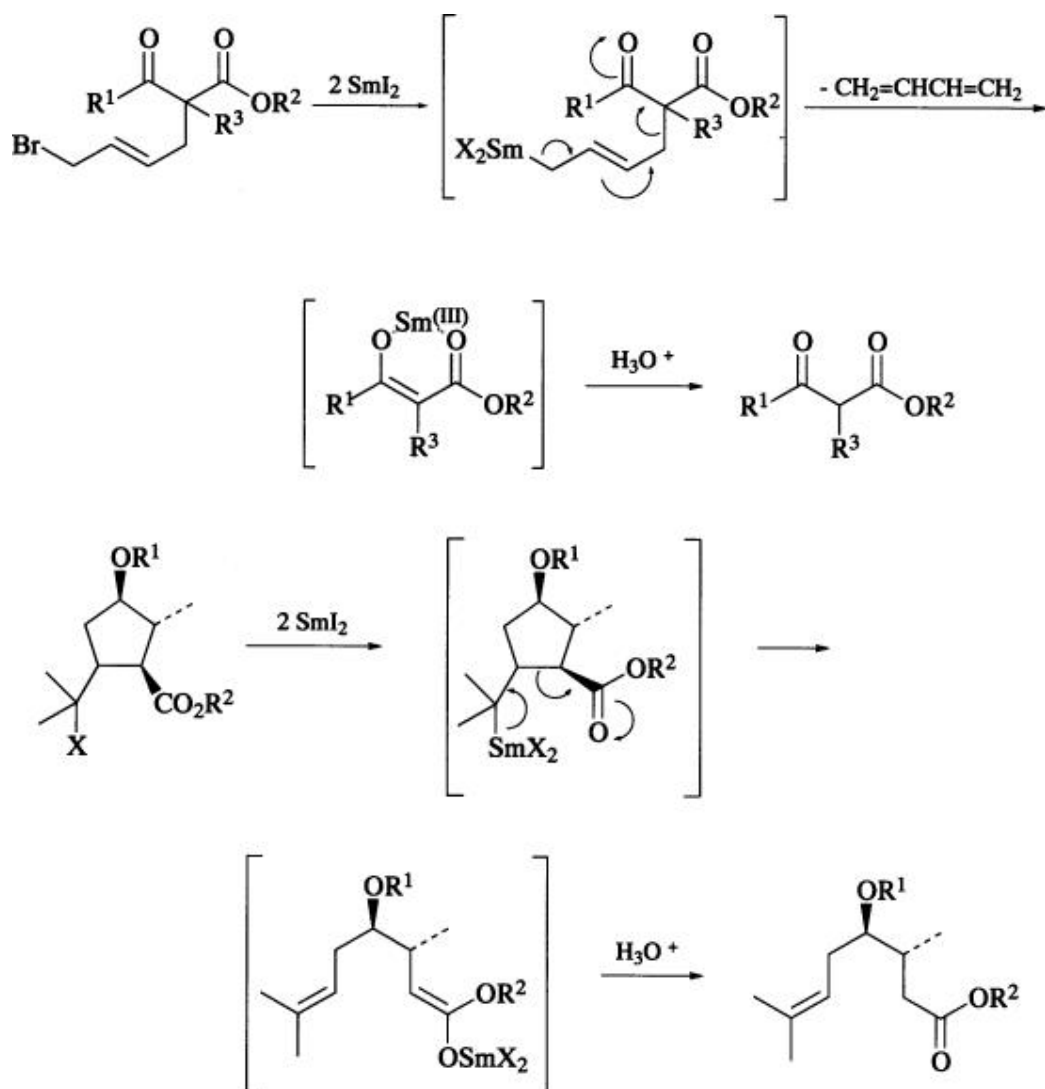
Reductive elimination reactions involving cyclopropylogous α -bromoketones are particularly interesting. (28) In these systems, near-complete stereospecificity is observed in the fragmentations. Ambiguities in the point of electron transfer from SmI$_2$ to the substrates make mechanistic interpretations extremely difficult. However, the fact that radical reducing agents (such as Bu$_3$SnH) render the process nonstereospecific rule out a radical fragmentation and suggest a fully concerted reaction.
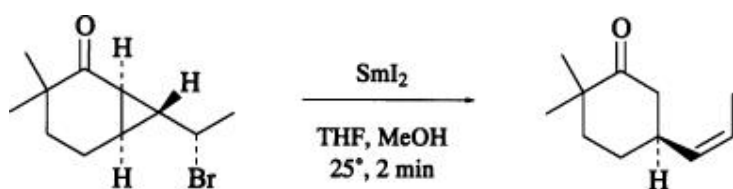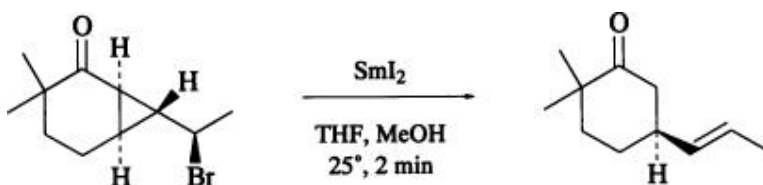
2.3. Reduction of Aldehydes and Ketones

The scope of carbonyl reductions with SmI_2 is not nearly so well delineated as that of Bouveault–Blanc or dissolving metal reductions of aldehydes and ketones. However, it seems likely that the same general mechanistic and stereochemical considerations are in play in all of these various protocols. Nevertheless, some general cautions may be in order concerning the mechanisms outlined below. First, the dimer model of alkali metal ketyls has been arbitrarily extended to that of samarium ketyls, even though there is no direct experimental evidence for (or against) such species. Second, the timing of electron transfer and proton transfer events in the reduction of carbonyl substrates by SmI_2 has not been investigated, and thus the mechanisms proposed are simply logical possibilities derived from other, more firmly established, processes.

Extensive studies on carbonyl reduction with a variety of different electron transfer agents have led to a reasonably clear picture of the mechanism of these transformations. (100-102) Single-electron transfer to the aldehyde or ketone generates a ketyl radical anion that can form dimeric or polymeric ion pairs (Eq. 1).
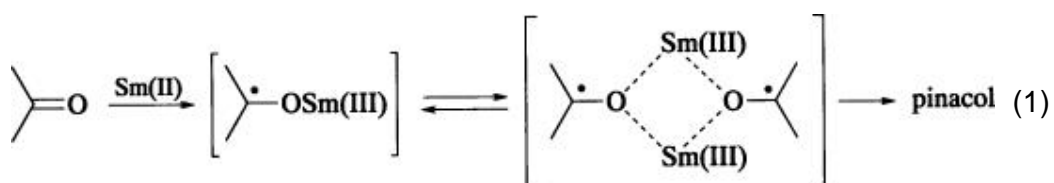
The nature and importance of the various species present in solution depend on the metal, the structure of the substrate, the solvent, the concentration, and the temperature. In the absence of good proton donors, collapse to a pinacol (Eq. 1) or disproportionation to a molecule of enolate and a molecule of alkoxide are the major pathways open to these ion pairs (Eq. 2). However, in the presence of a proton

$$\left[\begin{array}{c} Sm(III) \\ \diagdown O \diagup O \diagdown \\ Sm(III) \end{array} \right] \longrightarrow \left[\diagdown -OSm(III) \atop H \right] + \left[\diagdown -OSm(III) \right] \qquad (2)$$
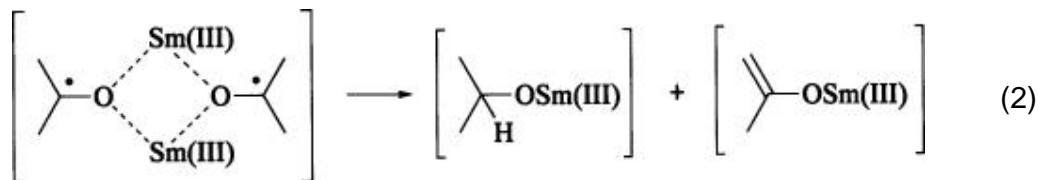
source (as most SmI$_2$-promoted reduction reactions of aldehydes and ketones are performed), two additional pathways become available. The first is a rapid disproportionation of the ketyl dimers to a molecule of alcohol and a molecule of ketone (Eq. 3). A second pathway invokes reversible protonation of the ketyl

$$\left[\begin{array}{c} Sm(III) \\ \diagdown O \diagup O \diagdown \\ Sm(III) \end{array} \right] \xrightarrow{H^+} \left[\diagdown -OSm(III) \atop H \right] + \diagdown =O + Sm(III) \qquad (3)$$
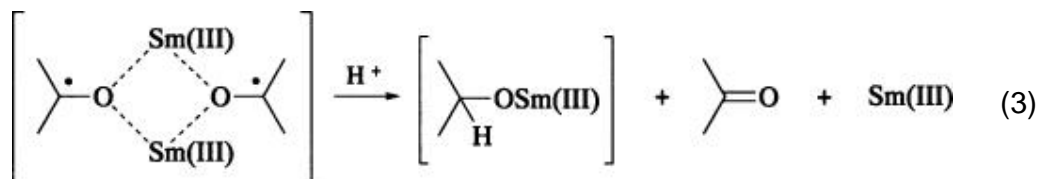
(monomer or dimer) to provide a carbinol radical. This undergoes a second electron transfer, generating a hydroxyalkyl carbanion that is protonated to afford the observed alcohol product (Eq. 4). The extent to which these diverse pathways

$$\left[\diagdown -OSm(III) \right] \xrightarrow{H^+} \left[\diagdown -OH \right] \xrightarrow{SmI_2} \left[\diagdown -OH \right] \xrightarrow{H^+} \diagdown -OH \atop H \qquad (4)$$
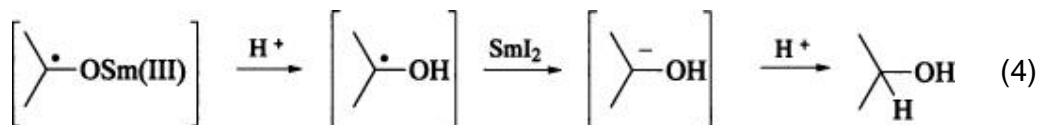
are followed is postulated to be a function of the acidity of the proton donor, the nature of the metal used for the reduction, and to some extent the structure of the substrate ketone or aldehyde. Because nothing is known of the structure or aggregation of samarium(III) ketyls, and the relative rates of the various processes outlined above are also unknown, any attempt to define more precisely the pathway traversed in SmI$_2$-mediated reductions would be highly speculative.

Very few details of the stereochemical issues involved in SmI$_2$-promoted carbonyl reductions have been elaborated. Those described, however, are consistent with the notion that the stereochemistry is determined by the relative conformational stabilities of ketyl intermediates. Cyclohexanones typically lead to equatorial alcohols. (41, 45) For example, 4-*tert*-butylcyclohexanone can be reduced under optimized conditions to a 93:7 mixture of *trans*- and *cis*-4-*tert*-butylcyclohexanols. Only very modest "anti-Cram" stereochemical control can be achieved in the reduction of chiral

acyclic ketones. (40, 41) Calculations have provided theoretical models and rationalizations for these experimental observations. (103) Finally, limited success has been achieved in attempts to induce asymmetry in the reduction of achiral ketones by using chiral protonating agents. (43)

Conjugated aldehydes and ketones provide mixtures of 1,2- and 1,4-reduction products. However, α , β -unsaturated esters and amides undergo selective conjugate addition with SmI₂. Mechanisms for the reduction of conjugated carbonyl systems would appear to be reasonably straightforward. (3, 50, 51, 104, 105) Many of the same factors involved in the mechanism of carbonyl reduction as outlined above apply to the α , β -unsaturated systems as well.
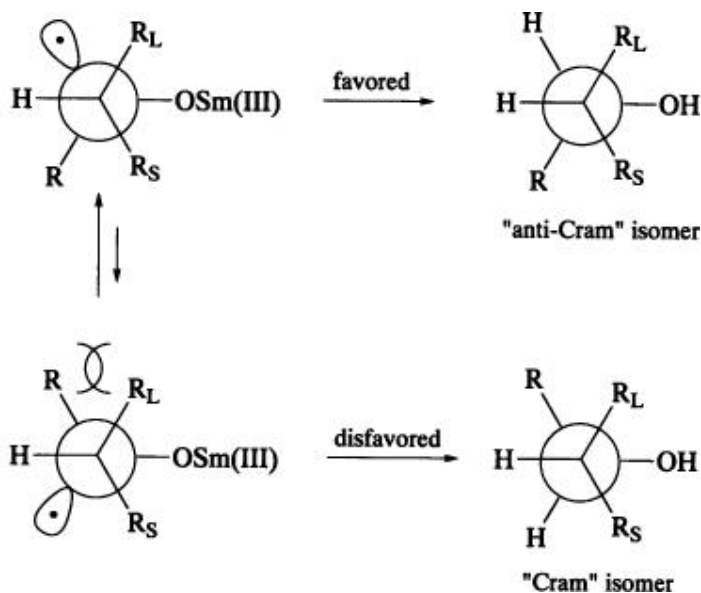
2.4. Reduction of Carboxylic Acids and Their Derivatives
Carboxylic acids and their derivatives are not readily reduced by single-electron transfer reductants, (106) and thus it is somewhat surprising that conditions have been developed that permit the reduction of these functional groups with SmI₂. (42, 46, 47) Under either acidic or basic conditions, the reduction of a variety of substituted aromatic acyl derivatives is relatively rapid.

Aromatic sodium carboxylates, carboxylic acids, carboxylic acid esters, and carboxylic acid amides react with SmI₂ under aqueous basic conditions to provide the corresponding benzylic alcohols. (42, 46, 47) The precise nature of the reducing agents formed under these conditions and definitive mechanisms for the reactions are somewhat speculative because no detailed studies have been performed. For example, it is conceivable that SmI₂ reacts with the bases

in these reactions, producing much more powerful reducing agents [SmX_2, X = OH, OR, NH_2, or perhaps even "ate" complexes of samarium(II)]. Although there is some doubt about the nature of the reducing agent, the timing of the various electron transfer and protonation steps are likely to be analogous to those of the ketone and aldehyde reductions outlined previously.

$$Ar-\overset{\overset{O}{\|}}{C}-X \xrightarrow{e^-} \left[Ar-\overset{\overset{OSm(III)}{|}}{\underset{\bullet}{C}}-X \right] \underset{}{\overset{H_2O}{\rightleftharpoons}} \left[Ar-\overset{\overset{OH}{|}}{\underset{\bullet}{C}}-X \right] \xrightarrow{e^-}$$

$$\left[Ar-\overset{\overset{OH}{|}}{\underset{-}{C}}-X \right] \xrightarrow{H_2O} \left[Ar-\overset{\overset{OH}{|}}{\underset{\underset{H}{|}}{C}}-X \right] \rightleftharpoons \left[ArCHO \right] \dashrightarrow ArCH_2OH$$

$$X = OH, OR, ONa, NH_2$$
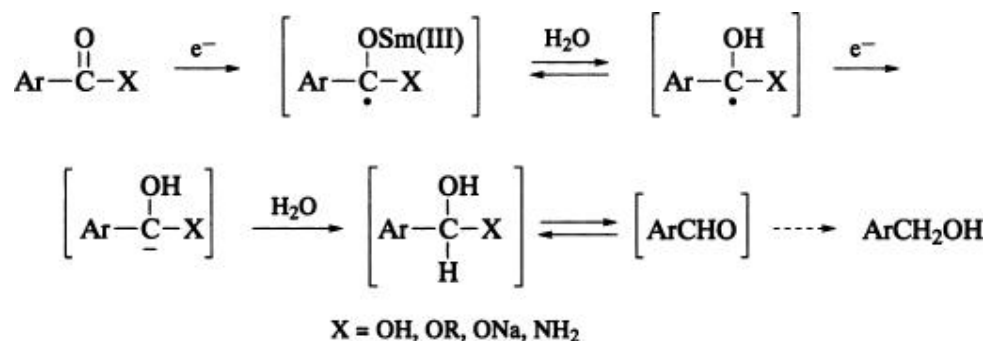
The presence of Lewis acidic samarium(III) ions could facilitate departure of the leaving group (X) in the tetrahedral intermediate leading to the aldehyde. From this point, reduction to the alcohol proceeds as described above for aldehyde and ketone substrates.

Under acidic conditions aromatic carboxylic acids and esters are converted to alcohols efficiently in very good yields. (46) Under such conditions electron transfer to the carbonyl system may be facilitated by protonation of the carbonyl group, rendering the system more easily reduced, owing to a lowering of the lowest unoccupied molecular orbital of the substrate. Subsequent electron transfer followed by proton transfer generates a tetrahedral intermediate, which can be protonated to ease departure of the leaving group. Decomposition of the tetrahedral intermediate again generates an aldehyde, which can be reduced to the benzyl alcohol.

$$Ar-\overset{\overset{O}{\|}}{C}-X \overset{H^+}{\rightleftharpoons} \left[Ar-\overset{\overset{+OH}{\|}}{C}-X \right] \xrightarrow{e^-} \left[Ar-\overset{\overset{OH}{|}}{\underset{\bullet}{C}}-X \right] \xrightarrow{e^-} \left[Ar-\overset{\overset{OH}{|}}{\underset{-}{C}}-X \right] \xrightarrow{H^+}$$

$$\left[Ar-\overset{\overset{OH}{|}}{\underset{\underset{H}{|}}{C}}-X \right] \xrightarrow{H^+} \left[Ar-\overset{\overset{OH}{|}}{\underset{\underset{H}{|}}{C}}-XH^+ \right] \rightleftharpoons \left[Ar-\overset{\overset{+OH}{\|}}{C}-H \right] \dashrightarrow ArCH_2OH$$

$$X = OH. OR$$
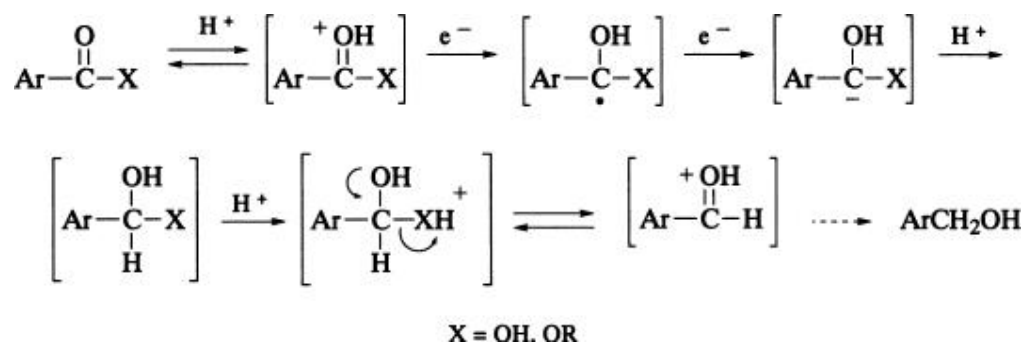
The addition of SmI_2 to primary amides in the presence of phosphoric acid

results in the production of aromatic aldehydes. This might be explained by a series of sequential proton transfers and electron transfers that result in the formation of an intermediate carbinolamine. Under the acidic conditions of the reaction, this carbinolamine may form a stable salt that resists reduction to the alcohol. (107) Decomposition of the ethanolamine salt upon aqueous workup thus provides the observed aldehyde products of the reaction.

$$Ar-\overset{O}{\overset{\|}{C}}-NH_2 \xrightleftharpoons{H^+} \left[Ar-\overset{+OH}{\overset{\|}{C}}-NH_2\right] \xrightarrow{e^-} \left[Ar-\overset{OH}{\overset{|}{\underset{\bullet}{C}}}-NH_2\right] \xrightarrow{e^-} \left[Ar-\overset{OH}{\overset{|}{\underset{-}{C}}}-NH_2\right]$$

$$\xrightarrow{H^+} \left[Ar-\overset{OH}{\underset{H}{\overset{|}{\underset{|}{C}}}}-NH_2\right] \xrightarrow{H^+} \left[Ar-\overset{OH}{\underset{H}{\overset{|}{\underset{|}{C}}}}-NH_3^+\right] \longrightarrow Ar-\overset{O}{\overset{\|}{C}}-H$$
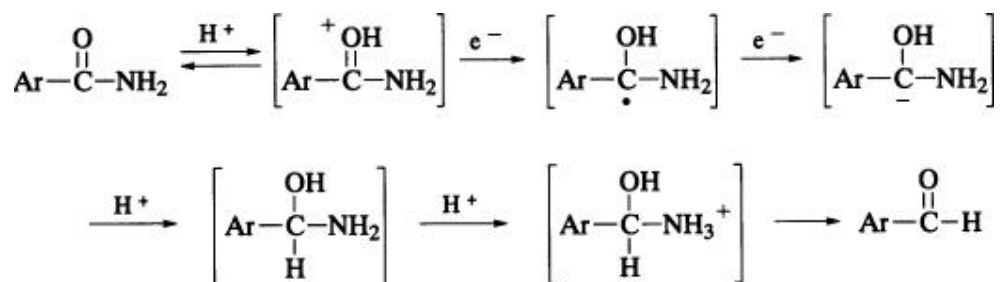
2.5. Reductive Cleavage of α -Heterosubstituted Carbonyl Compounds and Related Substrates

The most widely applied reduction process promoted by SmI_2 is the reductive cleavage of α -heterosubstituted carbonyl substrates. (7, 29, 49, 53-72) A wide variety of substituents can serve as leaving groups in this process, including hydroxy groups. (53-57)

$$RCHXCOY \xrightarrow[H^+]{2\,SmI_2} RCH_2COY$$

X = OH, OR, O₂CR, halide, OSiR₃, OSO₂Ar, SAr, S(O)Ar, SO₂Ar, OP(O)(OR)₂
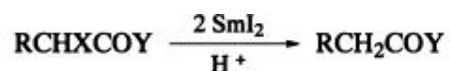
X = OH, OR, O_2CR, halide, $OSiR_3$, OSO_2Ar, SAr, S(O)Ar, SO_2Ar, OP(O)(OR)$_2$

Y = R, OR

Two limiting mechanisms can be envisioned for such transformations. In the first, initial electron transfer to the carbonyl generates a ketyl. This ketyl reacts immediately with a proton source, generating an α -hydroxy radical. Reduction of this radical to the anion with rapid β elimination affords an enol that tautomerizes to the observed carbonyl product. (53) It is likely that the oxophilicity and Lewis acidity of samarium(III) ions generated in the reduction are responsible for the success of this reaction with the wide variety of substituents, in many cases facilitating the departure of otherwise reluctant leaving groups. (108)
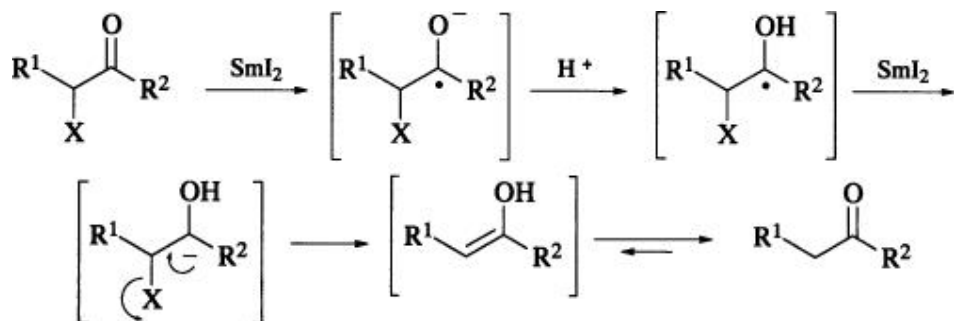
The second limiting mechanism involves initial dissociative electron transfer to an easily reducible α substituent. Subsequent reduction by a second equivalent of SmI$_2$ generates an enolate that undergoes protonation leading to the observed carbonyl product. (53) This type of mechanistic pathway is undoubtedly followed in substrates such as α -halo esters, wherein the halogen is far more easily reduced than the ester moiety, and is also an excellent leaving group.
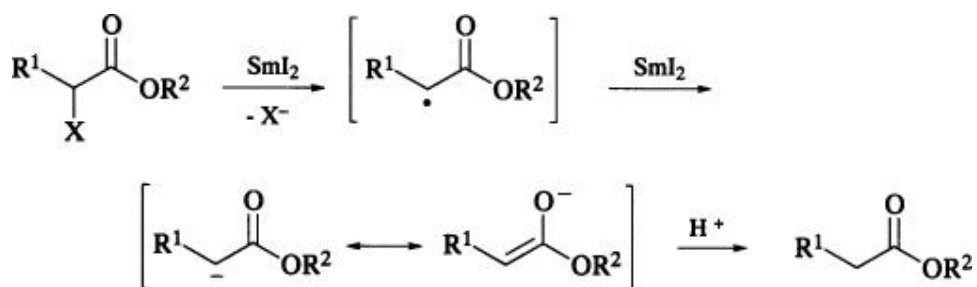
α , β -Epoxy ketones and α , β -epoxy esters comprise another subclass of α -heterosubstituted carbonyl substrates in which the mechanism for reductive cleavage must closely resemble that of other compounds wherein ketyl formation initiates the reaction. (67-69) The same fundamental mechanistic pathway is followed thereafter, resulting in the production of aldol products in which stereogenicity at the β carbon has remained intact throughout the process. Care must be taken in reactions with less easily reduced epoxy ester substrates because Lewis acid promoted ring opening of the epoxides competes with the reduction process if unoptimized solvent conditions are employed. (67) Nevertheless, this reaction provides an excellent entry to enantiomerically enriched α -unsubstituted aldol-type products that are sometimes difficult to access by more conventional means. (67-69)
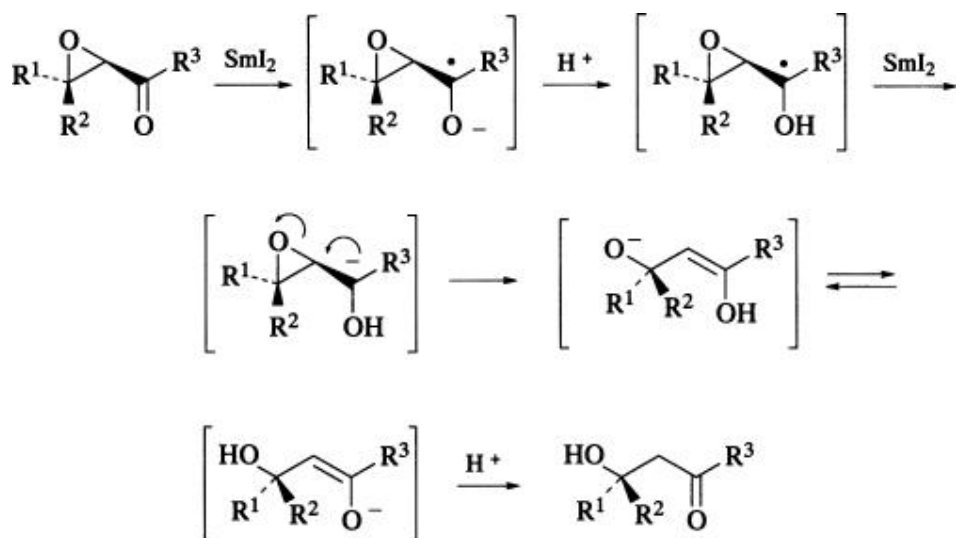
In addition to the diverse array of α substituents that can be reductively cleaved from carbonyl systems, other electron acceptors can be utilized for reductive cleavage processes. For example, α -heterosubstituted nitriles have also proven to be useful substrates for the reaction. (71, 72) Mechanisms similar to those of analogous α -heterosubstituted carbonyl substrates are undoubtedly in effect.
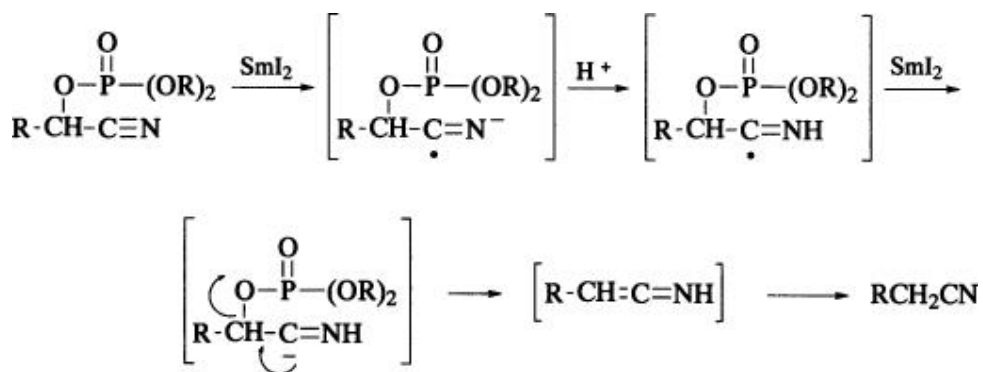
Finally, vinylogous epoxy carbonyl compounds and related vinyloxiranes also undergo facile reductive epoxide ring opening with SmI$_2$, providing δ -hydroxy- β , γ -unsaturated carbonyl substrates. (67, 70) In order to react efficiently, the substituent on the olefin in these systems must be a reasonably good electron-withdrawing group. This lowers the energy of the lowest unoccupied molecular orbital of the system, facilitating electron transfer in the crucial first step of the process. When electron-rich epoxy olefins are subjected to the

reaction, yields fall dramatically and substantial deoxygenation byproducts contaminate the reaction mixture (see below). (70) The key feature of these reductions with electron-deficient unsaturated epoxides is that a conjugated dienolate (or related species) is generated as an intermediate in the reaction. This is kinetically protonated, generating a nonconjugated olefin that resists isomerization under the rather mild reaction conditions. (70)
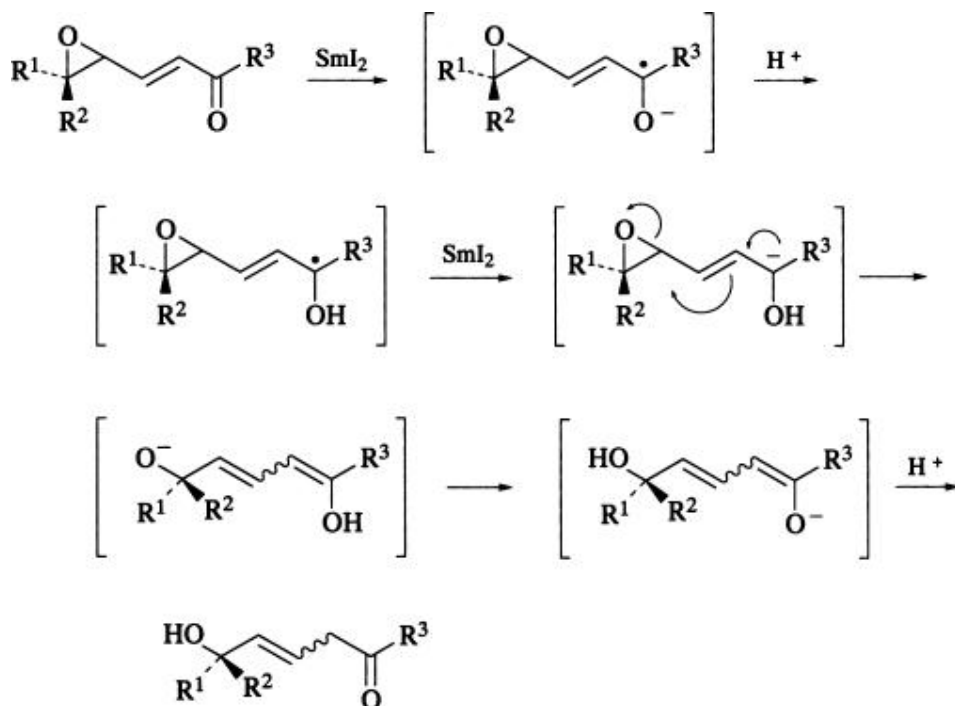
Starting from enantiomerically enriched epoxides, the overall process provides an excellent means to generate enantiomerically enriched allylic alcohols, although in some instances mixtures of diastereomeric alkenes are produced as a result of protonation of the dienolate. (70)

2.6. Reductive Cleavage of Cyclopropyl Ketones

The reductive cleavage of cyclopropyl ketones (61, 73, 74) has many similarities to that of the reduction of α -heterosubstituted carbonyl substrates. In both cases the process is initiated by single-electron transfer to the carbonyl, producing a samarium(III) ketyl. When a proton source is present, (61, 73) the ketyl is protonated and strain induced ring fragmentation of the cyclopropylcarbinyl radical thus generated affords a homoallylic radical. Electron transfer followed by proton transfer and protonation provides the observed products of the reaction.
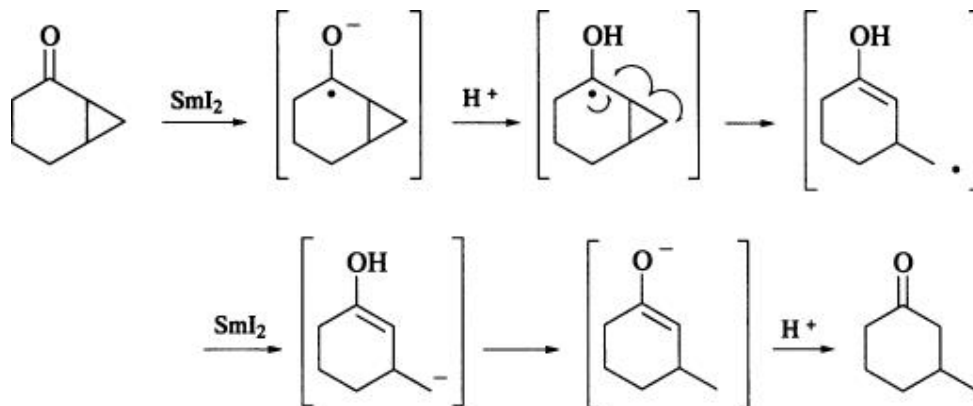
The mechanism and intermediates involved in the absence of a proton source are less clear. The latter conditions can be used in intramolecular carbon–carbon bond formation employing a judiciously placed sidechain on the ring possessing an unsaturated radical acceptor. (74) In the absence of such radicophiles, the homoallylic radical that is generated is presumably reduced to an organosamarium intermediate. However, trapping of such organosamariums with added electrophiles has not been observed. Indeed, when reactions conducted under aprotic conditions are quenched with added electrophiles, it is the samarium enolate that reacts. (74) Although no explanation has been provided for this observation, it is possible that the organosamarium is quenched by enolization of the starting ketone. The yields in these reactions wherein alkylsamariums would be generated are always less than 40%.

2.7. Deoxygenation Reactions

In contrast to α , β -epoxy ketones and vinylogous epoxy ketones in which the system is activated by an electron-deficient functional group, simple alkyl-substituted epoxides undergo a regiospecific but nonstereospecific deoxygenation, providing the corresponding alkenes as mixtures of diastereomers. (3, 75) One suggested mechanism for this process invokes a Lewis acid promoted ring opening of the epoxide, providing a mixture of iodohydrins or related species. (75) Reductive elimination of the intermediate thus generated provides the alkenes as mixtures of diastereomers.
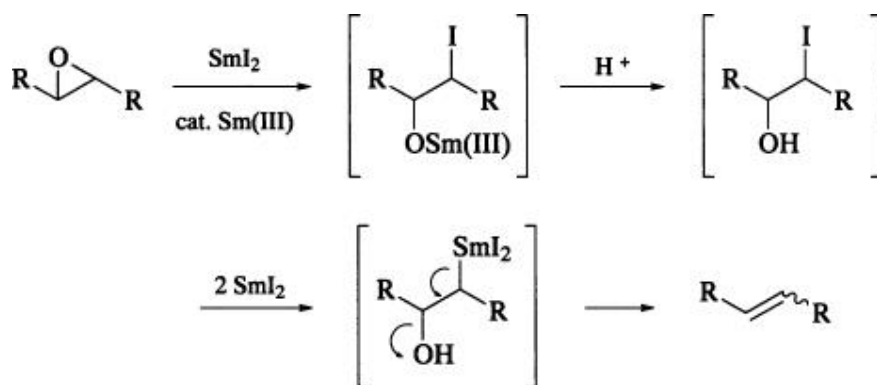
A second mechanistic scheme invokes direct reduction of the epoxide by samarium(II) in analogy to deoxygenation reactions promoted by a number of other low valent metal reductants. (109-113) By this pathway, intermediate radicals and subsequently anions are formed that eventually suffer β elimination as well. By either mechanistic pathway, it is probable that the presence of samarium(III) ions facilitates departure of the leaving group in the β -elimination process.
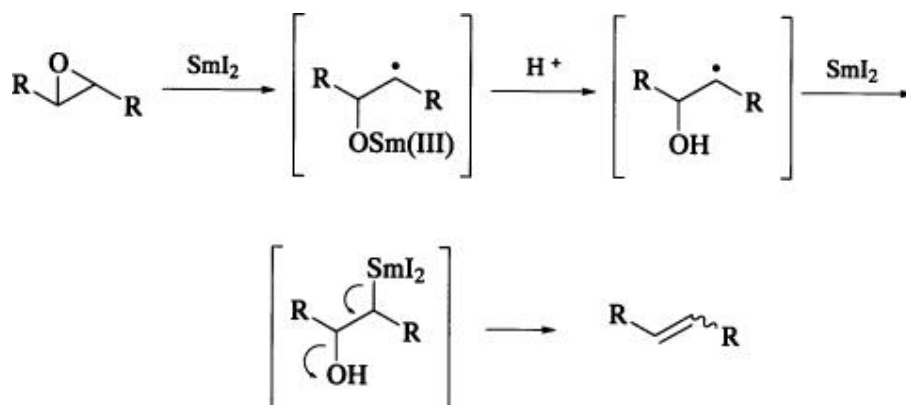
Although sulfoxides, phosphine oxides, nitrogen oxides, and arsine oxides all undergo deoxygenation with SmI_2, there is little information on the mechanisms of these processes. (41, 49, 76) Furthermore, no enantiomerically enriched phosphine oxides have been utilized in the reaction to determine if the process can be achieved stereospecifically.

2.8. Reduction of Nitrogen-Based Functional Groups
Reduction of nitroalkanes and aromatic nitro compounds can be stopped at the hydroxylamine stage or carried all the way to the amine, depending on the

reaction conditions. (49, 79, 80) With four equivalents of SmI$_2$ in THF/ MeOH for short periods of time (minutes), the hydroxylamines are produced. The mechanism is undoubtedly the same as that proposed for dissolving metal reduction of the same substrates. (104) A series of electron transfers from SmI$_2$ followed by proton transfers ultimately generates the hydroxylamine. Samarium(III) ions generated in the reaction mixture can be envisioned to facilitate departure of a hydroxy leaving group from one of the intermediates.
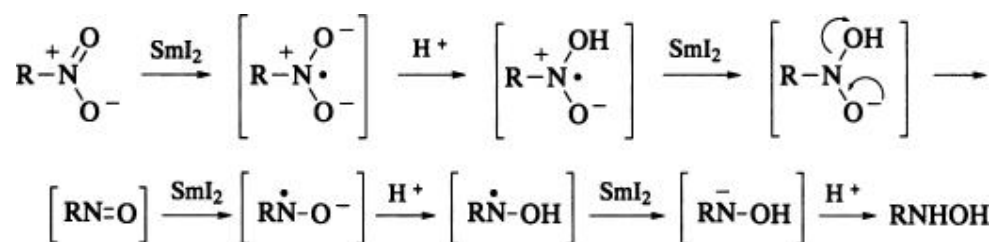
With six equivalents of SmI$_2$ over a period of several hours, the amines can be generated directly from the nitro compounds through the hydroxylamines by a mechanism involving electron transfer to the weak nitrogen–oxygen bond in the final stages of the reaction (vide infra).
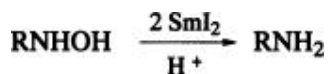
Nitriles are resistant to SmI$_2$ in THF/ MeOH at ambient temperatures, (3, 80) but aromatic nitriles do react under acidic or basic reaction conditions to provide the corresponding amines in excellent yields. (46) Under acidic conditions the process may be facilitated by protonation of the nitriles, which serves to activate the nitrile toward reduction by SmI$_2$. The mechanism for reduction could follow the classic electron transfer/proton transfer scheme.

$$RC{\equiv}N \xrightarrow[\;]{H^+} \left[RC{\equiv}\overset{+}{N}H \right] \xrightarrow{SmI_2} \left[R\overset{\bullet}{C}{=}NH \right] \xrightarrow{SmI_2} \left[R\overset{-}{C}{=}NH \right]$$

$$\xrightarrow{H^+} \left[\begin{array}{c} R \\ \diagdown \\ \diagup\;\;C{=}NH \\ H \end{array} \right] \xrightarrow{H^+} \left[\begin{array}{c} R \\ \diagdown \\ \diagup\;\;C{=}\overset{+}{N}H_2 \\ H \end{array} \right] \xrightarrow{SmI_2} \left[R\overset{\bullet}{C}HNH_2 \right]$$

$$\xrightarrow{SmI_2} \left[R\overset{-}{C}HNH_2 \right] \xrightarrow{H^+} RCH_2NH_2$$
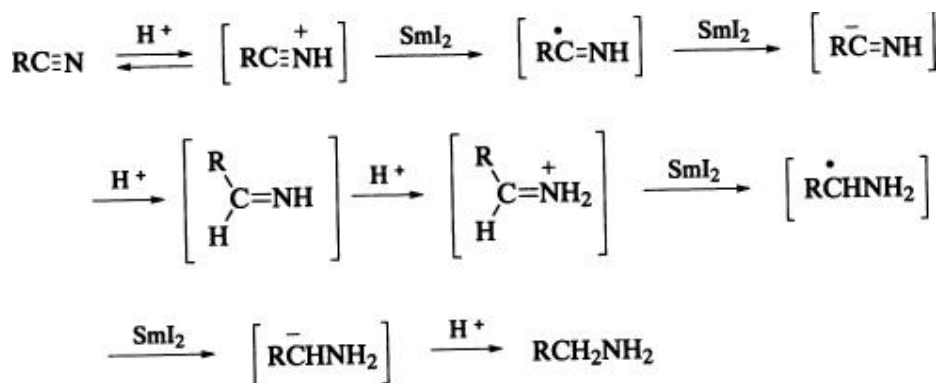
Alternatively, it has been suggested that phosphorylated imines, formed by addition of phosphoric acid to the nitriles, may be the intitial substrates for the reaction. (46)

$$RC{\equiv}N \xrightarrow{H_3PO_4} \left[\begin{array}{c} R{-}C{=}NH \\ | \\ O{-}P{-}(OR)_2 \\ \| \\ O \end{array} \right] \xrightarrow{SmI_2} \left[\begin{array}{c} R{-}\overset{\bullet}{C}{-}\overset{-}{N}H \\ | \\ O{-}P{-}(OR)_2 \\ \| \\ O \end{array} \right] \xrightarrow{H^+}$$

$$\left[\begin{array}{c} R{-}\overset{\bullet}{C}{-}NH_2 \\ | \\ O{-}P{-}(OR)_2 \\ \| \\ O \end{array} \right] \xrightarrow{SmI_2} \left[\begin{array}{c} R{-}\overset{-}{C}{-}NH_2 \\ | \\ O{-}P{-}(OR)_2 \\ \| \\ O \end{array} \right] \xrightarrow{H^+} \left[\begin{array}{c} R{-}CHNH_2 \\ | \\ O{-}P{-}(OR)_2 \\ \| \\ O \end{array} \right]$$

$$\xrightarrow[\;]{H^+} \left[\begin{array}{c} R{-}CH{-}NH_2 \\ | \\ O{-}P{-}(OR)_2 \\ \| \\ +OH \end{array} \right] \longrightarrow \left[\begin{array}{c} R \\ \diagdown \\ \diagup\;\;C{=}\overset{+}{N}H_2 \\ H \end{array} \right] \xrightarrow{SmI_2}$$

$$\left[R\overset{\bullet}{C}HNH_2 \right] \xrightarrow{SmI_2} \left[R\overset{-}{C}HNH_2 \right] \xrightarrow{H^+} RCH_2NH_2$$
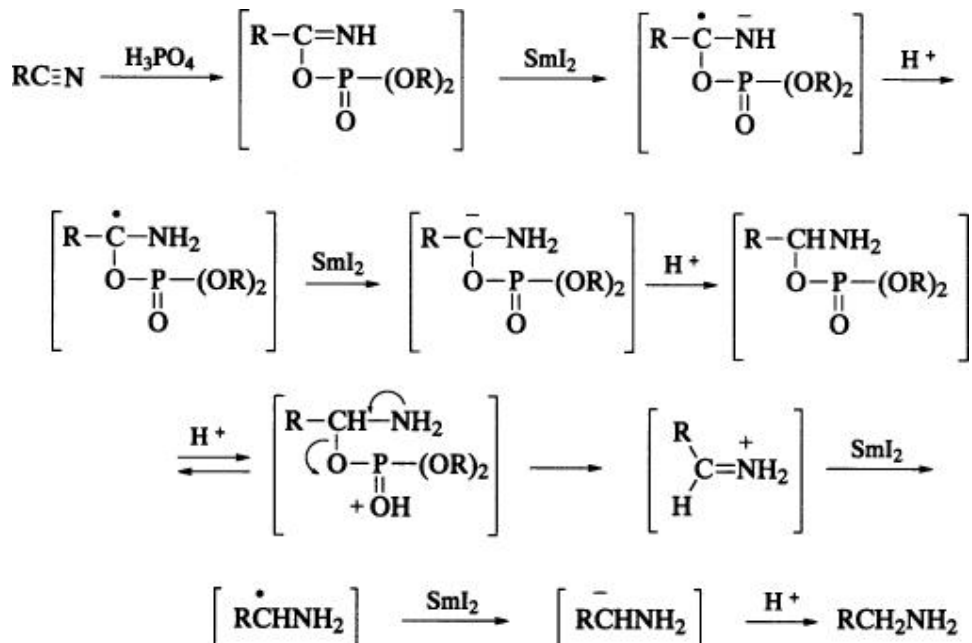
The species formed by addition of sodium hydroxide to SmI_2 is apparently a much more powerful reductant than SmI_2 itself. As proof of this, aryl chlorides are also extensively reduced during the reduction of aromatic nitriles with SmI_2 under basic conditions. (46) Thus, whatever the actual reductant is, it is also capable of reducing the nitrile very rapidly under these conditions. Samarium(III) ions formed during the reaction may ease electron transfer to the imine intermediate formed during the reaction.

$$RC\underset{\cdot}{\equiv}N \xrightarrow{\text{Sm(II)}} \left[R\overset{\bullet}{C}\underset{\cdot}{\overset{\bar{}}{=}}N \right] \xrightarrow{H_2O} \left[R\overset{\bullet}{C}{=}NH \right] \xrightarrow{\text{Sm(II)}} \left[R\bar{C}{=}NH \right]$$

$$\xrightarrow{H_2O} \left[\underset{H}{\overset{R}{\diagdown}}C{=}NH \right] \xrightarrow{\text{Sm(II)}} \left[\underset{H}{\overset{R}{\diagdown}}\overset{\bullet}{C}{-}\overset{\bar{}}{N}H \right] \xrightarrow{H_2O}$$

$$\left[\underset{H}{\overset{R}{\diagdown}}\overset{\bullet}{C}{-}NH_2 \right] \xrightarrow{\text{Sm(II)}} \left[\underset{H}{\overset{R}{\diagdown}}\bar{C}{-}NH_2 \right] \xrightarrow{H_2O} RCH_2NH_2$$
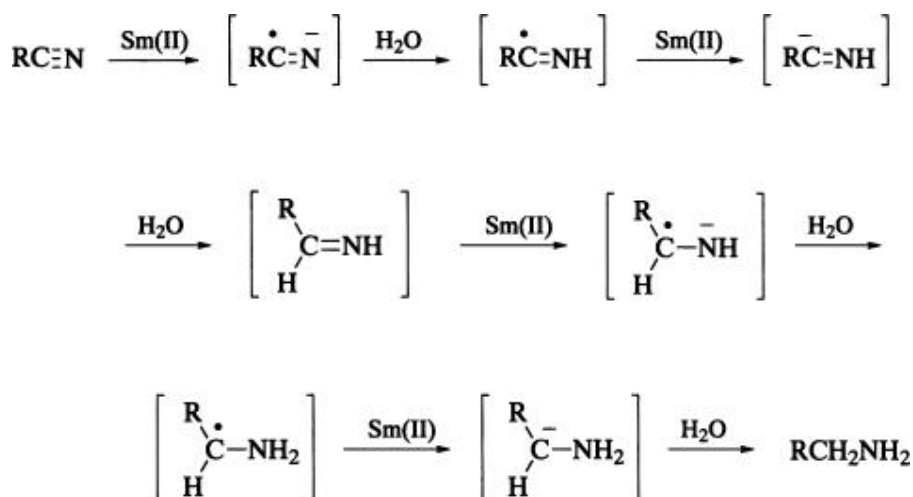
In direct analogy to the reduction of ketones, imines can be reduced with SmI$_2$ in THF/MeOH. (80, 81) The mechanism of these reactions is undoubtedly analogous to that of ketones as well.

$$\underset{R^1 \quad R^2}{\overset{NR^3}{\diagup\diagdown}} \xrightarrow{\text{SmI}_2} \left[\underset{R^1 \quad \bullet \quad R^2}{\overset{\bar{N}R^3}{\diagup\diagdown}} \right] \xrightarrow{H^+} \left[\underset{R^1 \quad \bullet \quad R^2}{\overset{NHR^3}{\diagup\diagdown}} \right] \xrightarrow{\text{SmI}_2}$$

$$\left[\underset{R^1 \quad - \quad R^2}{\overset{NHR^3}{\diagup\diagdown}} \right] \xrightarrow{H^+} \underset{R^1 \underset{H}{\diagup|\diagdown} R^2}{\overset{NHR^3}{}}$$
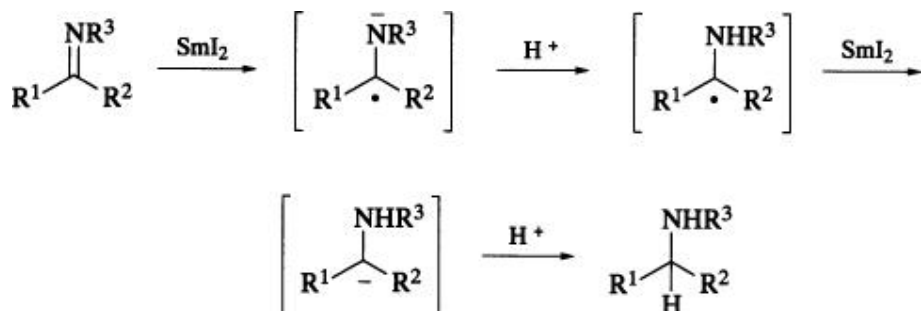
The mechanism for reduction of oximes to imines by SmI$_2$ (42, 80, 82) can be envisioned as being similar to that proposed for the electrochemical reduction of oximes. (104, 105) Further reduction of the imine thus generated to the amine follows the mechanism outlined above. A series of chiral 2-hydroximino amides of α -amino acids has been reduced with fair to good diastereoselectivities in the protonation of the amine α -carbanion. (82) There has been no rationalization for the sense of asymmetric induction observed.

Azo compounds react with two equivalents of SmI$_2$ in THF/MeOH to form hydrazines, (49) and these intermediates (and related acyl hydrazines) are reductively cleaved to amines with an excess of SmI$_2$. (80, 84)

$$RCH{=}NOH \xrightarrow{\text{SmI}_2} \left[R\overset{\bullet}{C}H{-}\overset{-}{N}OH \right] \xrightarrow{\text{H}^+} \left[R\overset{\bullet}{C}H{-}NHOH \right] \xrightarrow{\text{SmI}_2}$$

$$\left[\overset{\frown}{R\overset{\frown}{C}H{-}\underset{H}{\overset{-}{N}}{-}\overset{\frown}{OH}} \right] \longrightarrow \left[RCH{=}NH \right] \dashrightarrow RCH_2NH_2$$

$$RN{=}NR \xrightarrow{\text{SmI}_2} \left[R\overset{\bullet}{N}{-}\overset{-}{N}R \right] \xrightarrow{\text{H}^+} \left[R\overset{\bullet}{N}{-}NHR \right] \xrightarrow{\text{SmI}_2}$$

$$\left[R\overset{-}{N}{-}NHR \right] \xrightarrow{\text{H}^+} \left[RHN{-}NHR \right] \xrightarrow{\text{SmI}_2}$$

$$\left[\begin{array}{c} R\overset{\bullet}{N}H \\[2pt] + \\[2pt] R\overset{-}{N}H \end{array} \right] \begin{array}{c} \xrightarrow{\text{SmI}_2} \left[R\overset{-}{N}H \right] \xrightarrow{\text{H}^+} RNH_2 \\[18pt] \xrightarrow{\text{H}^+} RNH_2 \end{array}$$
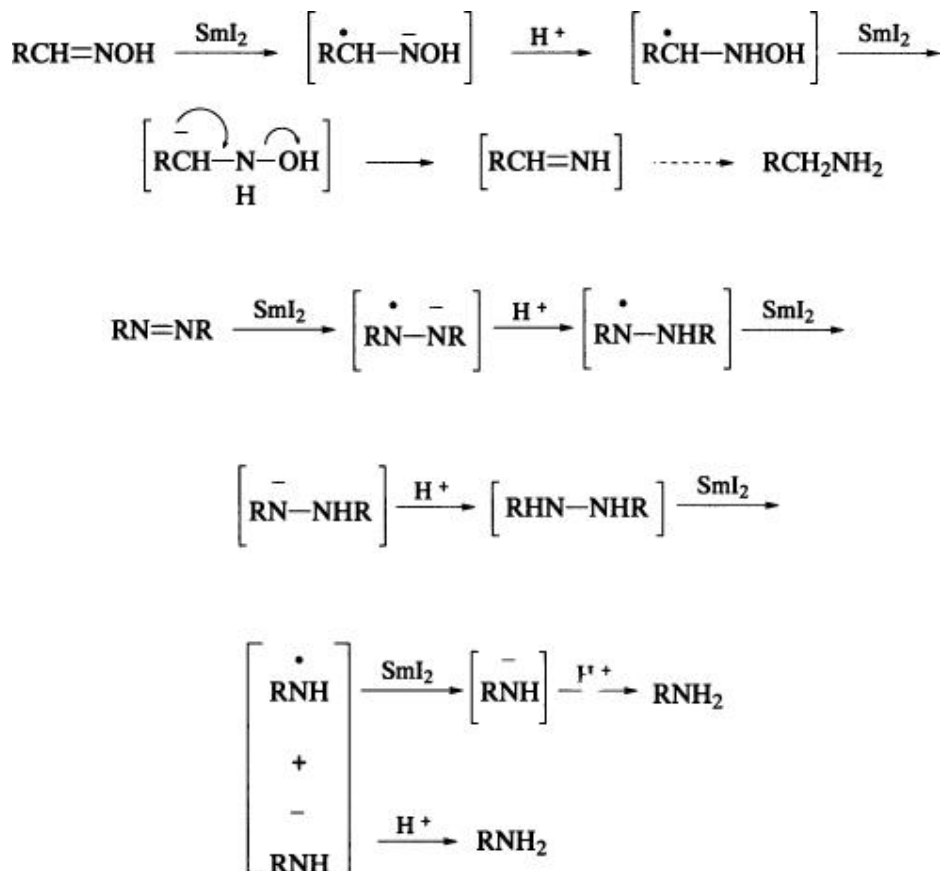
2.9. Reduction of Miscellaneous Functional Groups

As pointed out in some of the preceding examples, heteroatom–heteroatom bonds are readily cleaved by SmI$_2$. Thus peroxides also suffer rapid reductive bond cleavage, and bicyclic peroxides produce diols. (85, 86)

$$ROOR \xrightarrow{\text{SmI}_2} \begin{cases} RO{\bullet} \xrightarrow{\text{SmI}_2} RO^- \xrightarrow{\text{H}^+} ROH \\[14pt] RO^- \xrightarrow{\text{H}^+} ROH \end{cases}$$
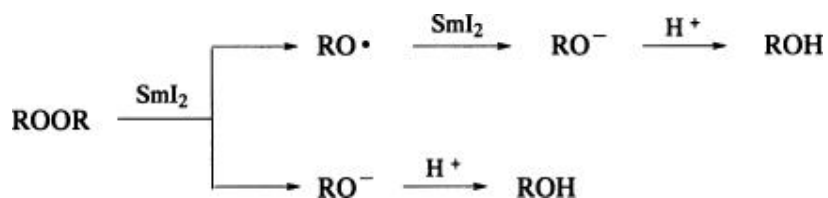
The nitrogen–oxygen bond of isoxazoles suffers the same fate, but in this case the enol oxygen is tautomerized to a ketone, and the imine equilibrates to an enamine in the final product. (25)

Halo phosphine oxides and halo phosphine sulfides undergo reduction to the

corresponding phosphines upon reduction by SmI$_2$. ([87](#)) The mechanism undoubtedly mimics that of reduction of alkyl halides by SmI$_2$, proceeding through radical and presumably anionic intermediates. In reactions with enantiomerically enriched substrates, substantial racemization occurs in the transformation from starting material to products. It is unclear whether this occurs as a result of epimerization of the intermediate radical or the anion. However, analogous anionic phosphorus complexes have been reported to maintain their stereochemistry.
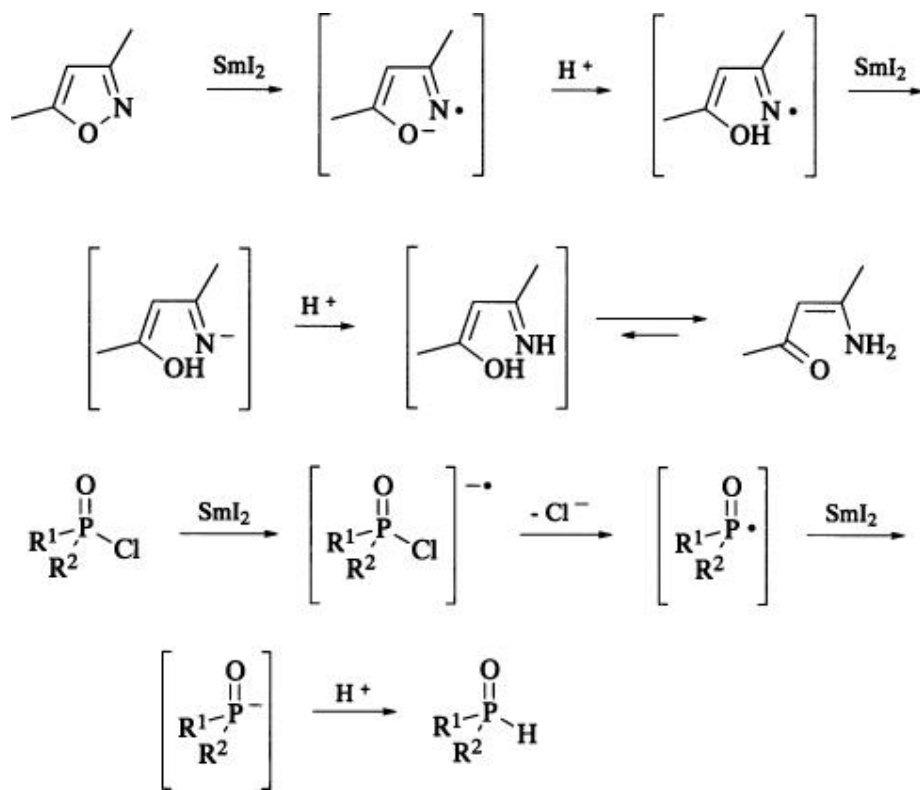
Samarium(II) iodide serves as the stoichiometric reductant in the palladium(0)-catalyzed reduction of allylic acetates. ([88](#)) In the process, the π-allylpalladium species initially formed is reduced by SmI$_2$, forming an allyl anion with regeneration of the palladium(0) catalyst. The allylic anion is subsequently quenched by isopropanol that is present in the reaction mixture. As a consequence of this mechanism, mixtures of regioisomeric and stereoisomeric alkenes are generally formed as products of the reactions.

$$R^1C\equiv C \quad \overset{OAc}{\underset{R^2}{\diagdown}} R^3 \xrightarrow{Pd(0)} \left[\overset{R^1}{\underset{L_2Pd}{\diagdown}} C=C=C \overset{R^3}{\underset{R^2}{\diagup}} \right]^+ \; {}^-OAc \xrightarrow{2\,Sm(II)}$$
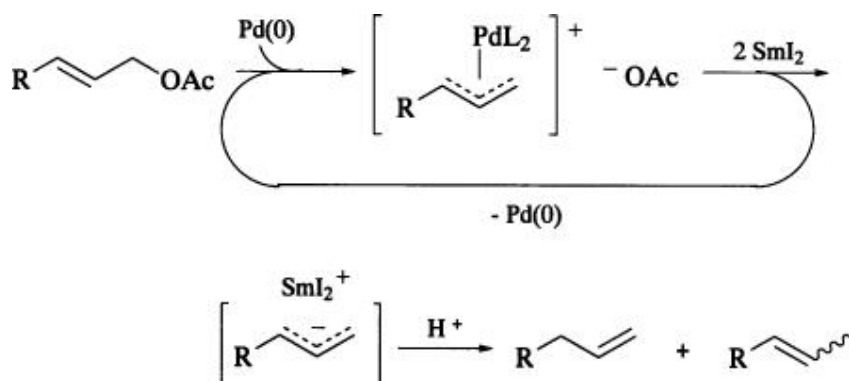
In an analogous process, propargyl acetates react under similar conditions to form allenes or alkynes. (89) The ratio of the two isomeric products is a function of the structure of the substrate as well as the protonating agent used in the reactions. Sterically bulky protonating agents typically provide a greater proportion of allene in these reactions, and the preference for allene formation is also enhanced in tertiary propargyl acetates relative to that of secondary and primary propargyl acetates.

$$\left[\overset{R^1}{\underset{X_2Sm}{\diagdown}} C=C=C \overset{R^3}{\underset{R^2}{\diagup}} \right] \rightleftharpoons \left[R^1C\equiv C \overset{SmX_2}{\underset{R^2}{\diagdown}} R^3 \right] \xrightarrow{H^+}$$

$$\overset{R^1}{\underset{H}{\diagdown}} C=C=C \overset{R^3}{\underset{R^2}{\diagup}} \quad + \quad R^1C\equiv C \overset{H}{\underset{R^2}{\diagdown}} R^3$$
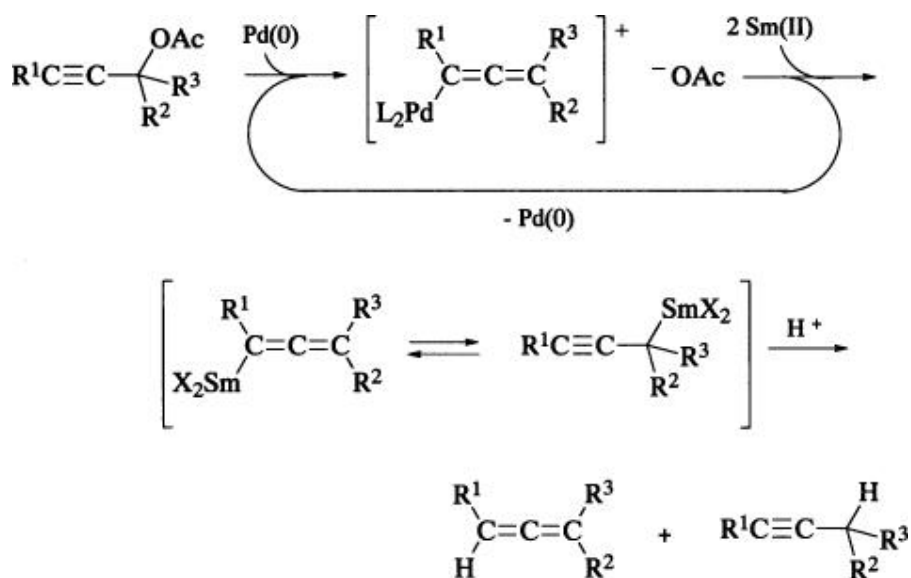
Samarium(II) iodide can also be utilized as the stoichiometric reductant in transition metal catalyzed reductions of alkynes to produce *cis*-alkenes. (91) Although

X$_2$Co(PPh$_3$)$_2$

SmX$_2$

SmX$_3$

$\overline{\text{X}}$Co(PPh$_3$)$_2$

H$^+$

SmX$_3$

HCoX(PPh$_3$)$_2$

RC≡CR

SmX$_2$, HX

X$_2$Co(PPh$_3$)$_2$

R   R

H   CoX(PPh$_3$)$_2$

R   R   R   R   SmX$_3$

H   H   HX   H   SmX$_2$
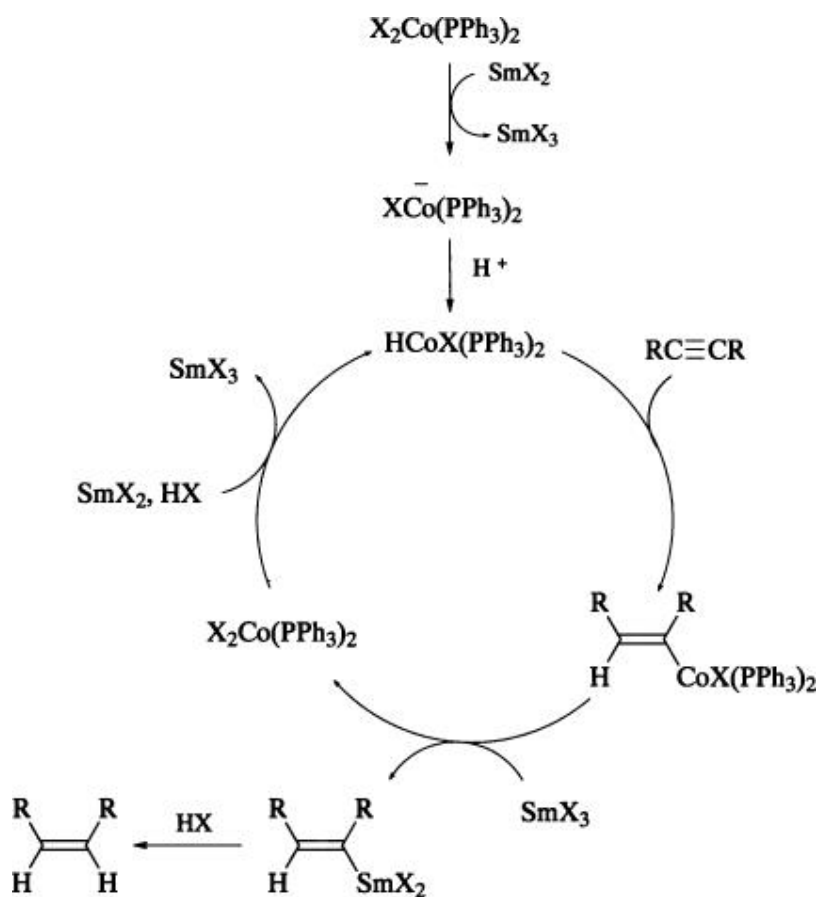
few mechanistic details exist for these transformations, transition metal hydrides are suspected as the reactive reducing agents in the reactions. Thus SmI$_2$ may serve as a reductant for CoCl$_2$·4PPh$_3$, which becomes protonated to generate HCoCl(PPh$_3$)$_2$, the active catalyst for the process. *cis*-Addition of the reactive hydride to the alkyne followed by transmetalation with SmX$_3$ may provide the corresponding alkenylsamarium and X$_2$Co(PPh$_3$)$_2$. The *cis* alkenes can be derived from the alkenylsamarium species by protonation, and the active catalyst would be regenerated from X$_2$Co(PPh$_3$) by reduction with SmI$_2$ and subsequent protonation.

Alternatively, the alkenylsamarium species could be derived from the alkenylcobalt species by a reductive transmetalation process, generating the anionic cobalt complex. Simple protonation of the latter species would again regenerate the active catalyst.
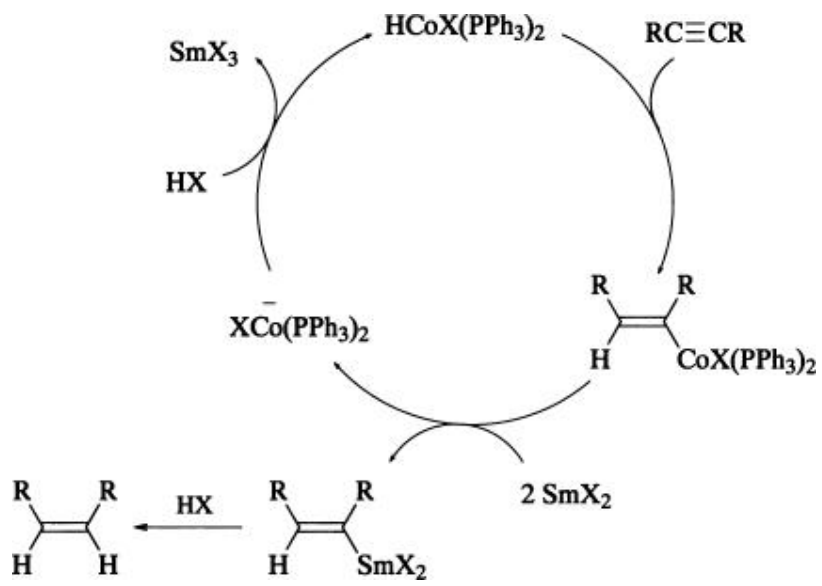
3. Scope and Limitations

3.1. Reduction of Organic Halides, Sulfonates, and Sulfones
In the presence of HMPA, SmI$_2$ appears to be a remarkably versatile and powerful reagent for the conversion of a variety of alkyl halides to the corresponding alkanes. (24) Primary, secondary, and even tertiary alkyl halides are reduced rapidly under very mild conditions. Although alkyl iodides and bromides react within minutes at room temperature, chloroalkanes require heating for several hours in THF for complete reaction. Selectivity for the reduction of alkyl bromides or alkyl iodides in the presence of chloroalkanes has not been specifically addressed. However, on the basis of the relative rates outlined above (24) and related data from intermolecular Barbier-type reactions, (3) high chemoselectivity in the reduction of bromochloroalkanes and chloroiodoalkanes can be anticipated. Although fluoroalkanes have apparently not been employed as substrates, it is likely that they are resistant to reduction under reasonable experimental conditions.
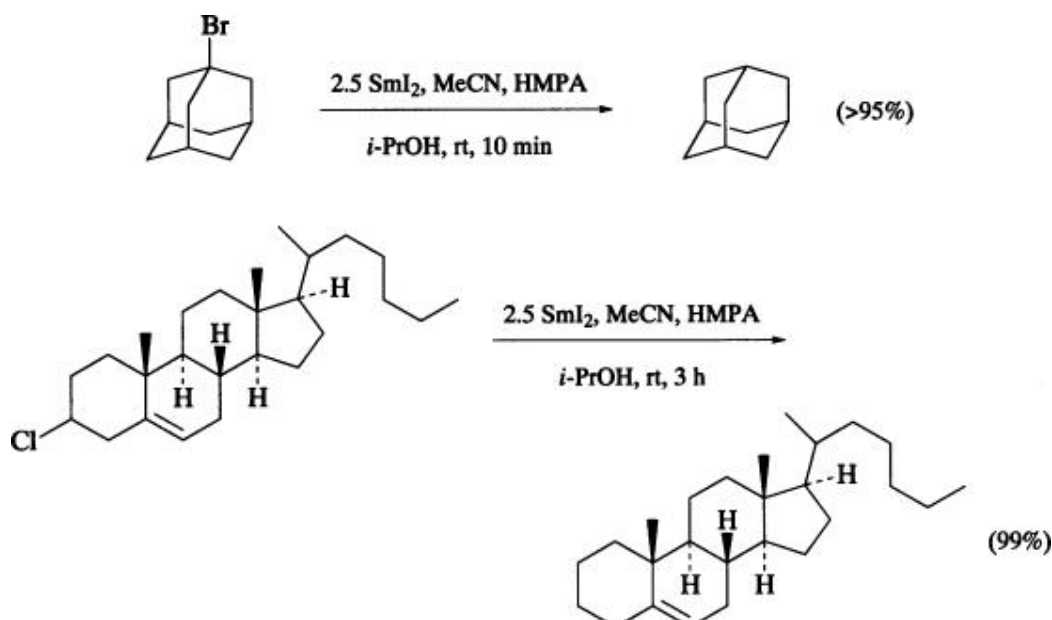
Several different functional groups can be tolerated under conditions required for alkyl halide reduction. These functional groups include alcohols, aromatic rings, ethers, and for most substitution patterns alkenes and esters. (24) Suitably disposed alkenes can trap radicals generated from alkyl halide precursors, and similarly esters (and other carboxylic acid derivatives) can undergo nucleophilic acyl substitution if five- or six-membered rings can result. The procedure for alkyl halide reduction is certainly not effective for substrates

possessing more easily reducible functional groups such as aldehydes, ketones, and conjugated carbonyl groups. Reduction of these functional groups or Barbier-type reactions compete with the alkyl halide reduction. Attempted reductions of alkyl halides in the presence of still other readily reduced functional groups or reactive electrophiles should be carried out with care.

Certain structural classes of alkyl halides may pose problems as well. For example, attempted reduction of geminal dihalides may lead to unwanted side reactions owing to carbene formation, (23, 29, 114) and alkyl halides possessing a leaving group β to the halide will undergo conversion to alkenes via a reductive β -elimination process. (26-28, 31, 33-39)

Alkyl tosylates can be reduced to the corresponding alkanes with SmI_2. (3) The scope of this transformation has not been fully explored. It has been suggested that the mechanism for this process involves an initial Finkelstein-type conversion of the tosylate to the corresponding alkyl iodide, which subsequently undergoes reductive cleavage. If this is the case, then the reduction will be restricted to alkyl tosylates that undergo facile conversion to the corresponding iodide under the reaction conditions.

Owing to the intervention of radical intermediates in the reduction of alkyl halides, an obvious limitation to SmI_2-promoted reductions is the loss of stereochemistry that will result in nearly all cases when chiral alkyl halide substrates are reduced. One exception is the retention observed in reduction of some cyclopropyl halides, in which configurational stability is conferred on the intermediates of the reduction process. (92)
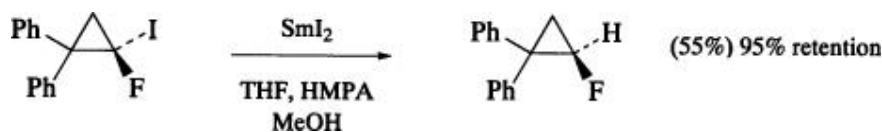
Aryl iodides, aryl bromides, and even aryl chlorides are all reduced effectively by SmI_2 in the presence of HMPA. (24) Although somewhat less well studied, alkenyl halides also appear to be suitable substrates for reduction reactions. The intermediacy of rapidly inverting vinyl radicals would appear to prevent stereospecific reduction of diastereomeric alkenyl halides.
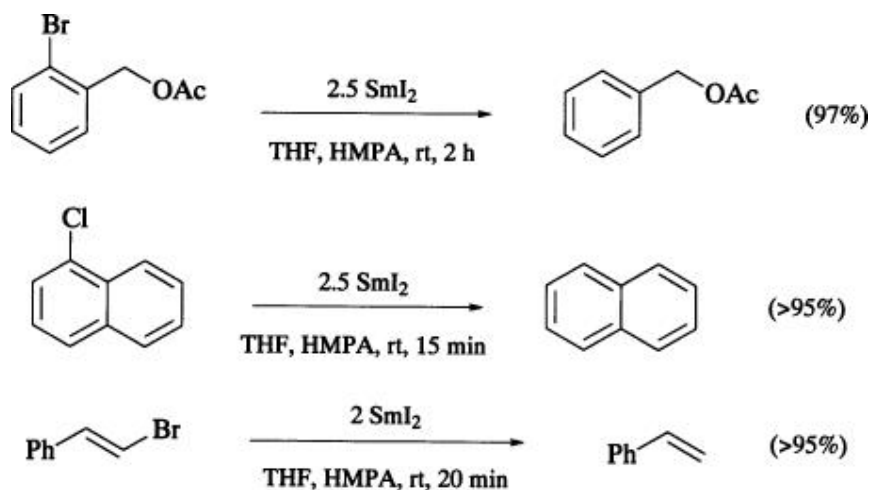
Neither allylic halides nor benzylic halides are effectively reduced to the corresponding alkanes with SmI_2 in THF. In both sets of substrates, extensive reductive dimerization occurs. (3) However, these substrates have not been subjected to reductions employing SmI_2 in HMPA, and perhaps under these conditions a clean reduction can be achieved. (115)

Alkyl phenyl sulfones and alkenyl *tert*-butyl sulfones are reductively cleaved by SmI_2 in the presence of HMPA, providing the corresponding hydrocarbons. (33) These reactions can be acccomplished in spite of the fact that diaryl sulfones and dialkyl sulfones have been reported to be converted to the corresponding sulfides under nearly the same reaction conditions. (41, 76) Perhaps even more surprising is the fact that the alkenyl sulfones can be reductively cleaved without interference from competitive conjugate reduction. Although further studies will be required to outline the full scope of this process, it is clear that the procedure is fairly chemoselective (tolerating alcohols, esters, benzyl ethers, and aromatic systems), and thus may be of reasonable synthetic utility.
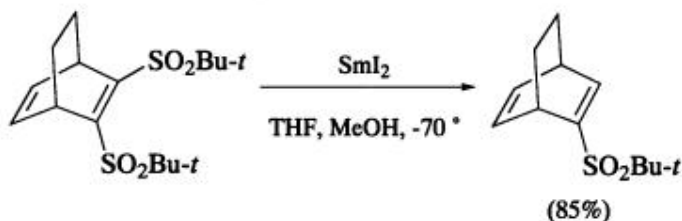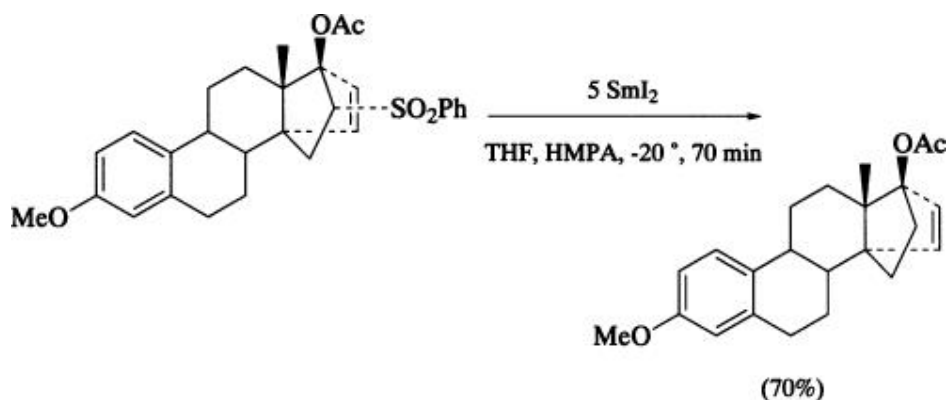
3.2. Reductive Elimination/Fragmentation Reactions

Reductive cleavage of β -halo ethers and β -acyloxy halides is a general reaction, but tertiary alkyl halides have not been employed as substrates. Although only modest effort has been devoted to this reaction as a synthetic tool, substrates examined to date make it clear that ketones, esters, alcohols, and alkynes do not react under conditions required for the β -elimination processes. Reactions proceed under mild conditions using both chloride and bromide precursors. (26, 31, 34-36) The procedure would thus appear to be a reliable, chemoselective method for the deprotection of appropriately protected (β -haloethyl-substituted) alcohols and amines in highly functionalized molecules, (35, 36) and for the construction of olefins from suitable geminally substituted substrates. Additionally, the reductive fragmentation reaction can be utilized as a mechanistic tool to probe for the intermediacy of organosamarium intermediates in processes promoted by SmI$_2$. (18, 73) 1,2-Dihaloalkenes and 1,2-dihaloarenes have not been subjected to reduction by SmI$_2$. However, because alkenyl and aryl radicals generally undergo hydrogen atom abstraction from the solvent more rapidly than they are reduced to the anion, (24, 93-95, 97, 98) it is not likely that such substrates would lead to alkynes or benzynes, respectively.
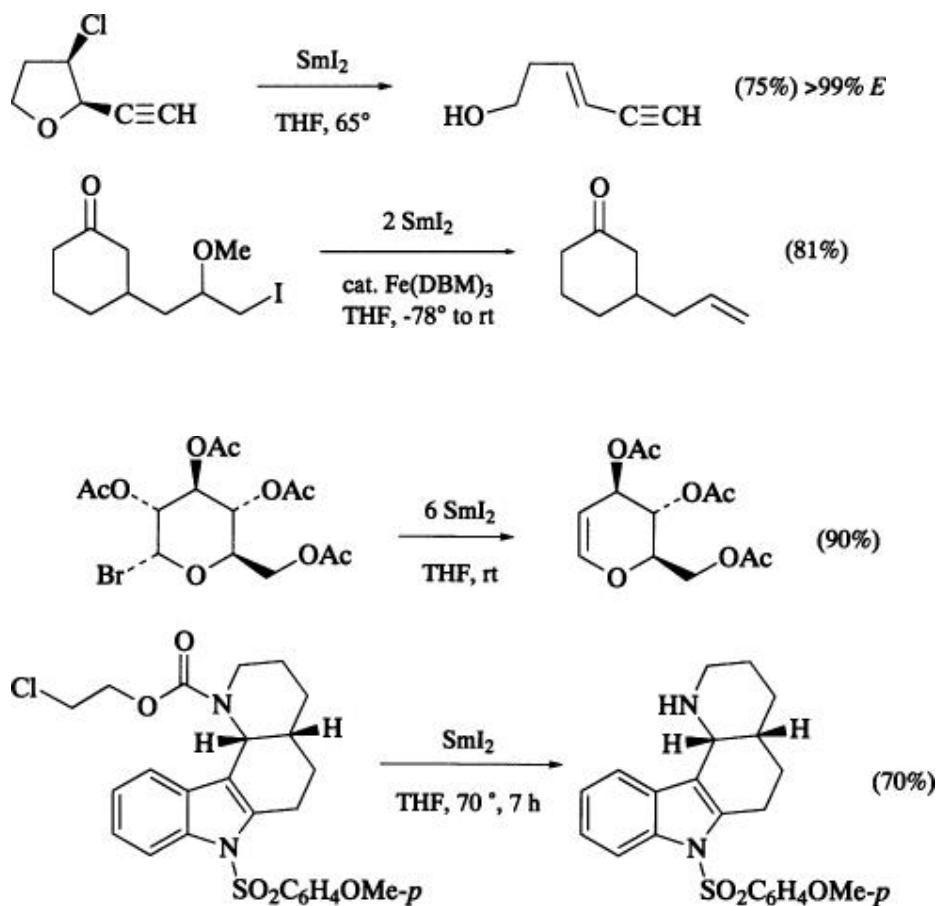
Only two α , β -disulfones have been reduced by SmI$_2$, but yields are high in both cases, and thus the expectation is that a diverse range of such substrates might undergo reductive elimination. (33) There are some reservations in this expectation, however, because of the results obtained in the reductive elimination of β -hydroxy sulfones. Thus although reductive cleavage of alkyl imidazolyl sulfones in this series proceeds very effectively, alkyl phenyl sulfones subjected to identical reaction conditions lead only to the recovery of starting material or to desulfonated alcohol. (33, 37)

$$\text{(87\%) 5:1 } E/Z \quad (64)$$

(91%)
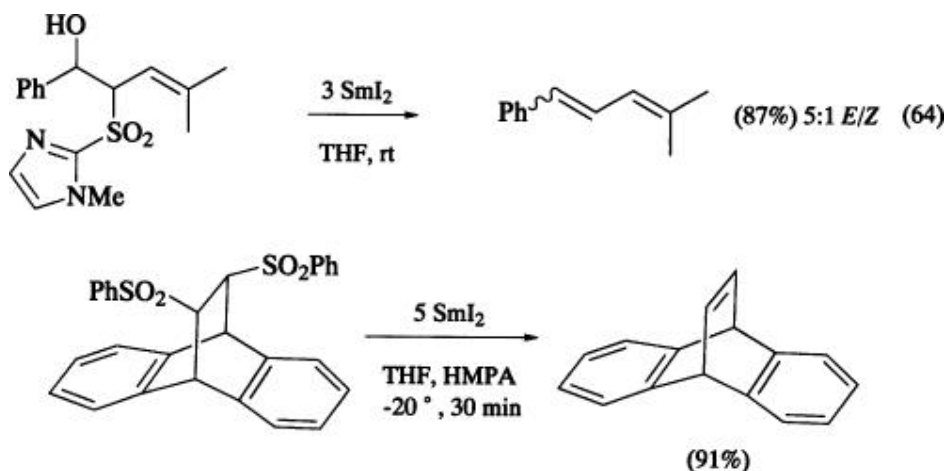
The reductive elimination of enolates is an intriguing reaction that has seen only preliminary development with SmI$_2$ utilized as the reducing agent to induce the fragmentation. In certain cases it has the potential to generate stereocontrolled, highly functionalized acyclic structural units from readily available cyclic precursors. (27, 28, 38, 39)
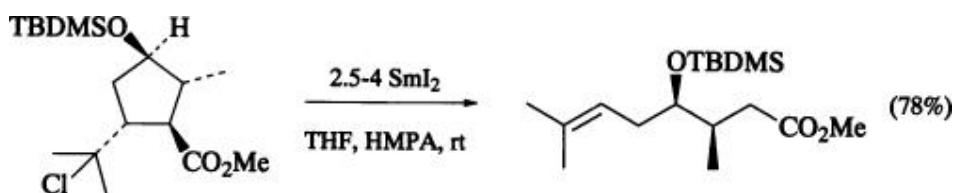
3.3. Reduction of Aldehydes and Ketones

The reduction of aldehydes and ketones by SmI$_2$ has not been explored in great detail. In the few examples that are reported, the reaction works reasonably well on some simple substrates. (3) Competitive rate studies indicate that SmI$_2$ is highly chemoselective for the reduction of aldehydes in the presence of ketones. (3) Additionally, ketones can be reduced in the presence of esters (45) and, to some extent, α , β -unsaturated esters. (44) Chemoselectivity in the presence of halides is difficult to achieve because of competitive Barbier-type reactions, although alkyl chlorides will survive the reaction conditions if HMPA is not employed as a cosolvent. The ability of other reducible functional groups to remain intact during carbonyl reduction has yet to be submitted to close scrutiny.

Diastereoselectivity in the reduction of aldehydes and ketones with SmI$_2$ in most cases is not high, (40, 41) although in specific instances preference for

the equatorial alcohol in six-membered ring systems can be quite respectable. (41, 45) Although reasonably high enantioselectivities have been achieved in the reduction of benzil to benzoin using SmI$_2$ as a reductant along with chiral protonating agents, (43) this approach to asymmetric synthesis is unlikely to be competitive with other available methods.
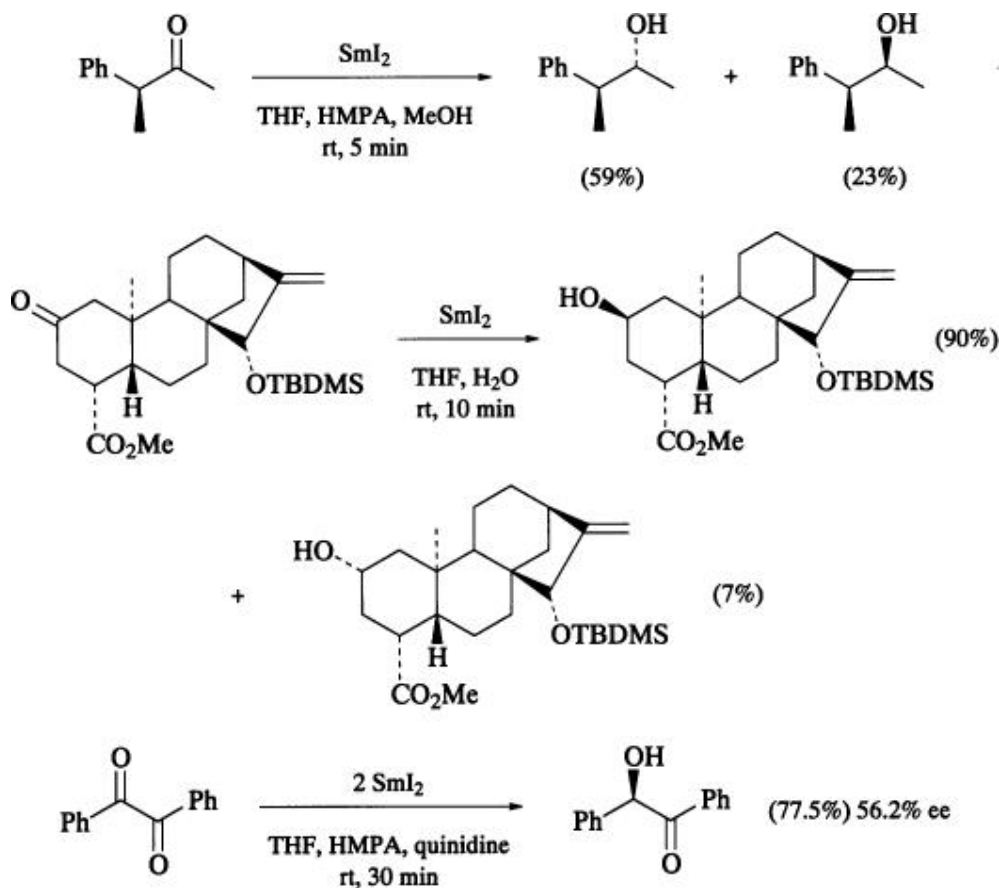
3.4. Reduction of Carboxylic Acids and Their Derivatives

Carboxylic acids, carboxylic acid amides, and carboxylic acid esters are quite resistant to reduction by SmI$_2$ in THF or even in THF/HMPA. However, under acidic (aqueous phosphoric acid) or basic (e.g., aqueous sodium hydroxide) conditions, reduction of aromatic carboxylic acids and their derivatives can be effected within seconds. (42, 46, 47) Under basic conditions the reduction of simple, unfunctionalized aliphatic carboxylic acids also proceeds in good-to-excellent yields, but the acidic reaction protocol appears applicable only to aromatic carboxylic acids. There is no information on the scope of the reaction with regard to the nature of the alcohol-derived portion of the ester, but for those esters that possess alkyl units that can form reasonably stable radicals, the electron transfer nature of the reaction may lead to the

intervention of radical cleavage processes leading to undesired byproducts. (116, 117) Furthermore, because of the powerfully reducing reaction conditions, only a very limited array of functionality can be tolerated in these transformations.

$$PhCO_2H \xrightarrow{\begin{array}{c} 4\ SmI_2 \\ \hline THF,\ H_2O,\ 8\ NaOH, \\ rt,\ 60\ s \\ \hline 4\ SmI_2 \\ \hline THF,\ H_3PO_4\ (85\%), \\ rt,\ 3\ s \end{array}} \begin{array}{c} PhCH_2OH \\ (91\%) \end{array}$$
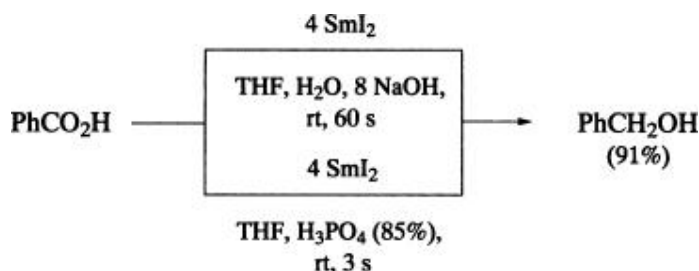
As might be expected, based upon the reduction of carboxylic acids in basic media, sodium benzoate is also readily reduced in aqueous SmI_2, providing a good yield of benzyl alcohol. (47) Anhydrides and carboxylic acid halides, however, are poor substrates for SmI_2-based reduction under either anhydrous or aqueous conditions. Under anhydrous conditions the acyl anion intermediate generated upon initial reduction of the acid halide by SmI_2 is acylated, leading to the generation of α -diketones and α -ketols. (48) Even under aqueous conditions substantial dimerization occurs, and the process is therefore not synthetically useful.

Methyl benzoate can be reduced under acidic or basic conditions to provide benzyl alcohol, (42, 46) but this reduction for nonaromatic esters has not been examined, and the reaction is not likely to be general.

$$PhCO_2Me \xrightarrow{\begin{array}{c} 4\ SmI_2 \\ \hline THF,\ H_2O,\ 8\ KOH, \\ rt,\ 8\ min \\ \hline 4\ SmI_2 \\ \hline THF,\ H_3PO_4\ (85\%), \\ rt,\ 3\ s \end{array}} \begin{array}{c} (68\%) \\ PhCH_2OH \\ (72\%) \end{array}$$
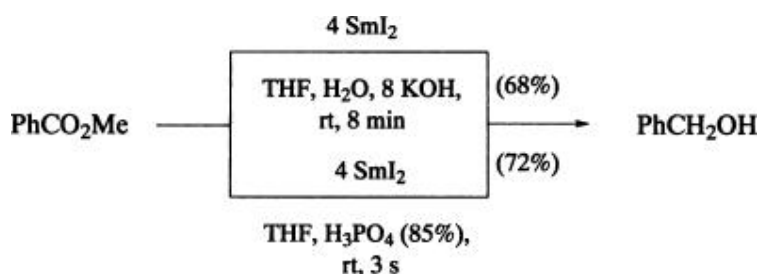
Curiously, aromatic carboxamides are reduced to benzyl alcohols under basic conditions. (42) The reaction under acidic conditions provides the corresponding benzaldehydes in excellent yield. (46) Unfortunately, the reaction in both cases appears limited to primary amides. Secondary amides,

hydrazides, and hydroxamic acids give mixtures of products in modest yields. Consequently, this process, too, appears of quite limited synthetic value.

$$PhCONH_2 \begin{cases} \xrightarrow[\substack{THF,\ MeOH,\ 8\ KOH \\ rt,\ 123\ s}]{4\ SmI_2} PhCH_2OH \quad + \quad PhCH_2NH_2 \\ \qquad\qquad\qquad\quad (68\%) \qquad\qquad (8\%) \\ \\ \xrightarrow[\substack{THF,\ 85\%\ H_3PO_4 \\ rt.\ 3\ s}]{4\ SmI_2} PhCHO \\ \qquad\qquad\qquad\quad (>99\%) \end{cases}$$
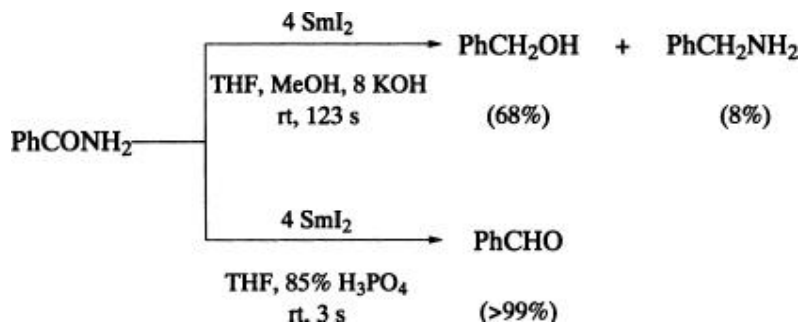
3.5. Reduction of Conjugated Carbonyl Substrates

Reduction of α , β -unsaturated aldehydes and ketones with SmI_2 invariably leads to mixtures of 1,2- and 1,4-addition products, and to products in which both the olefin and the carbonyl group have been reduced. (3) In some cases, extensive polymerization is observed as well. Consequently, with the exception of benzoquinone and perhaps its analogs, (49) clean reductions in such systems seem difficult to achieve.

On the other hand, the reduction of conjugated esters and amides by SmI_2 is a quite useful process, proceeding within minutes in *N,N*-dimethylacetamide with an added proton source. (3, 50-52) The nature of the solvent is reported to be critical for success in these conjugate reductions, although there is some controversy surrounding this point. Thus HMPA is reported to lead to extensive reductive dimerization of the unsaturated systems in one study, (51) an observation that is disputed in a second investigation. (60) With the exception of tetrasubstituted systems, all substitution patterns about the olefin have been examined in conjugate reductions of unsaturated esters and amides, and all proceed in reasonable yields. Little information is available about other functional groups that might be compatible with the reactions.
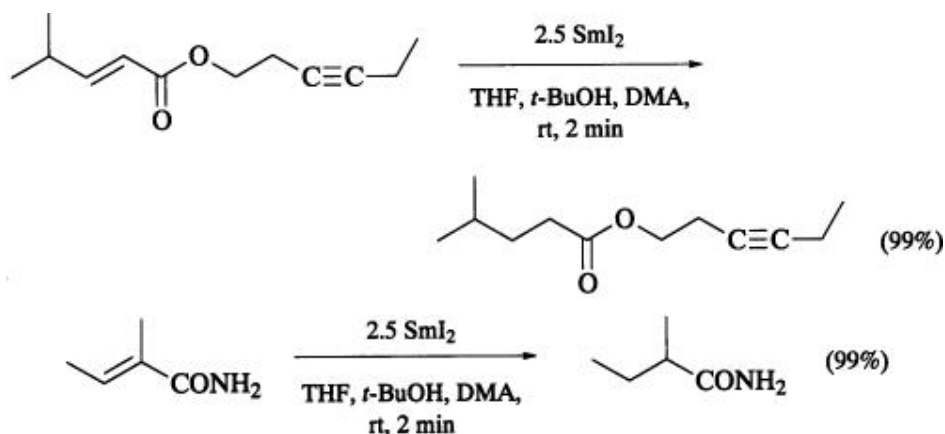
Conjugated carboxylic acids and anhydrides can also be reduced to the saturated derivatives in the presence of SmI$_2$. (50) For these substrates, THF/HMPA appears to be the solvent of choice. Di-, tri-, and tetrasubstituted olefins have all been examined, and modest to excellent yields are maintained throughout the series.
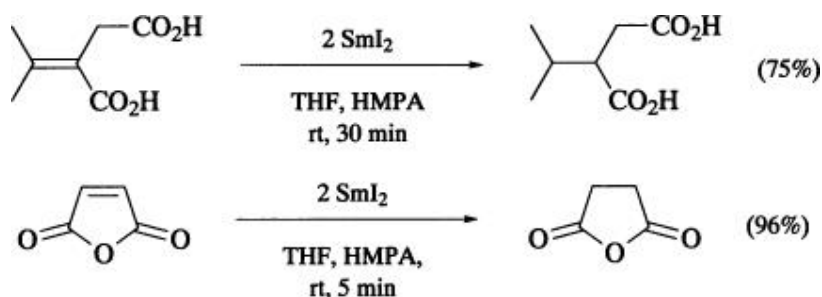
3.6. Reductive Cleavage of α -Heterosubstituted Carbonyl Compounds and Related Substrates

The most broadly applied reduction processes promoted by SmI$_2$ are the reductive cleavage reactions of various α -heterosubstituted carbonyl compounds. These reactions are general for both the types of α -heterosubstituents that may be employed, as well as for the carbonyl substrates that undergo the transformation. For example, the reductive cleavage of both α -halo ketones and α -halo esters with SmI$_2$ can be effected under extremely mild conditions, affording the dehalogenated products in virtually quantitative yields. (8, 29, 49, 53) Both bromide and chloride precursors have been utilized for the reaction, and ketones, acyclic esters, and lactone substrates have been employed successfully as well. The facility with which α -heterosubstituents are cleaved permits their selective removal in the

presence of other alkyl halides, (29) and it is likely that the process can be carried out in the presence of most other functional groups as well.
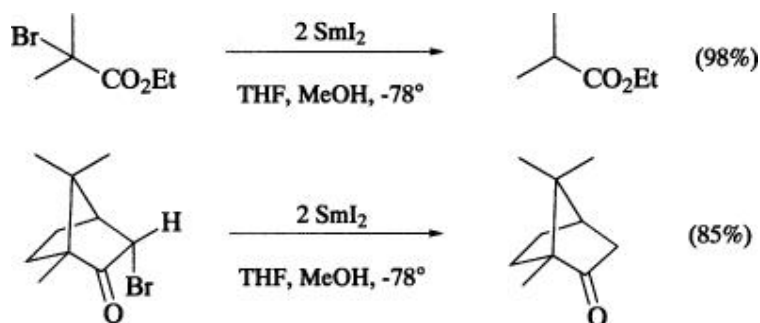
One of the unique features of SmI₂ is its ability to effect the reduction of α -hydroxy carbonyl substrates. (53-55, 57) Several different reaction protocols have been developed for this process, and it can be utilized most effectively with α -hydroxy esters and α -hydroxy lactones. Under optimized reaction conditions these transformations transpire at room temperature within hours, and yields are uniformly high. (54, 55) The reductive cleavage of α -hydroxy ketone substrates is less extensively established. (53, 57) and the best reaction protocol has perhaps not yet been developed. Nevertheless, it is obvious that this transformation can be applied to most systems, and it is likely to prove general.
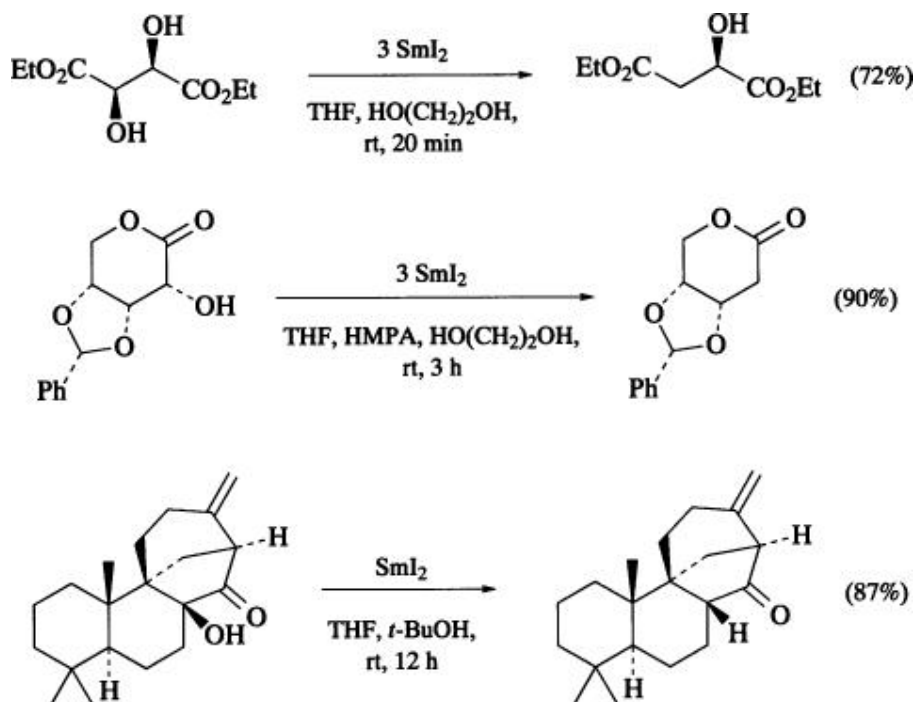
In a similar fashion, α-alkoxy, α-silyloxy, α-carboalkoxy, and α-tosyloxy carbonyl substrates are all rapidly reduced by SmI_2, and several different reaction protocols have been developed to carry out these transformations. (53-55, 58-66) With simple ketone substrates bearing such α substituents, reactions are nearly always carried out in THF at –78° and are complete within minutes, providing nearly quantitative yields of the desired products. (53, 59-64, 66) Because of the facility with which these reactions proceed, most functional groups (e.g., isolated ketones, esters, halides, and nitriles) are compatible with the extraordinarily mild reduction conditions required. α-Heterosubstituted ester and lactone substrates are more difficult to reduce, and thus reactions are typically performed at ambient temperatures in THF/HMPA. (53-55, 58) Nevertheless, the desired materials are isolated in excellent yields, and in terms of both the α-heterosubstituent and the structure of the ester, the process is highly general.
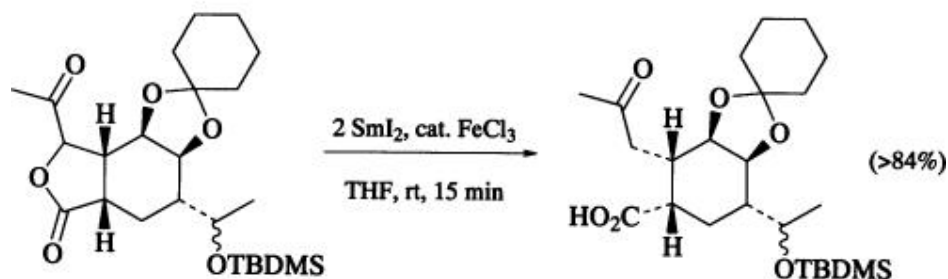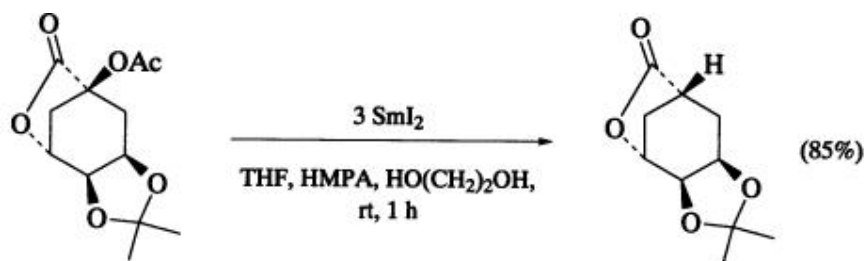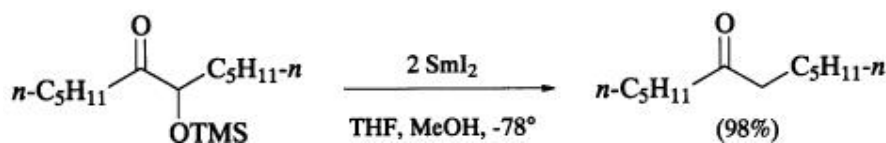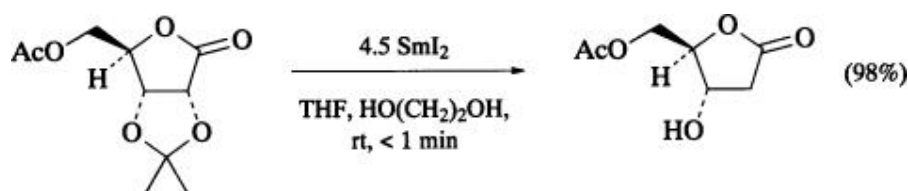
Product mixtures are often observed when α , β -diheterosubstituted lactones are reduced with SmI$_2$. (55, 65) For such substrates, the enolate that initially forms after reductive cleavage of the α -heterosubstituent may be protonated or may lead to rapid β elimination. The β elimination is usually prevented when substrates possess a β -alkoxy substituent and when reactions are carried out in THF/ethylene glycol mixtures. (55) However, the unsaturated lactones are synthesized predominantly, if not exclusively, when reductions are carried out with β -acyloxy substrates in THF alone or in THF with added pivalic acid or acetic acid. (55, 65)
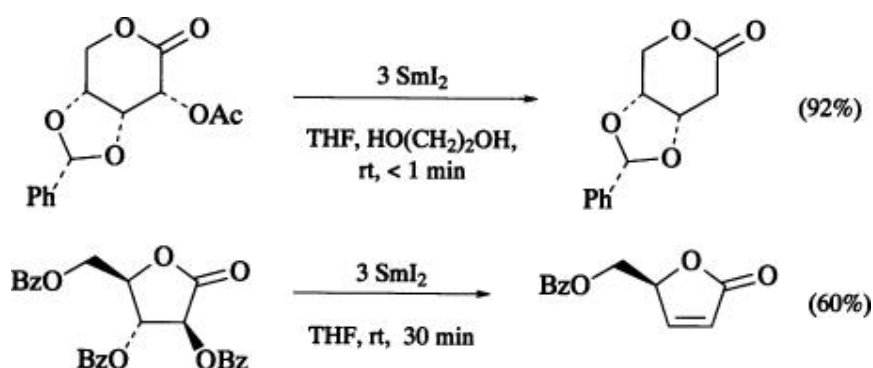
Only three α -thiosubstituted ketones have been subjected to reduction by SmI$_2$, but the α -thiophenyl ether, α -phenyl sulfoxide, and α -phenyl sulfone of cyclohexanone are all reduced in reasonable yields (64–88%). (53) This provides some confidence that the process can be generalized in more diverse systems.
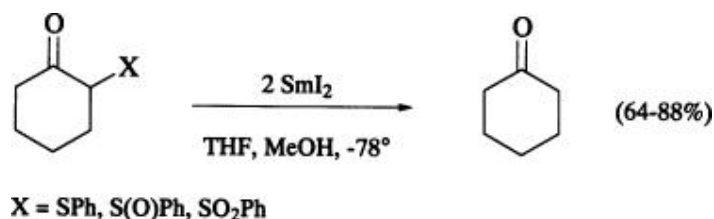
Reductive cleavage reactions of α -heterosubstituted carbonyl substrates have been extended to α , β -epoxy carbonyl substrates. (67-69) Reactions proceed rapidly at very low temperatures in THF solvent (–90°) for epoxy ketones, (69) but epoxy esters appear to react best in

THF/HMPA/*N,N*-dimethylaminoethanol solvent systems at room temperature. (67, 68) Diverse systems have been examined in which both substitution and orientation about the epoxy carbonyl centers vary, and excellent yields are realized in virtually every case. Conditions required for reduction of epoxy ketones permit most functional groups (e.g., isolated ketones, esters, halides, and amines) to be present in substrates of interest, but the situation with less easily reduced epoxy esters has not been established. Of some significance is the fact that nonracemic α , β -epoxy carbonyl substrates can be reduced to aldol-type products with little or no epimerization through a retroaldol-aldol sequence. (67-69) This provides a novel route to α -unsubstituted, enantiomerically enriched aldol products that are typically difficult to access by more traditional means.
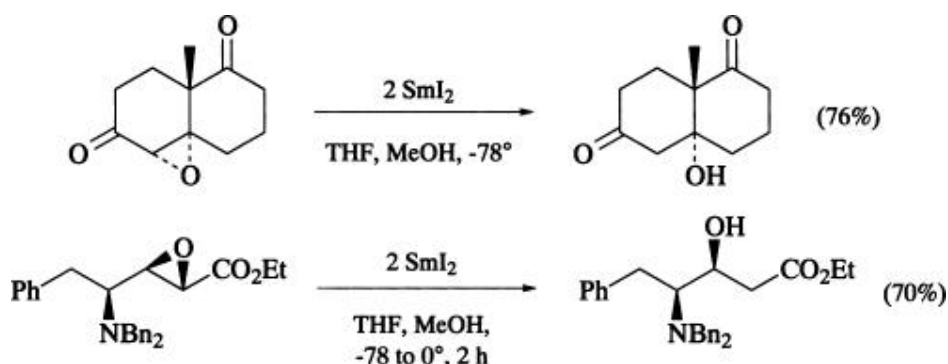
Vinylogous epoxy carbonyl compounds are also extremely reactive with SmI$_2$, providing the δ -hydroxy- β , γ -unsaturated carbonyl products in excellent yields. (67, 70) In fact, unsaturated epoxides bearing cyano groups, sulfones, phosphonates, and thioesters on the olefin work as well as ketones and esters in activating the substrate toward reduction. Unactivated epoxy alkenes undergo much slower reactions, and mixtures of diastereomeric alkenes result. (70) In virtually every successful reductive cleavage reaction, kinetic protonation of the intermediate dienolate (or analog) leads to exclusive formation of the nonconjugated olefin, and under the mild reaction conditions little, if any, conjugated material is produced. All substitution patterns about the epoxide and the alkene units in these systems work quite well, although stereoisomeric mixtures of unsaturated products are often isolated. As with the simple α , β -epoxy ketones, the use of enantiomerically enriched substrates provides a facile route to nonracemic allylic alcohols with complete retention of stereochemistry. (70)
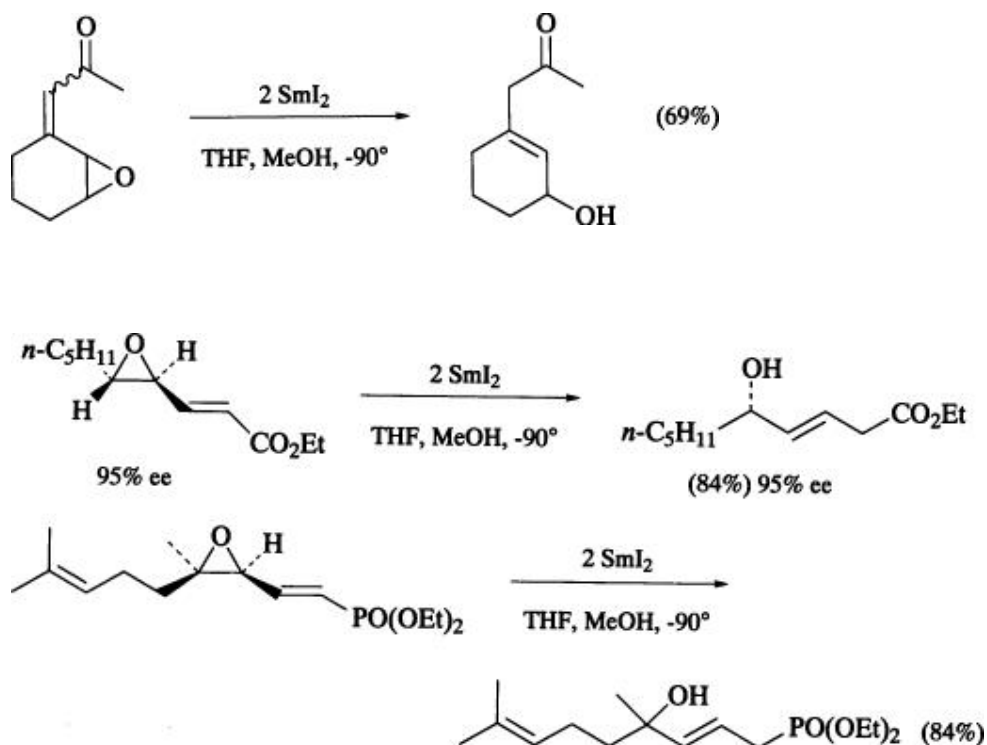
Cyanohydrin reactions carried out with lithium cyanide in the presence of diethyl phosphorocyanidate generate intermediate α -cyanophosphates. These α -heterosubstituted nitriles are efficiently reduced by SmI$_2$ in THF/methanol, providing the unsubstituted nitriles. (71) Kinetic protonation of the intermediate anion generated is evident in these substrates, because allylic and propargylic α -cyanophosphates are cleaved to provide exclusively the β , γ -unsaturated nitriles.
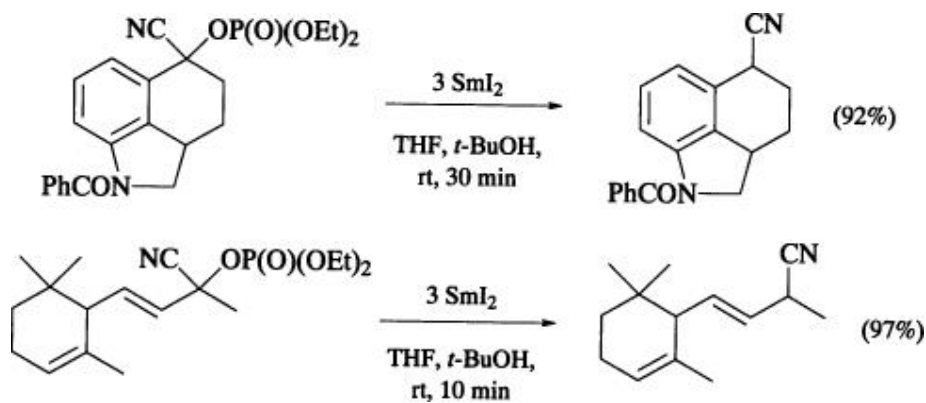
3.7. Reductive Cleavage of Cyclopropyl Ketones

Stereoelectronically controlled radical ring opening of cyclopropyl ketones by SmI$_2$-promoted reduction of acyl cyclopropanes occurs in modest to good yields. (61, 73, 74) The number of examples tested is quite limited at this point, but the process would appear to have some utility. Yields are higher when the reaction is carried out under protic conditions, in which case both the organosamarium and samarium enolate intermediates generated in the process are immediately protonated. (61, 73) Esters, alkenes, and methoxyethoxymethyl ethers can withstand the reaction conditions; however, heterosubstituents α to the carbonyl are reduced at the same or more rapid rates than the cyclopropyl ketone. (61, 73, 74)
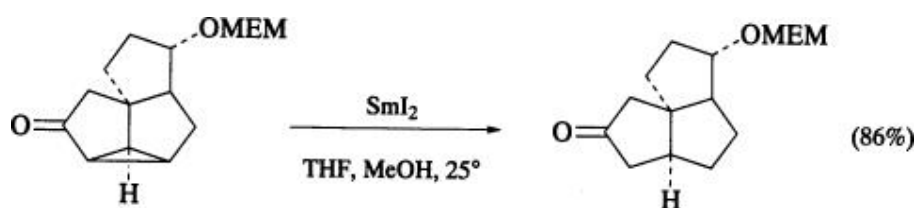
3.8. Deoxygenation Reactions

Samarium(II) iodide effects the deoxygenation of a variety of functional groups, and thus has proven itself synthetically useful for such transformations. Epoxides, for example, can be reduced effectively to the corresponding alkenes with SmI$_2$. In THF/alcohol solvent mixtures, Lewis acid promoted epoxide rearrangements compete with the deoxygenation, and as a consequence mixtures of alkene, ketone, and alcohol can result. (3) On the other hand, when reductions are carried out in HMPA/*N,N*-dimethylaminoethanol, the Lewis acid promoted epoxide ring opening is inhibited, and clean conversion to the alkenes results. (75) Although deoxygenations carried out under such conditions are completely regiospecific, they are not stereospecific. The deoxygenation thus affords both diastereomeric alkenes. These deoxygenations can be carried out in the presence of esters, but the tolerance of other functional groups has not been examined.
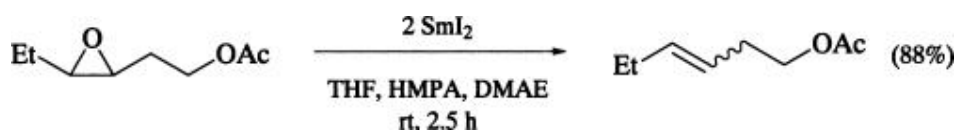
The SmI$_2$-promoted reduction of sulfoxides to sulfides is an extraordinarily rapid and facile process when carried out in THF/HMPA, (41, 76) but it is much slower in THF alone. (3) Dialkyl, diaryl, and aralkyl sulfoxides are all converted

to the corresponding sulfides in virtually quantitative yields, and the reaction can be carried out in the presence of ester and even ketone groups. (41, 76)
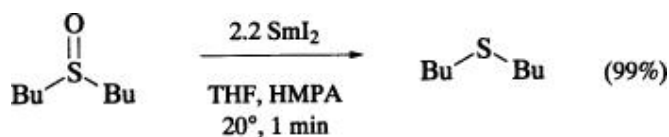
The remarkable effects of HMPA on SmI$_2$-promoted deoxygenation reactions is also demonstrated in reductions of sulfones. Thus, although studies indicate that sulfones are resistant to reduction by SmI$_2$ carried out in THF, reactions performed in THF/HMPA demonstrate that diaryl sulfones can be reduced to sulfides in nearly quantitative yields. (41, 76) Dialkyl sulfones are converted in only modest yields even with use of the THF/HMPA solvent system. For aryl alkyl sulfones, reductive cleavage may be a competitive process (see above). (33)
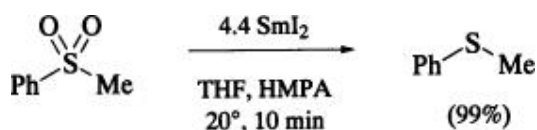
N-Oxides, triphenylphosphine oxide, and triphenylarsine oxide are all effectively deoxygenated with SmI$_2$ under relatively mild reaction conditions. (41, 49, 76) With the exception of the phosphine oxides, it does not appear that HMPA is necessary for these conversions because the reactions can be carried out efficiently in THF alone.
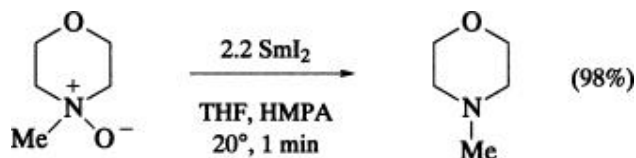
3.9. Reduction of Nitrogen-Based Functional Groups

Selective reduction of several nitrogen-based functional groups by SmI$_2$ has been examined, and useful procedures have emanated from these studies. For example, the reduction of nitro groups can be effectively controlled to provide either hydroxylamines or amines, depending upon the stoichiometry and duration of the reaction. In the presence of four equivalents of SmI$_2$ for

short periods of time (less than five minutes), both nitroalkanes and nitroaromatics are reduced to hydroxylamines in modest to excellent yields. (79) With six to eight equivalents of SmI$_2$ over a period of hours, the corresponding amines are synthesized in equally good yields. (49, 79, 80) Amines, nitriles, *tert*-butyldiphenylsilyl ethers, and some acetals generally remain intact during such reactions, but in one case an ester functionality led to a complex mixture of reaction products. (79) Both reductions to hydroxylamines and to amines would appear to be quite general in scope and of synthetic utility for a wide range of substrates.
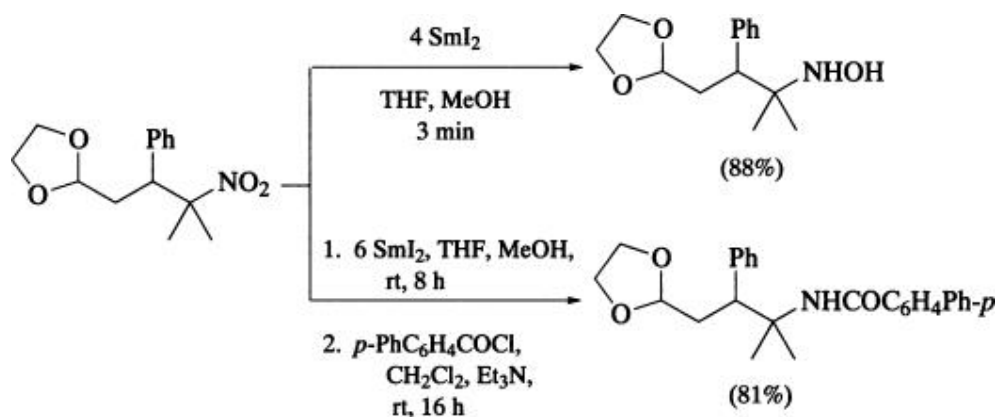
Aromatic nitriles are reportedly unreactive toward SmI$_2$ in THF/MeOH solvent mixtures, (80) but by using either acidic (aqueous phosphoric acid) or basic (aqueous potassium hydroxide) reaction conditions these substrates can be effectively converted to the corresponding amines. (46) In aromatic nitrile substrates containing an aromatic chloride, both the nitrile and the halide are reduced by SmI$_2$ under basic conditions. Reduction of the halide can be prevented, however, when acidic conditions are used. These transformations appear quite limited not only because of the lack of chemoselectivity, but also because alkyl nitriles provide only modest yields of the desired amines (46) or are completely unreactive. (80)
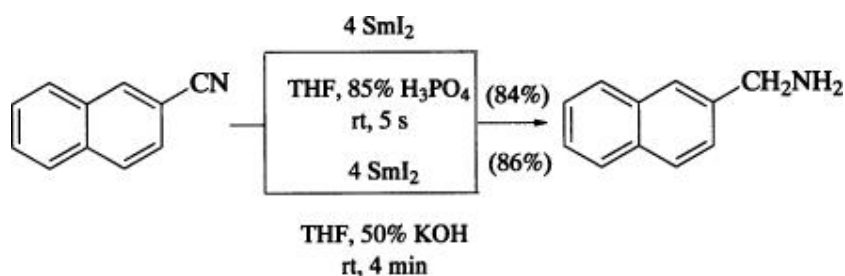
Only three imines have been employed as substrates in SmI_2-promoted reductions. (80, 81) Yields in these cases are high, but with such a limited database it is difficult to extrapolate the generality of such transformations.

$$PhCH=NPh \xrightarrow[\substack{THF,\ MeOH \\ rt,\ 24\ h}]{2.5\ SmI_2} PhCH_2NHPh \quad (80\%)$$
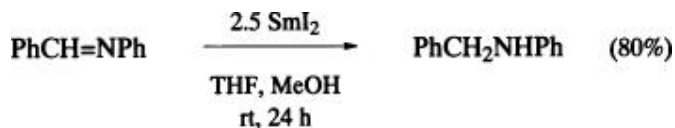
Although oximes as a general class have not been examined for their ability to take part in SmI_2-mediated reductions, (42, 80) 2-hydroximino amides of α-amino acids have been extensively investigated as precursors to dipeptides. (82) Reductions of chiral amino acid precursors to the desired amines occur in good yields, and with fair to good diastereoselectivities (1,4-asymmetric induction).
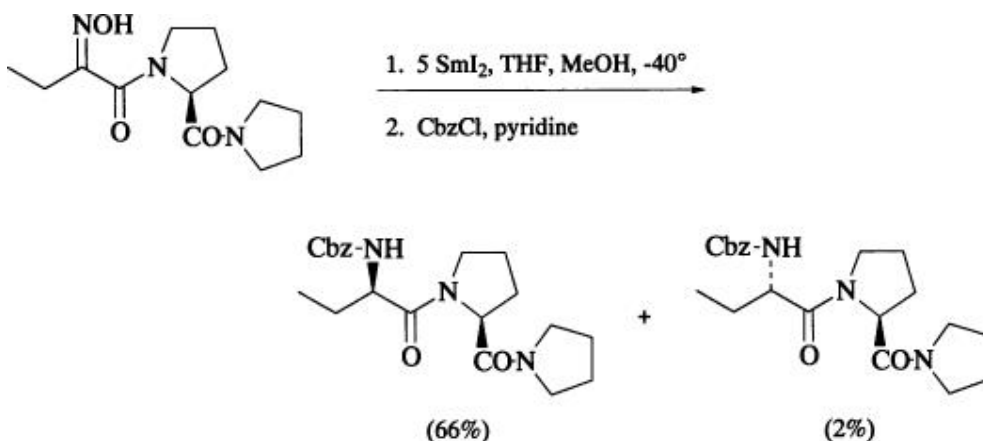
A single azo compound, azobenzene, has been reduced by SmI_2. With two equivalents of SmI_2, diphenylhydrazine is isolated, (49) but with eight equivalents of SmI_2 the hydrazine intermediate initially generated is reductively cleaved in modest yield to provide two equivalents of aniline. (80)

Although hydrazines have not been generally examined for their susceptibility to SmI_2-promoted reductive cleavage, indications are that such reactions are slow (four days at ambient temperature) and rather inefficient. (80) In contrast, N-acylhydrazines are rather good substrates for this reaction. (84) The reductive cleavage takes place within 30 minutes and provides acceptable

yields of the desired amines. This transformation is useful for the cleavage of enantiomerically enriched *N*-acylhydrazines, affording optically active amines.
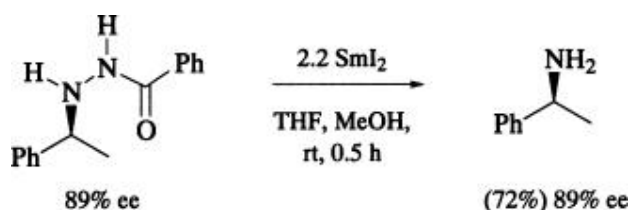
3.10. Reduction of Miscellaneous Functional Groups

Various other functional groups, some in very limited samplings, have been subjected to reduction by SmI_2. In addition, SmI_2 has been utilized as a stoichiometric reductant in processes catalyzed by transition metals. A number of these transformations are outlined in this section.

Peroxides are quite efficiently reduced by SmI_2 in THF. (85, 86) The process has been utilized to release the diol functionality in bicyclic peroxides. The reaction can be carried out in the presence of alcohols, alkenes, and primary alkyl tosylates.
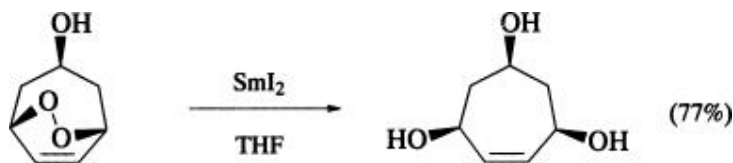
The heteroatom–heteroatom bond in isoxazoles can also be cleaved efficiently by SmI_2. (25) Although esters survive the process intact, aldehydes and benzylic halides located off the isoxazole ring appear to be reduced in preference to the nitrogen-oxygen bond.
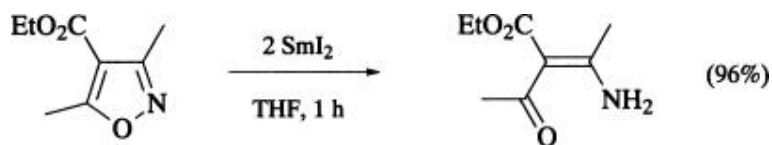
A reasonably broad array of chloro phosphine oxides and chloro phosphine sulfides have been subjected to reduction with SmI_2. (87) Reaction of the

chloride proceeds smoothly in THF at room temperature to provide the corresponding P-H compound, without interference from deoxygenation of the phosphorus–oxygen bond in the final product. In some cases, reductive dimerization is a minor side reaction. Phosphine oxides are generally reduced more quickly than their phosphine sulfide analogs, and increasing the number of alkoxy groups attached to phosphorus dramatically increases reaction times required for complete reduction and markedly decreases the yield of the desired products as well. Somewhat unexpectedly, the reduction occurs with substantial loss of stereochemistry at an asymmetric phosphorus center. Consequently, it does not seem likely that the process will be useful for the reduction of enantiomerically enriched starting materials.
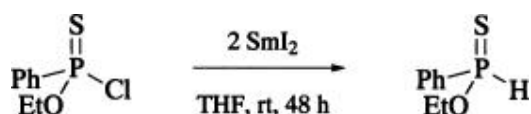
Allylic acetates are reduced to alkenes in high yields with SmI_2 and 2-propanol in the presence of a catalytic amount of palladium(0) catalyst. (88) Unfortunately, mixtures of regioisomeric and stereoisomeric alkenes are generated in these reactions, detracting from the synthetic utility of the process.
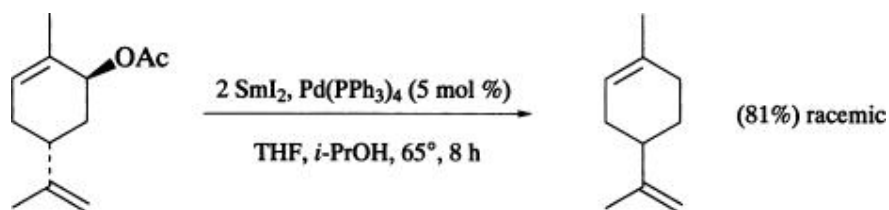
In contrast to the palladium(0)-catalyzed reduction of allylic acetates, conditions for reductive cleavage of propargyl γ -lactones have been developed to the point whereby some control for the synthesis of allenes can be achieved. (89) Thus tertiary propargylic carboxylates usually provide allenes exclusively in the reaction with SmI_2-palladium(0). Secondary carboxylates and γ -lactones provide mixtures of allene and alkyne products, with allenes typically predominating. On the other hand, primary carboxylates often lead to product mixtures in which the alkyne products predominate.

Reaction scheme:

$n\text{-}C_8H_{17}C{\equiv}C$ (attached to furanone lactone ring with =O)

1. 2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%),
   THF, i-PrCHOHPr-i,
   -40°, 2 h

2. CH$_2$N$_2$

$$\underset{H}{\overset{n\text{-}C_8H_{17}}{\diagdown}}C{=}C{=}C\underset{(CH_2)_2CO_2Me}{\overset{H}{\diagup}}$$
(66%)
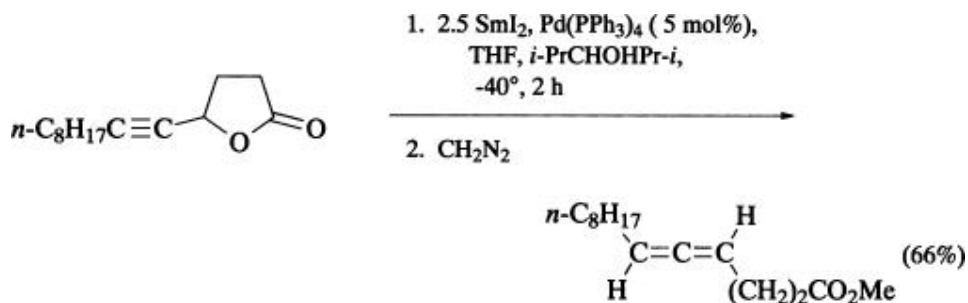
Some success has been achieved in accomplishing selective reduction reactions of alkynes in which SmI$_2$ is used as the stoichiometric reductant in THF, and cobalt, nickel, or iron salts are employed as catalysts. (91) The method has been touted as a means to prevent overreduction of the *cis*-alkene intermediates that commonly plague transition metal catalyzed hydrogenation reactions. Under optimized reaction conditions, diphenylacetylene is selectively reduced to *cis*-stilbene in 99% yield, and the selectivity for this product with respect to *trans*-stilbene and 1,2-diphenylethane is >99:1. In two different alkyne substrates, reasonably high selectivity for the *E* isomer is observed when HMPA is added to the reaction mixture. Only a limited number of substrates have been examined in these hydrogenation studies, and the one functionalized molecule studied (a propargyl alcohol) leads to a mixture of alkene, allene, and alkyne. Thus although the method may be of use for hydrocarbon substrates, considerable development will be required before it can be viewed as a general method for the stereoselective reduction of alkynes.

PhC≡CPh

2 SmI$_2$, CoCl$_2$•4 PPh$_3$ (3 mol%)
———————————————————
THF, AcOH, rt, 30 min

(cis-stilbene: Ph, Ph on top; H, H on bottom) (>99%)

PhC≡CPh

2 SmI$_2$, NiCl$_2$•4 PPh$_3$ (3 mol%)
———————————————————
THF, HMPA, i-PrOH, rt, 30 min

(trans-stilbene: Ph, H on top; H, Ph on bottom) (81%)
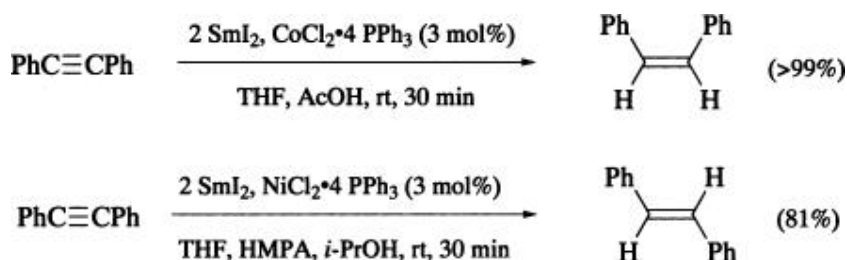
4. Comparison with Other Methods

Given the very fundamental nature of the processes outlined in this chapter and the numerous other methods that have been developed to effect these same transformations, it would be impossible to compare SmI_2 with every other reducing agent for each individual class of compounds in a succinct manner. However, an attempt is made to compare some of the more useful reductions achieved by SmI_2 to those of other more popular methods.

4.1. Reduction of Organic Halides, Sulfonates, and Sulfones

There are scores of reducing agents, including many low-valent metals or metal complexes, which have proven effective for the reduction of organic halides. As might be expected, there are significant areas where SmI_2 is effective and those where other reducing agents certainly surpass its ability. Samarium(II) iodide cannot be employed to reduce allylic halides or benzylic halides, and chiral alkyl halides will undergo nonstereospecific reduction. However, SmI_2 is a versatile reagent that can be utilized to reduce both sp^3 (primary, secondary, and tertiary) and sp^2-hybridized organic halides with reasonable efficiency. Perhaps one of the most useful characteristics of the reagent is that these reductions can be performed in the presence of unprotected alcohols and, in general, esters. This, plus the ability to vary the solvent to increase at will the reactivity and selectivity of the reducing agent, makes it likely that SmI_2 can be utilized for reduction of organic halides in the presence of many other functional groups as well.

The direct reduction of alkyl sulfonates to alkanes by SmI_2 appears promising, but because only a single example has been examined (2) extrapolation to other systems is premature. Samarium(II) iodide may not be as general or as selective as the more traditional hydride reducing agents in this respect. (118)

Samarium(II) iodide has shown tremendous promise in the reduction of α , β -unsaturated sulfones to the corresponding alkenes without significant interference from conjugate reduction of the double bond. (32, 33) In this regard it is a considerable improvement over other reducing agents, including sodium amalgam and sodium dithionite. (118) The reduction of alkyl aryl sulfones is also competitive with dissolving metal reductions and sodium amalgam in alcohol as a means to cleave the sulfone moiety, although the scope of the reaction with regard to the tolerance of various functional groups is of some concern (33) and reduction to sulfides may also compete. (41, 76)

4.2. Reductive Elimination/Fragmentation Reactions

The SmI_2-mediated reductive elimination of appropriately functionalized 1,2-disubstituted substrates is competitive with many other methods previously developed for the same transformation. (118) Drawbacks to the SmI_2 route are

that it is not stereospecific, although in some cases it is more diastereoselective than sodium-promoted processes. ([34]) It may also be more tolerant of different functional groups (e.g., unprotected alcohols, esters) ([31], [35]) than other methods. Furthermore, in direct comparison with sodium amalgam, SmI_2 has displayed enhanced efficiency for the reduction of β-hydroxy sulfones, ([37]) and thus it may be used as an alternative reagent in the conventional Julia sequence for the synthesis of alkenes.

A unique process that deserves further study is the fragmentation of γ-halo carbonyl substrates by SmI_2. ([27], [28], [38], [39]) Although the full scope of this reaction is unknown at the present time, this distinctive transformation cannot be effected by other reductants like tri-*n*-butyltin hydride/azobis(isobutyronitrile) or zinc in acetic acid. ([27]) The SmI_2 promoted process thus certainly deserves further study.

4.3. Reduction of Aldehydes and Ketones

As a general rule, SmI_2 will not compete with the numerous hydride reducing agents that have been developed for the chemoselective and stereoselective reduction of acyclic aldehydes and ketones. ([118]) However, in limited cases it may provide advantages over other single electron transfer agents that might normally be utilized for reductions. Samarium(II) iodide is generally more chemoselective than these other reagents, and in reductions of chiral cyclohexanones, higher selectivity for the equatorial alcohol isomer may be expected under optimized conditions using SmI_2. ([41], [45]) This latter aspect of the chemistry bears further exploration.

4.4. Reduction of Carboxylic Acids and Their Derivatives

Although conditions for the SmI_2-mediated reduction of carboxylic acids and various derivatives have been developed, by and large these methods are not particularly useful for the synthesis of alcohols. ([42], [46], [48]) In general the reaction conditions are not amenable to the incorporation of other functionality in substrates of interest, and for the most part the method is restricted to aromatic carboxylic acids and carboxylic acid derivatives. Consquently, it is unlikely that SmI_2-promoted reductions of carboxylic acids and their derivatives will compete with those of more established, general methods. ([118])

4.5. Reduction of Conjugated Carbonyl Substrates

Although SmI_2 provides mixtures of products in the reduction of conjugated aldehydes and ketones, it has proven to be quite general and selective for the conjugate reduction of α, β-unsaturated carboxylic acids and their derivatives (esters and amides). ([50], [51]) Perhaps most useful among these is the reduction of the unsaturated carboxylic acids themselves, ([50]) because relatively few general methods for this conversion exist. ([118]) This reactivity pattern is useful for the direct reduction of unsaturated carboxylic acids because it circumvents synthetic designs requiring conjugate reduction

through an ester where inefficient protection–deprotection schemes are necessitated.

4.6. Reductive Cleavage of α -Heterosubstituted Carbonyl Compounds and Related Substrates

The reduction of α -heterosubstituted carbonyl compounds and related substrates has long been recognized as a useful synthetic transformation, and many different reagents have been developed to realize this conversion. (53, 118) Among the more widely utilized methods are zinc metal and chromium(II) ion-induced reductions, which require the use of acidic media for extended reaction times, often at elevated temperatures. Only a limited array of functionality can be tolerated under such conditions. Other methods (e.g., dissolving metal reductions, phosphorus-based or silicon-based reducing agents) either lack chemoselectivity or have not been thoroughly investigated to ascertain the scope of their capabilities. Thus SmI_2 appears to be among the more versatile and useful of the reagents available for this transformation.

Of notable interest is the ability of SmI_2 to cleave α -hydroxy carbonyl substrates by a reductive process. (53-57, 118) Because it is one of only a handful of reagents for this particular transformation and because the SmI_2-mediated method appears to be mechanistically distinct from the others, it is likely to find considerable use in this transformation.

Likewise the reductive cleavage of α , β -epoxy ketones and α , β -epoxy esters with SmI_2 is a highly useful tool for the construction of aldol-type products. (67-69) Although several other methods have been developed for the same process, (69, 118) SmI_2 is certainly competitive, if not superior, to these with respect to yields, versatility, and selectivity.

Among the reagents reported to cleave vinyloxiranes in a reductive process, SmI_2 may be unique in terms of its specificity and overall capabilities. (67, 72, 118) The observed regioselectivity of the final products, along with the generality of the process for a host of activated substrates, combine to make SmI_2 the reagent of choice for such conversions.

Reductive cleavage of cyano phosphates with SmI_2 provides a facile entry to the corresponding nitriles. (71, 72) Previous attempts at this and related conversions with other reducing agents resulted either in complete failure or in methods with rather severe limitations. (72, 119) Thus SmI_2 fills a useful niche, permitting the rather direct formation of one-carbon homologated nitriles from aldehyde and ketone precursors.

4.7. Reductive Cleavage of Cyclopropyl Ketones

As a general rule the reductive cleavage of cyclopropyl ketones has seen little development as a synthetic method for the synthesis of open-chain ketones.

(74) Nevertheless, of the few strategies that have been developed for such processes (e.g., photochemical and radical methods), conversions mediated by SmI$_2$ would appear to be competitive based upon the limited number of substrates examined.

4.8. Deoxygenation Reactions

Although SmI$_2$ is reasonably effective for the deoxygenation of epoxides to produce the corresponding alkenes, (3, 75) the lack of stereospecificity engendered in this process makes it of limited utility relative to the numerous methods exhibiting this feature. (118)

A number of methods have been developed for the deoxygenation of sulfoxides and *N*-oxides, but only a handful of methods are available for the deoxygenation of sulfones and phosphorus oxides. Consequently, the ability of SmI$_2$ to deoxygenate these functional groups clearly represents a potentially significant procedure. (75) If the limited number of substrates subjected to these deoxygenations could be expanded, providing a better idea of the scope of the reaction, SmI$_2$ could well prove to be the reagent of choice for such operations.

4.9. Reduction of Nitrogen-Based Functional Groups

There are notable areas of success in SmI$_2$-mediated reductions of functional groups involving nitrogen. One example is the reduction of nitro groups, wherein appropriate control of stoichiometry and reaction conditions permits the isolation of either hydroxylamines or amines. (79) This method is fully comparable to alternative procedures for other representative syntheses of alkyl hydroxylamines and alkyl amines from nitro precursors.

On the other hand, the reduction of aromatic nitriles to amines must be performed under rather harsh (acidic or basic) reaction conditions. (46) Consequently, there is little tolerance for other functionality. Furthermore, the method is not applicable to alkyl nitriles, and thus the countless other reagents that can be utilized for the synthesis of amines from nitriles are probably best used for this transformation. (118)

Only three imines have been reduced to the corresponding amines with SmI$_2$, (80, 81) and with such a limited database it is risky to speculate on the scope of this reaction in relation to other methods for the same transformation.

The enhanced chemoselectivity of SmI$_2$ relative to that of lithium aluminum hydride, sodium borohydride, and borane has made it an attractive alternative to these more traditional reagents for the diastereoselective reduction of 2-hydroximino amides. (82) It is likely that with further development more uses of the reductant with similar substrates will be possible.

Although hydrazines in general react slowly with SmI$_2$, acyl hydrazines are excellent substrates for the reagent. (84) Because of the lack of studies wherein functional group compatibility and other factors are available, direct comparison with other potential reducing agents is difficult. However, SmI$_2$ appears to be an excellent reagent for this type of reductive cleavage reaction.

4.10. Reduction of Miscellaneous Functional Groups

Limited data are available on the reduction of other functional groups with SmI$_2$. In reactions with bicyclic peroxides, the reagent appears comparable to zinc/acetic acid for the reductive cleavage, and may hold an advantage in systems with acid-sensitive arrays of functionality. (85)

The reduction of halo phosphine oxides and halo phosphine sulfides holds some promise as a general method for the synthesis of phosphine oxides and phosphine sulfides, but unfortunately will not compete with routes that provide these materials in enantiomerically pure form. (87)

Similarly, the palladium(0)-catalyzed reductive cleavage of allylic acetates (88) and propargyl acetates (89) is somewhat limited in scope given the mixtures of products that are typically generated. Nevertheless, the SmI$_2$-mediated process would appear comparable in many respects to those transformations using ammonium formate, borohydride, trialkyltin hydride, and other reducing reagents.

There is some promise for the use of transition metal catalyzed hydrogenations of alkynes to stereodefined alkenes using SmI$_2$ as a stoichiometric reductant. (91) Although innumerable other catalysts and synthetic methods have been developed for this transformation, (118) the method using SmI$_2$ has demonstrable selectivity for alkene formation, and under suitable reaction conditions both the *cis*- and *trans*-olefinic isomers can be generated with considerable selectivity. However, substantial development of the method will be required before it can be considered a general method for the selective hydrogenation of alkynes to alkenes.

5. Experimental Conditions

Pure samarium(II) iodide is a deep blue, air-sensitive compound. Consequently, all manipulations involving this material must be carried out in an inert atmosphere (e.g., argon or nitrogen). However, SmI_2 is not so air-sensitive that glovebox techniques or even Schlenk-type glassware must be utilized, and thus normal benchtop techniques for the handling of air-sensitive materials suffice. Somewhat surprisingly, SmI_2 does not react appreciably with water over several hours, and is clearly even less reactive toward other protic solvents (e.g., alcohols). Consequently, these may be added as cosolvents to reactions of SmI_2 in the presence of various organic substrates with little or no detrimental effect to the reducing agent, and in fact may be necessary for the efficacy of the reactions themselves.

Most often solutions of SmI_2 in THF are utilized to effect the desired transformations. Although solutions of SmI_2 in THF are commercially available, it is very easy to prepare the reagent in situ. As far as can be determined, yields in the published preparations are virtually quantitative and thus these methods provide a rapid and convenient source of the reducing agent. Perhaps the most convenient method is the oxidation of samarium metal with diiodomethane. (6) The oxidant in this case is a liquid that can be injected into a rapidly stirring slurry of samarium metal in THF. Another efficient method for the preparation of SmI_2 employs 1,2-diiodoethane as the oxidant. (3-5) The only drawbacks to this procedure are that the oxidant must be purified to some extent before use, and the fact that the oxidant is a solid. This makes its introduction to the slurry of samarium metal somewhat less convenient than the diiodomethane route. The other methods for preparation of SmI_2 (using iodine (8) or trimethylsilyl chloride/sodium iodide (9) as the oxidant) suffer from either extremely long reaction times or require less useful solvent systems and are therefore much less generally utilized. Samarium(II) iodide can be stored as a solution in THF for reasonably long periods of time, particularly when it is stabilized by a small amount of samarium metal. (3-5) Alternatively, the solvent may be removed altogether, providing $SmI_2(THF)_n$ powder. (3-5)

The SmI_2 prepared by these methods can be characterized in solution in several different ways, including techniques involving absorption spectroscopy, magnetic susceptibility measurements, titration of samarium ions with *N,N,N¢,N¢*-tetramethylethylenediamine, potentiometric titrations of iodide ion, and acidometric titration and reaction of iodine, which measures the reductive capability of the solutions. (3, 4) The last method serves for the rapid and convenient determination of the molar concentration of SmI_2 in, for example, THF solution.

Because SmI_2 is a one-electron reducing agent, synthetic conversions that

require a net two-electron reduction necessitate the addition of two molar equivalents of SmI_2. Similarly, four-electron conversions require four molar equivalents, and so forth. In published experimental procedures it is not unusual to find that an excess of SmI_2 is used in certain difficult conversions, although in general it is sufficient to utilize a stoichiometric amount of the reagent or a slight excess to effect complete reaction.

The vast majority of reactions employing SmI_2 are carried out in THF, and because SmI_2 is conveniently generated in this solvent this makes the in situ preparations particularly useful. However, there is a dramatic solvent effect on the ability of SmI_2 to reduce various functional groups. (24, 41) In general polar aprotic solvents such as acetonitrile, *N,N¢*-dimethylpropyleneurea, tetramethylurea, *N,N*-dimethylformamide, *N,N*-dimethylacetamide, 1-methyl-2-pyrrolidinone, *N,N,N¢,N¢*-tetramethylethylenediamine, and in particular, HMPA greatly enhance the reducing power of SmI_2. The precise reason for this dramatic activation is unknown, but could be attributed to deaggregation of SmI_2 (the solution structure of SmI_2 in THF is unknown) or *f*-orbital perturbation owing to ligand field effects in the presence of the strong donor ligands, raising the energy of the highest occupied molecular orbital (electron-donating orbital) and thereby increasing the samarium(II)/samarium(III) cell electromotive force. (120) In fact, a combination of these two effects might be responsible. Whatever the reason, reports in the literature reveal that the reduction potentials of several lanthanides are strongly dependent on the associated ligand(s). (121-124) As an example, a negative shift of 0.86 V in the reduction potential of europium(III) is observed upon addition of 5% dimethyl sulfoxide by volume as cosolvent in propylene carbonate. (124, 125) Similar effects are observed for the reduction potentials of samarium(III) and ytterbium(III).

Some explanation for the unique nature of the interaction of HMPA with lanthanide ions and its effect on the reduction potential may be derived from the X-ray crystal structures of various lanthanide(III) ion–HMPA complexes. Crystal structures of such complexes reveal that in all cases the HMPA molecules are coordinated via their oxygen atoms. For example, reaction of ytterbium(III) chloride with excess HMPA in THF produces $YbCl_3(HMPA)_3$ in quantitative yield. (126) The X-ray crystal structure determination reveals that HMPA molecules occupy the two axial positions and an equatorial position in the distorted octahedron of this complex. Remarkably, further studies reveal that the maximum number of HMPA ligands able to bind to any of the lanthanide(III) perchlorates is six. (127) Thus, in all cases (Ln = La – Lu), treatment of $LnCl_3$ with three equivalents of silver perchlorate followed by addition of excess HMPA results in the isolation of crystals that correspond to complexes with the stoichiometry $[Ln(HMPA)_6](ClO_4)_3$. These results are in stark contrast to studies using dimethyl sulfoxide or *N,N*-dimethylacetamide

complexes, in which the number of ligands decreases with decreasing ionic radius of the lanthanides. (128, 129) The singular ability of HMPA to activate Sm(II) may thus be attributed to its unique binding and stabilization of Sm(III) cations generated as a result of electron transfer.

The only drawback to the unique effect of HMPA activation of SmI$_2$ is that HMPA is a potent carcinogen, and thus must be handled with extreme care. However, unlike many of their main group and transition metal counterparts, inorganic lanthanide complexes themselves are generally classified as nontoxic when introduced orally, and only modestly toxic when injected. (18) Although toxicity may vary to some extent based on the ligands attached to the metal, in nearly all cases the lanthanide complexes are converted to hydroxides immediately upon ingestion, and thus are believed to be poorly absorbed in the digestive tract.

Another important factor in the efficacy of many SmI$_2$-promoted reductions is the presence of a proton source in the reaction mixture. Often, yields of the desired products are greatly enhanced when reactive intermediates such as enolates, alkoxides, or organosamariums are quenched immediately by in situ proton sources such as water, aliphatic alcohols, carboxylic acids, glycols, or amino alcohols in the reaction mixture. Furthermore, in some cases the presence or absence of a proton source may be the major determinant in mechanistic pathways followed by reactive intermediates. For example, treatment of aldehydes and ketones with SmI$_2$ in the presence of protic solvents generally leads to clean reduction to the corresponding alcohols. In the absence of such additives, ketyl dimerization occurs, leading to the efficient production of pinacols. (18, 22, 100, 101)

Iron(III) salts have been found to catalyze various carbon–carbon bond-forming reactions promoted by SmI$_2$ (e.g., Barbier-type reactions). (3, 18, 21, 22) However, such catalysts have only rarely been utilized for selective reduction reactions. Additionally, some highly specific reactions have been developed in which SmI$_2$ serves as a stoichiometric reductant for processes promoted by palladium(0) (88-90) or transition metal catalysts. (91) As a general rule, though, the potential role of catalysts in SmI$_2$-mediated reactions has not been explored.

Finally, workup procedures for SmI$_2$-promoted reactions may vary considerably depending on the stability of the desired products. If the organic products of the SmI$_2$-promoted reactions are stable to aqueous acids, aqueous hydrochloric acid can be utilized to quench the reaction. With this protocol the samarium salts generated as a result of the reaction are water soluble and are easily removed in the aqueous layer. For acid-sensitive organic products, mildly basic solutions or pH 7-8 buffers may be utilized to quench the reaction

mixtures. In such cases the samarium salts are typically insoluble, but do form a suspension in the aqueous phase from which the desired organic product can be extracted by standard experimental procedures.

6. Experimental Procedures

$$Sm \ + \ ICH_2CH_2I \ \longrightarrow \ SmI_2 \ + \ CH_2=CH_2$$

6.1.1.1. Samarium(II) Iodide (Preparation of the Reducing Agent from Samarium Metal Using 1,2-Diiodoethane as the Oxidant) (3-5)
The synthesis of samarium(II) iodide was performed under a nitrogen atmosphere. In a standard procedure, 1.504 g (10 mmol) of samarium powder was placed in a Schlenk tube. A 50-mL tetrahydrofuran solution of 1,2-diiodoethane (1.410 g, 5 mmol) was slowly added. The reactants were vigorously stirred with a magnetic stirrer. After a short induction period, a deep blue-green color appeared. After one hour, a 0.1 M solution of samarium(II) iodide in tetrahydrofuran was obtained. Titrations showed that the yield of the reaction was quantitative. Such solutions can be stored for long periods of time without a decrease in Sm(II) concentration if kept under an inert atmosphere and in the presence of a small amount of samarium metal.

$$Sm \ + \ ICH_2I \ \longrightarrow \ SmI_2 \ + \ 0.5 \ CH_2=CH_2$$

6.1.1.2. Samarium(II) Iodide (Preparation of the Reducing Agent from Samarium Metal Using Diiodomethane as the Oxidant) (6)
Samarium metal powder (0.15 g, 1 mmol) was added under a flow of argon to an oven-dried roundbottomed flask containing a magnetic stirring bar and a septum inlet. The flask and the samarium metal had been flame-dried and cooled under a stream of argon. Tetrahydrofuran (10 mL) was added. The vigorously stirred slurry of samarium metal and tetrahydrofuran was cooled to 0°, and neat diiodomethane (0.228 g, 0.85 mmol) was added. The resulting green slurry was stirred at 0° for 15 minutes, then allowed to warm to room temperature and vigorously stirred for an additional hour. The resulting solution of samarium(II) iodide was a deep blue color.

$$Sm \ + \ I_2 \ \longrightarrow \ SmI_2$$

6.1.1.3. Samarium(II) Iodide (Preparation of the Reducing Agent from Samarium Metal Using Iodine as the Oxidant) (7)

Iodine (5.1 g, 20 mmol) was added with stirring to a mixture of 40-mesh samarium powder (3.3 g, 22 mmol) and dry tetrahydrofuran (200 mL) under argon. The initial mildly exothermic reaction subsided in several minutes to form a yellow suspension of SmI_3. The mixture was then heated at reflux with stirring. The color of the suspension gradually turned from yellow to green and finally to an intense blue-green. Heating at reflux overnight provided a 0.1 M solution of SmI_2.

$$Sm + 2\,Me_3SiCl + 2\,NaI \longrightarrow SmI_2 + Me_3SiSiMe_3 + 2\,NaCl$$

6.1.1.4. Samarium(II) Iodide (Preparation of a Samarium Iodide Equivalent in Acetonitrile Solvent) (8)

To a solution of sodium iodide (0.9 g, 6 mmol) in dry acetonitrile (20 mL) was added chlorotrimethylsilane (0.76 mL, 6 mmol) followed by samarium powder (2 mmol) under a nitrogen atmosphere at room temperature. The samarium gradually reacted and the color of the solution turned to deep green, indicating the production of a samarium(II) iodide equivalent.

6.1.1.5. 1-Phenyldec-1-yne (Generation of Alkylidenecarbenes from 1,1-Dibromoalk-1-enes) (23)

A solution of 1,2-diiodoethane (3.55 mmol) in benzene (32 mL) **[Caution: Potent Carcinogen]** and hexamethylphosphoric triamide (3.6 mL) **[Caution: Potent Carcinogen]** was added to 40-mesh samarium powder (5.32 mmol) under nitrogen. Gentle heating was required to initiate the reaction. The reaction mixture was stirred for 5 days at room temperature to afford a purple solution of samarium(II) iodide in benzene–hexamethylphosphoric triamide **[Caution: Potent Carcinogen]** . The concentration of SmI_2 was determined by titration using iodine under nitrogen according to the method of Imamoto and Ono. (8) To the purple solution of samarium(II) iodide thus generated (4 mL of a 0.094 mol dm^{-3} solution, 0.38 mmol) was added a solution of 1,1-dibromo-2-phenyldec-1-ene in benzene **[Caution: Potent Carcinogen]** at room temperature under nitrogen. After stirring for 10 minutes, the mixture was quenched with dilute hydrochloric acid, and then extracted with diethyl ether. The organic layer was dried and concentrated to afford a crude mixture that was purified by preparative TLC to afford the title compound in 67% yield, along with 8% of 2-phenyl-1-decene.
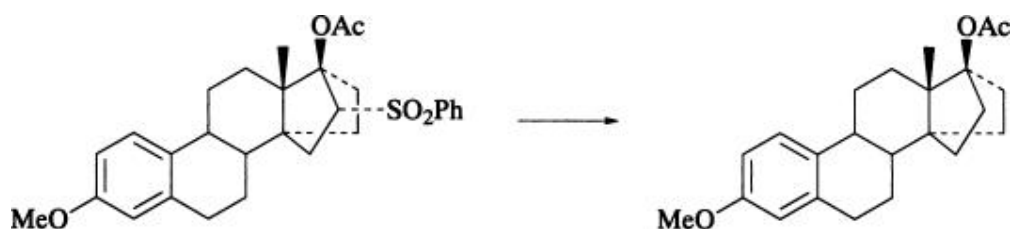
6.1.1.6. 3-Methoxy-14,21-cyclo-19-norpregna-1,3,5(10)-trien-17-ol Acetate (Reductive Desulfonylation Reactions) (33)

Under an atmosphere of argon, 0.494 g of (16 α ,17 α)-3-methoxy-16-(phenylsulfonyl)-14,21-cyclo-19-n orpregna-1-3,5(10)-trien-17-ol acetate was dissolved in 50 mL of a freshly prepared solution of samarium(II) iodide–tetrahydrofuran (approximately 0.1 M). This mixture was cooled to –20° under stirring and hexamethylphosphoric triamide (4 mL) **[Caution: Potent Carcinogen]** was added dropwise by syringe, whereupon the color of the solution changed from blue to purple. After 90 minutes, the reaction was terminated with aqueous ammonium chloride (5 mL). Most of the tetrahydrofuran was removed in vacuo by rotary evaporation. The product was precipitated by addition of cold hydrochloric acid (0.5 M) and isolated by suction–filtration. The solid residue was dissolved in ethyl acetate, and the resulting organic phase was washed with aqueous sodium thiosulfate solution, followed by brine, and then dried over anhydrous sodium sulfate. Chromatography of the crude product on silica gel (hexane-ethyl acetate, 9:1) provided 0.308 g (87%) of the title compound, mp 119–120° (acetone-hexane).
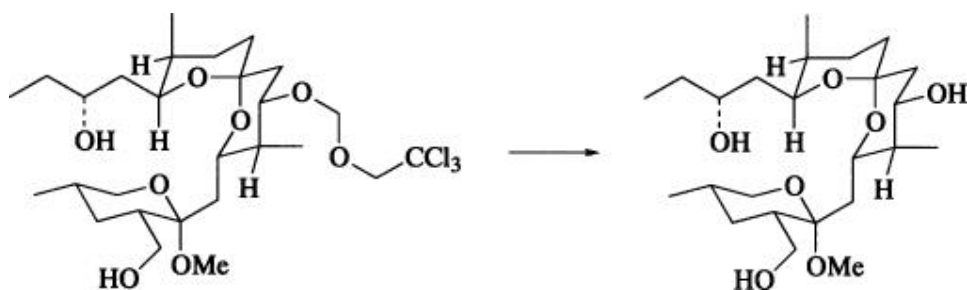
6.1.1.7. [6R-(6 α [2S(R*),3S*],8 β (2S*,3S*,5S*),9 β ,10 β)]- α -Ethyl-10-hydroxy-3,9-dimethyl-8-[tetrahydro-3-(hydroxymethyl)-2-methoxy-5-methyl-2H-pyran-2-yl]-1,7-dioxaspiro[5.5]undecane-2-ethanol [Deprotection of (2,2,2-Trichloroethoxy)methoxy Ethers by Reductive β -Elimination] (35)*

[6R-(6 α [2S*(R*),3S*],8 β (2S*,3S*,5S*),9 β ,10 β)]-α-Ethyl-10-[(2,2,2-trichloroethoxy) methoxy]-3,9-dimethyl-8-[tetrahydro-3-(hydroxymethyl)-2-methoxy-5-methyl-2H-pyran-2-yl]-1,7-dioxaspiro[5.5]undecane-2-ethanol (6.2 mg, 10.2 µmol) was azeotropically dried with two 1-mL portions of toluene and was subsequently dissolved in 0.8 mL of tetrahydrofuran. Freshly prepared samarium(II) iodide (71.2 mmol, 0.72 mL, 0.10 M in tetrahydrofuran) was introduced in one portion, affording a dark blue solution. After 35 minutes at ambient temperature, the reaction was diluted with 15 mL of diethyl ether and was extracted with 10 mL of saturated aqueous potassium carbonate. The aqueous extract was washed with 10 mL of ethyl acetate, and the combined organic layers were washed successively with 15 mL of saturated aqueous sodium sulfite and 15 mL of brine, dried (anhydrous sodium sulfate), filtered, and concentrated. Purification of the residue by flash chromatography (1 × 18 cm, linear gradient of 60–80% ethyl acetate/hexane) yielded 3.2 mg (71%) of the title compound as a clear oil. This material proved identical in all respects (^{1}H NMR, optical rotation, TLC, GC coinjection, mass spec) with natural material.
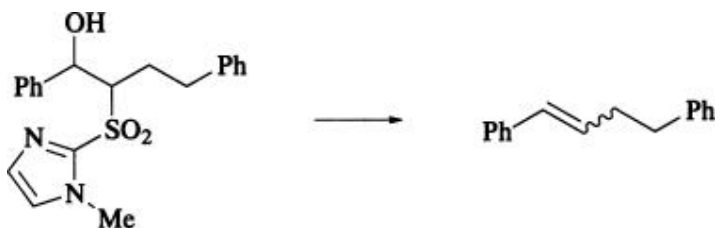
6.1.1.8. 1,4-Diphenylbut-1-ene (Reductive Elimination of β -Hydroxy Imidazoyl Sulfones) (37)
To a stirred solution of samarium(II) iodide (1.5 mmol) in tetrahydrofuran (12 mL) was rapidly added a solution of β -[(1-methyl-1H-imidazol-2-yl)sulfonyl]- α -phenylbenzenebutanol (0.185 g, 0.5 mmol) in tetrahydrofuran (6 mL) under an argon atmosphere. After 15 minutes at room temperature the reaction was still blue because of the excess of SmI$_2$ utilized. The reaction mixture was then poured into a 10% solution of sodium thiosulfate (20 mL) and extracted with ethyl acetate. The residue was chromatographed over silica gel (hexane–ethyl acetate, 99:1) to provide 0.085 g (82%) of the title compound as an 8:1 mixture of E/Z olefins. Satisfactory spectral data (IR, ^{1}H NMR,^{13}C NMR, and mass spectral data) were obtained for the product, the spectra matching that of material previously described in the literature.

6.1.1.9. (R)-Benzoin (Enantioselective Reduction of Ketones) (43)
Benzil (30 mg, 0.14 mmol) and quinidine (93 mg, 0.28 mmol) were dissolved in tetrahydrofuran (1.8 mL), and to this solution hexamethylphosphoric triamide (0.1 mL) **[Caution: Potent Carcinogen]** and then samarium(II) iodide–tetrahydrofuran (0.1 mol dm^{-3}, 2.8 mL, 0.28 mmol) were added under an atmosphere of argon. After stirring for 30 minutes at room temperature, hydrochloric acid (0.1 mol dm^{-3}, 5 mL) was added and the mixture was extracted with benzene **[Caution: Potent Carcinogen]** . The organic phase was washed with brine, aqueous sodium thiosulfate, brine, 3 mol dm^{-3} hydrochloric acid (20 mL), and brine successively, and dried over anhydrous magnesium sulfate. Benzene was removed and the residue was adsorbed on a silica gel column (Wako gel C-300, 7 g, 1.80 × 8 cm) and eluted with benzene (400 mL) **[Caution: Potent Carcinogen]** . The eluate was concentrated and the residue (18.2 mg) was analyzed by HPLC using a chiral column (Chiralcel OD; hexane:2-propanol, 9:1). Benzil (22.4%), benzyl phenyl ketone (trace), and benzoin (77.5%) were detected, and the ena ntiomers of benzoin were completely separated. Under these reaction conditions the benzoin was generated in 56.2% ee (*R* isomer predominating).

6.1.1.10. (2S,4S,5R,'S)-3-Oxazolidinecarboxylic Acid,
2-(3-Methoxy-1-methyl-3-oxopropyl)-4-methyl-5-phenyl Methyl Ester and
(2S,4S,5R,1'R)-3-Oxazolidinecarboxylic Acid,
2-(3-Methoxy-1-methyl-3-oxopropyl)-4-methyl-5-phenyl Methyl Ester
(Reduction of α , β -Unsaturated Carbonyl Substrates) (52)
A solution of (2*S*,4*S*,5*R*)-3-oxazolidinecarboxylic acid, 2-(3-methoxy-1-methyl-3-oxo-1-propeny)-4-methyl-5-phenyl methyl ester (56.5 mg, 0.18 mmol of an 88:12 mixture of *E*:*Z* isomers) in tetrahydrofuran/water (5/1) was treated with a 0.1 M tetrahydrofuran solution of samarium(II) iodide (8.8 mL, 0.88 mmol) at room temperature and under nitrogen until a persistent blue color was obtained. The mixture was extracted

with diethyl ether. The organic extracts were dried over anhydrous sodium sulfate and filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography (*n*-hexane/ethyl acetate, 75/25) to provide the title compounds in 33% yield as a 9:1 mixture of 1¢*S*:1¢*R* isomers. ^{1}H NMR (CDCl$_3$, 200 MHz): δ 0.82 (3H, d, *J* = 7.1 Hz), 1.05 (3H, d, *J* = 6.1 Hz), 2.25–2.70 (2H, m), 2.85 (1H, m), 3.71 (3H, s), 3.76 (3H, s), 4.81 (1H, m), 5.04 (1H, d, *J* = 2.8 Hz), 5.14 (1H, d, *J* = 6.0 Hz), 7.25–7.46 (5H, m). ^{13}C NMR (CDCl$_3$, 50 MHz): δ 12.74, 16.06, 32.7, 37.7, 51.58, 52.51, 56.34, 80.556, 91.12, 125.9, 127.7, 128.2.

6.1.1.11. 5-Iodo-1-phenyl-1-pentanone (Reduction of α -Acyloxy Ketone Substrates) (53)

To a slurry of samarium powder (0.32 g, 2.1 mmol) in 2 mL of tetrahydrofuran at room temperature was added a solution of 1,2-diiodoethane (0.56 g, 2 mmol) in 2 mL of tetrahydrofuran. The resultant olive-green slurry was stirred at ambient temperature for 1 hour, after which time the resulting dark blue slurry of samarium(II) iodide that had formed was cooled to –78° and treated with a solution of 2-acetoxy-5-iodo-1-phenyl-1-pentanone (0.35 g, 1 mmol) in 1 mL of methanol and 2 mL of tetrahydrofuran. The resultant brown mixture was stirred for 10 minutes at –78°, warmed to room temperature, and then poured into saturated aqueous potassium carbonate. The aqueous phase was extracted with diethyl ether (5 × 10 mL) and the combined extracts were dried (anhydrous magnesium sulfate). Evaporation of the solvent left a solid that was recrystallized from diethyl ether to afford 0.24 g (87%) of the title compound, mp 72–73°. IR (CCl$_4$): 1690 cm^{-1}. ^{1}H NMR (CCl$_4$): δ 7.9 (m, 3H), 7.4 (m, 3H), 3.2 (t, *J* = 6 Hz, 2H), 2.9 (t, *J* = 7.5 Hz, 2 H), 1.8 (m, 4H). ^{13}C NMR: δ 199.26, 136.63, 132.90, 128.21 (2 C), 127.84 (2 C), 37.09, 32.85, 24.92, 6.12. Exact mass spectral analysis, calcd for C$_{11}$H$_{13}$IO, 288.0012; found, 288.0011.

6.1.1.12. 1,8-Dichloro-11,11-dimethoxy-3-exo-hydroxytetracyclo[6.2.1.0^{2,7}.0^{4,1} ^{0}] undec-5-en-9-one (Reductive Cleavage of α -Halo Ketones) (29)

A solution of 1,8,10-trichloro-11,11-dimethoxy-*exo*-hydroxytetracyclo[6.2.1.0^{2,7}.0^{4,10}]undec-5-en-9-one (0.34 g, 1 mmol) in a tetrahydrofuran–methanol solution (3 mL, 2:1) was added to a solution of samarium(II) iodide (2.8 equiv, 6 mL) at –78°. The reaction mixture was allowed to warm to room temperature and stirred overnight (16 hours). The reaction mixture was worked up by pouring it into saturated aqueous potassium carbonate (25 mL) and extracting the resultant mixture with ethyl acetate (50 mL). The organic layer was washed with water and brine and dried (anhydrous magnesium sulfate). The residue obtained after removal of solvent under reduced pressure was applied to a silica gel column. Elution with 10% ethyl acetate–hexane furnished the title compound (218 mg, 68%), mp 148–149°. IR (KBr): 3526, 2951, 1764, 1215, 1087, 933, 787 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ 2.87 (ddd, J = 8.8, 4.5, 2.4 Hz, 1H), 2.95 (d, J = 9.3 Hz, 1H), 3.30–3.22 (m, 1H), 3.32 (dd, J = 5.7, 1.4 Hz, 1H), 3.37 (dd, J = 8.1, 2.4 Hz, 1H), 3.55 (s, 3H), 3.70 (s, 3H), 3.98 (dd, J = 9.3, 1.8 Hz, 1H), 5.91 (ddd, J = 8.3, 5.7, 1.1 Hz), 6.32 (ddd, J = 8.3, 7.1, 1.44 Hz, 1H). ^{13}C NMR: δ 197.49, 137.81, 127.52, 99.15, 85.17, 83.56, 78.30, 62.58, 52.09, 49.57, 48.66, 46.75. Anal. Calcd for C$_{13}$H$_{14}$O$_4$Cl$_2$: C, 51.31; H, 4.64; Cl, 23.00. Found: C, 51.24; H, 4.61; Cl, 22.77.
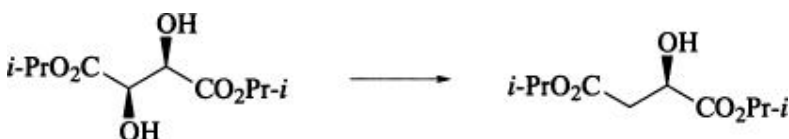
6.1.1.13. (R)-Diisopropyl Malate (Reduction of α -Hydroxy Ester Substrates) (54)

To a mixture of (*R,R*)-diisopropyl tartrate (148 mg, 0.63 mmol) and a samarium(II) iodide–tetrahydrofuran solution (1.9 mmol, 0.1 mol dm^{-3}, 19 mL) was added dropwise a solution of ethylene glycol (0.5 mL) in tetrahydrofuran (19 mL) over a period of 30 minutes at room temperature. After stirring for an additional 30 minutes, the reaction mixture was exposed to air to quench the excess samarium(II) iodide. Ethylene glycol (0.57 mL), silica gel (approximately 3 g), and hexane (10 mL) were added and the mixture was stirred for 10 minutes. Chromatographic purification (silica gel, hexane/ethyl acetate, 3:1) provided the title compound (137 mg, 99%) as an oil.
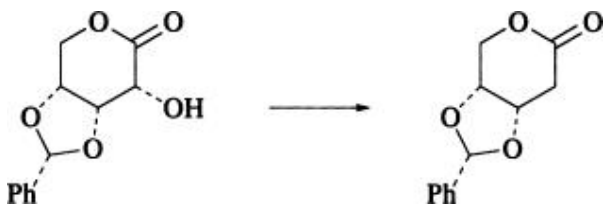
6.1.1.14. (R)-2-Deoxy-3,4-O-(phenylmethylene)-D-erythro-pentanoic Acid, δ-Lactone (Reduction of α-Hydroxy Aldonolactones) (55)

To a solution of (R)-3,4-O-(phenylmethylene)-D-ribonic acid, δ-lactone (236 mg, 1.0 mmol), anhydrous ethylene glycol (650 μL, 12 equiv), and hexamethylphosphoric triamide (1.5 mL) **[Caution: Potent Carcinogen]** in tetrahydrofuran (10 mL) was added dropwise a solution of 0.1 M samarium(II) iodide in tetrahydrofuran (30 mL, 3 mmol, 3 equiv) at room temperature under argon. After stirring for 3 hours, the mixture was quenched with saturated aqueous sodium bicarbonate, then extracted with ethyl acetate. The organic layer was washed with aqueous sodium thiosulfate, brine, and water, and then dried. The volatiles were removed and the residue was chromatographed to afford 199 mg (90%) of the title compound, mp 138–139°. [α]$_D$ = −167.9° (c 1.47). Characterization was accomplished by comparison with known physical constants from the literature. Additionally, a correct microanalysis was obtained, and the compound was further characterized by 300 MHz ^{1}H NMR.

6.1.1.15. (1¢R*,3R*,4S*,4aR*,7S*,8aS*)-3,4,4a,7,8,8 α-Hexahydro-7-hydroxy-4-methyl-3-(1¢-methylprop-2¢-enyl)-2(1H)-naphthalenone (Reduction of α-Alkoxy Ketone Substrates) (63)

To a slurry of samarium powder (2.6 g, 17.2 mmol) in 18 mL of tetrahydrofuran at 25° was added 1,2-diiodoethane (4.34 g, 17.21 mmol) in 18 mL of tetrahydrofuran via cannula over 15 minutes. The transfer was completed with 5 mL of tetrahydrofuran. A dark blue-green color developed. After being stirred at 25° for 1 hour the solution was cooled to −78° and (1R*,1¢R*,3R*,4S*,4aR*,7S*,8aS*)-1,7-epoxy-3,4,4a,7,8,8a-hexahydro-4-metyl-3-(1¢-methylprop-2¢-enyl)-2(1H)-naphthalenone (1.7 g, 7.3 mmol) in 24 mL of tetrahydrofuran was added over 10 minutes via cannula. The transfer was completed with 5 mL of tetrahydrofuran. The reaction mixture was stirred

for 30 minutes, followed by addition of 30 mL of saturated aqueous potassium carbonate. The reaction mixture was warmed to 25°, the organic layer was separated, and the aqueous layer was extracted with four 100-mL portions of diethyl ether. The organic extracts were combined, washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo to yield 1.71 g of crude title compound that was utilized without further purification in a subsequent experiment. A sample of the material was purified by preparative TLC (25% ethyl acetate/hexanes) for spectral analysis. ^{1}H NMR (500 MHz, CDCl$_3$): δ 1.2 [d, $J = 8$ Hz, 6H, CH$_3$ (1²,4)], 1.6 (m, 2H), 1.75 (m, 1H), 1.95 (m, 1H), 2.05 (s, 1H), 2.3 (m, 2H), 2.55 (m, 1H), 4.3 [br s, 1H, H(7)], 4.95 [d, $J = 7$ Hz, 1H, H(3¢)], 5.0 [d, $J = 14$ Hz, 1H, H(3')], 5.9 [m, 3H, H(5,6,2')]. IR (neat): 3420, 2960, 1700 cm^{-1}. LRMS (EI) m/z 234 (M$^+$), 216 (M$^+$–H$_2$O), 201 (M$^+$–CH$_5$), 166.

6.1.1.16. trans-Hexahydro-4a-hydroxy-8a-methyl-1,6(2H,5H)-naphthalenedione (Reduction of α , β -Epoxy Ketones) (69)

To a slurry of samarium powder (0.32 g, 2.1 mmol) in 2 mL of tetrahydrofuran at room temperature was added a solution of 1,2-diiodoethane (0.56 g, 2 mmol) in 2 mL of tetrahydrofuran. The resultant olive-green slurry was stirred at ambient temperature for 1 hour, after which time the resulting dark blue slurry of samarium(II) iodide that had formed was cooled to –90° and treated with a solution of (1a α ,4a α ,8aR*)-tetrahydro-4a-methyl-(1aH)-naphth[1,8a-b]oxirene-2,5(3H,6H)-dione (0.19 g, 1.00 mmol) in 1 mL of methanol and 2 mL of tetrahydrofuran. The resultant brown mixture was stirred for 5 minutes at –90°, quenched at this temperature by the addition of saturated aqueous potassium carbonate or pH 8 phosphate buffer, and then warmed to room temperature. The aqueous phase was extracted with diethyl ether (5 × 10 mL), and the combined organic extracts were dried (anhydrous magnesium sulfate). Evaporation of the solvent left a solid that was recrystallized from diethyl ether to afford 0.14 g (76%) of the title compound, mp 186–187°. IR(CHCl$_3$/DMSO): 3330, 1700 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ 2.9–1.5 (m, 13H), 1.3 (s, 3H). ^{13}C NMR (CDCl$_3$/DMSO-d_6): δ 213.59, 209.74, 79.04, 50.56, 49.87, 36.95, 35.93, 32.18, 27.35, 19.92, 19.79. Exact mass spectral analysis, calcd for C$_{11}$H$_{16}$O$_3$, 196.1099; found, 196.1105.
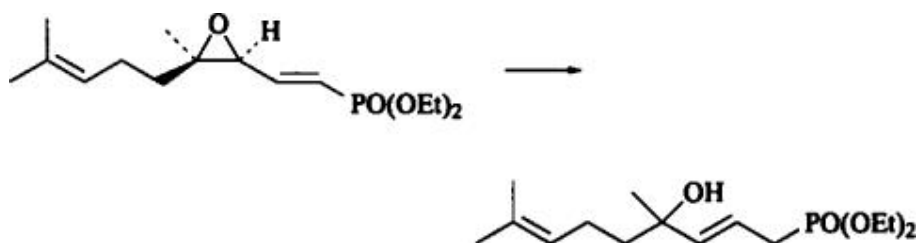
6.1.1.17. Diethyl [(2E)-4,8-Dimethyl-4-hydroxy-2,7-nonadien-1-yl]phosphonate (Reduction of Vinyl Oxiranes) (70)

To a slurry of samarium powder (0.32 g, 2.1 mmol) in 2 mL of tetrahydrofuran at room temperature under argon was added a solution of 1,2-diiodoethane (0.56 g, 2 mmol) in 2 mL of tetrahydrofuran. The resultant olive-green slurry was stirred at ambient temperature for 1 hour, after which time the resulting dark blue slurry of samarium(II) iodide was cooled to –90° and treated with a solution of diethyl [(3R*,4S*)-(1E)-4,8-dimethyl-3,4-epoxy-1,7-nonadien-1-yl]phosphonate (0.233 g, 0.077 mmol) in 2 mL of tetrahydrofuran and 1 mL of methanol. The resultant brown reaction mixture was stirred for 5 minutes at –90°, quenched at this temperature by the addition of pH 8 phosphate buffer, and then warmed to room temperature. The aqueous phase was extracted with diethyl ether (5 × 3 mL), the combined extracts were dried (anhydrous magnesium sulfate/potassium carbonate or anhydrous sodium sulfate), and the volatiles were removed in vacuo. The remaining oil was kugelrohr distilled (bp 100°, 0.1 mm Hg) to provide 0.197 g (84%) of the title compound. IR (neat): 3400, 1250, 1040 cm^{-1}. ^{1}H NMR: δ 5.7 (m, 2H), 5.1 (m 1H), 4.1 (m, 4H), 2.64 (d, J = 6 Hz, 1H), 2.54 (d, J = 6 Hz, 1H), 2.0 (m, 2H), 1.8–1.2 (m, 19H). ^{13}C NMR: δ 142.33, 131.06, 124.19, 115.91, 72.17, 61.68, 42.08, 31.10, 28.30, 27.38, 25.31, 22.45, 17.29, 16.14. Exact mass spectral analysis, calcd for $C_{15}H_{30}O_4P$, 305.1882; found, 305.1904.
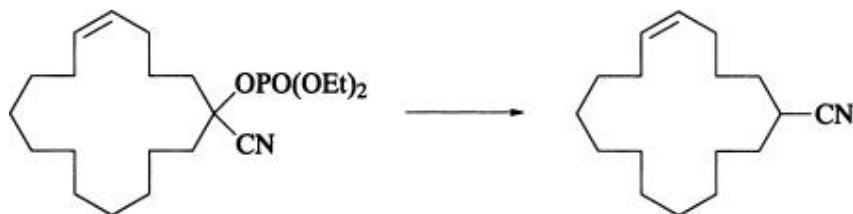
6.1.1.18. Cyclohexadec-5-enecarbonitrile (Reduction of α -Heterosubstituted Nitriles) (72)

Cyclohexadec-5-enone (0.5 mmol) was stirred with $O,O\text{¢}$-diethyl phosphorocyanidate (245 mg, 1.5 mmol) and lithium cyanide (24.5 mg, 1.5 mmol) in 10 mL of tetrahydrofuran for 10–30 minutes at room temperature. Water (10 mL) was added, and the mixture was extracted with ethyl acetate–hexane (1:1, 50 mL). The extract was washed with brine (2 × 20 mL), dried (anhydrous magnesium sulfate), and evaporated under reduced pressure. A solution of the crude cyanophosphate thus formed and *tert*-butanol (37 mg, 0.5 mmol) in 5 mL of tetrahydrofuran was added to a solution of samarium(II) iodide, prepared from samarium metal (345 mg, 2.3 mmol) and 1,2-diiodoethane (413 mg, 1.5 mmol) in 10 mL of tetrahydrofuran at room temperature. The reaction mixture was quenched by addition of 10% hydrochloric acid (10 mL) and extracted with diethyl ether (2 × 50 mL). The extracts were washed with 5% sodium thiosulfate (10 mL), water (10 mL) and brine (10 mL) and dried (anhydrous magnesium sulfate). After removal of the solvent, the residue was purified by column chromatography (benzene–hexane, 1:1, **[Caution: Potent Carcinogen]**) to provide the title compound (97%) as a colorless oil, bp 156° (2 mm Hg). IR (film): 2240 cm^{-1}. ^{1}H NMR: δ1.1–1.7 (m, 22H), 2.2 (br s, 4H), 2.5 (m, 1H), 5.3 (m, 2H). Mass spectrum, *m/z* 247 (M$^+$). HRMS calcd for $C_{17}H_{29}$, 247.2298; found, 247.2299. Anal. Calcd for $C_{17}H_{29}N$: C, 82.85; H, 11.82; N, 5.66. Found: C, 82.51; H, 11.97; N, 5.72.

6.1.1.19. N-Hydroxy 2-(tert-Butyldiphenylsiloxy)ethanamine (Reduction of Nitro Compounds to Hydroxylamines) (79)

To a solution of freshly prepared samarium(II) iodide (4 mmol) in 30 mL of tetrahydrofuran was rapidly added a solution of 2-(tert-butyldiphenylsiloxy)-1-nitroethane (1 mmol) in a 2:1 mixture of tetrahydrofuran/methanol (6 mL). The reaction mixture was stirred at room temperature for 3 minutes, poured into a 10% solution of sodium thiosulfate (30 mL) and extracted with ethyl acetate several times. The residue was chromatographed over silica gel (ethyl acetate) to provide the title compound in 79% yield, mp 68–69°. IR (CHCl$_3$) 3580, 3260, 2920, 1470, 1425, 1110 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.70 (m, 4H), 7.43 (m, 6H), 6.32 (br, 2H), 3.85 (t, J = 5.1 Hz, 2H), 3.08 (t, J = 5.1 Hz, 2H), 1.09 (s, 9H). ^{13}C NMR (60 MHz, CDCl$_3$): δ 135.53, 133.38, 129.72, 127.73, 60.02, 55.61, 26.84, 19.20. Mass spectrum: *m/z* 298 (M$^+$-17, 1). Anal. Calcd for $C_{18}H_{25}NO_2Si$: C, 68.52; H, 7.99; N, 4.44; Found: C, 68.79; H, 8.03; N, 4.30.

6.1.1.20. [S-(R*,S*)]-[1-Methyl-2-oxo-2-[2-(1-pyrrolidinylcarbonyl)-1-pyrrolidiny l] ethyl]-Carbamic Acid, Phenylmethyl Ester (Reduction of 2-Hydroxyimino Amides) (82)

To a solution of
(S)-1-[2-(hydroxyimino)-1-oxopropyl]-2-(1-pyrrolidinylcarbonyl)pyrrolidine
(51.0 mg, 0.20 mmol) in methanol (10 mL) and tetrahydrofuran (4.0 mL) was
added a solution of samarium(II) iodide in tetrahydrofuran (10 mL, 0.1 M,
10 mmol) under argon at –40°. The resulting mixture was stirred for 1 hour.
The reaction mixture was quenched with a mixture of pH 7 buffer (2.5 mL) and
methanol (2.5 mL) at –40°. The reaction mixture was poured into 10%
aqueous potassium carbonate solution and extracted with dichloromethane.
The organic layer was dried over anhydrous magnesium sulfate and the
solvent was removed under reduced pressure. Dichloromethane (10 mL) was
added to the residue, and carbobenzoxy chloride (0.04 mL, 0.3 mmol) and
pyridine (0.03 mL, 0.3 mmol) were added to this solution. After stirring for 1
hour at 0°, the reaction mixture was quenched with brine and extracted with
dichloromethane. The organic layer was dried over an hydrous magnesium
sulfate. Subsequently, the solvent was removed and the crude product was
purified by silica gel TLC (ethyl acetate) providing the title compound (60.8 mg,
82% yield).
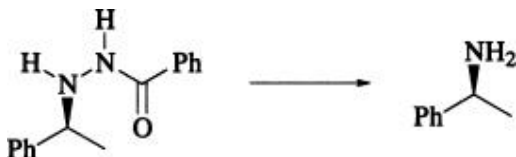
6.1.1.21. (S)-(–)- α -Methylbenzylamine (Reductive Cleavage of the Nitrogen–Nitrogen Bond of N-Aroylhydrazines) (84)

To (S)-(–)-1-phenyl-1-(2-benzoylhydrazino)ethane (0.40 g, 1.66 mmol, 89% ee)
in methanol (7 mL) was added rapidly dropwise a solution of samarium(II)
iodide (3.5 mmol, 70 mL of a 0.05 M solution in tetrahydrofuran). After
complete addition, the reaction was allowed to stir for 30 minutes. The reaction
was then concentrated on a rotary evaporator, and to the resulting residue was
added 1 M hydrochloric acid (15 mL). The aqueous layer was extracted with

diethyl ether (8 × 25 mL). The aqueous layer was made basic to litmus by the addition of 3 M sodium hydroxide and then was extracted with diethyl ether (8 × 25 mL). The combined ether extracts were diluted with pentane (1:1) and dried over a small amount of anhydrous magnesium sulfate. Concentration of the diethyl ether/pentane solution on a rotary evaporator provided the title compound (0.144 g, 72%) as a colorless oil, $[\alpha]_D^{20} = -37.1°$ (c 1.33, C_6H_6). ^{1}H NMR (CDCl$_3$): δ 1.40 (d, J_{HH} = 6.3 Hz, 3H, CH_3), 1.70 (br, 2H, NH), 4.14 (q, J_{HH} = 6.3 Hz, 1H, CH), 7.25 (m, 1H, Ph), 7.45 (m, 4H, Ph). The enantiomeric purity of the product was determined to be 89% ee using capillary GC methods [J & W Cyclodex B column, 80°, isothermal, R isomer retention time 20.57 minutes; S isomer retention time 21.33 minutes].
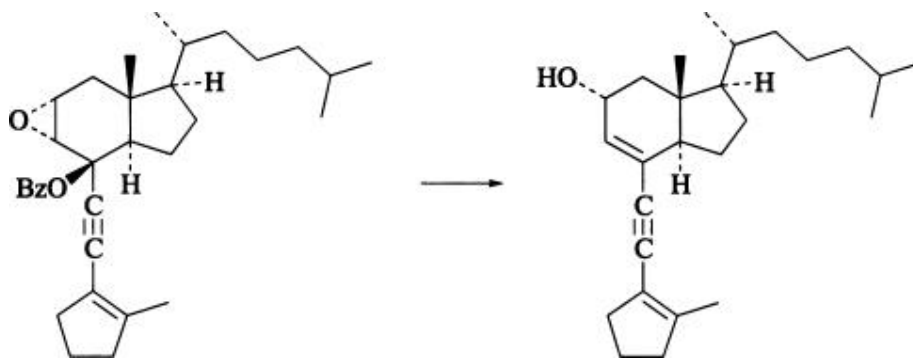
6.1.1.22. A-Nor-9,10-secocholest α -5(10),8-dien-6-yn-11 α -ol
(Palladium-Promoted Reductive Cleavage of Propargyl Carboxylates) (90)
To a suspension of samarium powder (0.451 g, 3.0 mmol) in dry tetrahydrofuran (5 mL) was added a solution of 1,2-diiodoethane (0.724 g, 2.57 mmol) in tetrahydrofuran (5 mL) under argon at room temperature via cannula. After stirring for 1 hour, a deep blue solution was obtained, and a solution of A-nor-9 α ,11 α -oxido-9,10-secocholesta-5(10)-en-6-yn-8 β -yl benzoate (0.251 g, 0.51 mmol) and tetra kis(triphenylphosphine)palladium(0) (0.018 g, 3 mol %) in tetrahydrofuran (7 mL) was added via cannula. The deep blue color persisted, and the solution was stirred for one hour. Water (5 mL) was added, and the mixture was stirred until it became yellow. Solid sodium carbonate was added to separate the layers, the entire mixture was extracted with diethyl ether (2 × 25 mL), and the organic layers were combined and dried. Concentration gave a dark orange oil that was subjected to HPLC purification (10% ethyl acetate/hexanes) to provide 0.168 g (89%) of the title compound as a viscous oil. ^{1}H NMR (CDCl$_3$): δ 0.72 (s, 3H, C$_{18}$CH_3), 0.85 (overlapping d, J = 6.7 Hz, 6 H, C$_{26,27}$2 CH_3), 0.95 (d, J = 6.2 Hz, 3H, C$_{21}$CH_3), 1.84 (s, 3H, C$_{19}$CH_3), 4.41 (ddd, J = 1.9, 7.0, 3.1 Hz, 1H), 5.91 (dd, J = 3.1, 3.1 Hz, 1H).

7. Tabular Survey

Tables I–X are organized in the sequence used in the Scope and Limitations section. Literature coverage through 1992 is as exhaustive as possible, using both computer scanning services and hand searches. Unspecified yields are denoted by (–).

Tables I–X are ordered by increasing carbon number of the basic structural unit of the educt, omitting the carbon count of, for example, protecting groups or the alcohol portion of a carboxylic ester.

Abbreviations used in all of the tables are as follows:

Ac	acetyl
Bn	benzyl
Bz	benzoyl
C_6H_{11}	cyclohexyl
Cbz	carbobenzyloxy
DBM	dibenzoylmethanato
DMA	*N,N*-dimethylacetamide
DMAE	*N,N*-dimethylaminoethanol
DMF	*N,N*-dimethylformamide
DMPU	*N,N¢*-dimethylpropyleneurea
ee	enantiomeric excess
HMPA	hexamethylphosphoric triamide
MEM	methoxyethoxymethyl
MOM	methoxymethyl
NMP	1-methyl-2-pyrrolidinone
rt	room temperature
SEM	2-(trimethylsilyl)ethoxymethyl
TBDMS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
THF	tetrahydrofuran
TMEDA	*N,N,N′,N′*-tetramethylethylenediamine
TMS	trimethylsilyl
TMU	tetramethylurea
Tol	tolyl
Tr	triphenylmethyl

Ts   *p*-toluenesulfonyl

Table I. Reduction of Organic Halides, Sulfonates, and Sulfones

[View PDF]

Table II. Reductive Elimination/Fragmentation Reactions

[View PDF]

Table III. Reduction of Aldehydes and Ketones

[View PDF]

Table IV. Reduction of Carboxylic Acids and Their Derivatives

[View PDF]

Table V. Reduction of Conjugated Carbonyl Substrates

[View PDF]

Table VI. Reductive Cleavage of α -Heterosubstituted Carbonyl Compounds and Related Substrates

View PDF

Table VII. Reductive Cleavage of Cyclopropyl Ketones

View PDF

Table VIII. Deoxygenation Reactions

View PDF

Table IX. Reduction of Nitrogen-Based Functional Groups

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Table X. Reduction of Miscellaneous Functional Groups

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Table I. REDUCTION OF ORGANIC HALIDES, SULFONATES, AND SULFONES
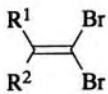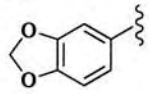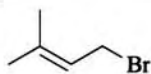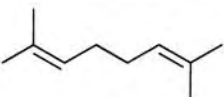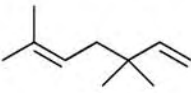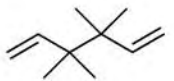
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
		A. Organic Halides and Sulfonates	

C_2

$$R^1C\equiv CR^2 \ + \ \text{(I)} \ + \ \text{(II)} \ + \ \text{(III)}$$

I **II** **III**

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
$R^1 = C_6H_{11}$; $R^2 = H$	2.5 SmI$_2$, C$_6$H$_6$, HMPA, rt, 10 min	**I** (86)	23
$R^1 = C_6H_{13}$; $R^2 = H$	"	**I** (90)	23
$R^1 = C_8H_{17}$; $R^2 = H$	"	**I** (74)	23
$R^1 = $ Me; $R^2 = $	"	**I** (41)	23
$R^1 = C_8H_{17}$; $R^2 = $ Ph	8 SmI$_2$, THF, HMPA, rt	**I** (27) + **II** (39) + **III** (6)	23
	2.5 SmI$_2$, C$_6$H$_6$, HMPA, rt, 10 min	**I** (67) + **II** (8)	23

C_5

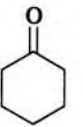| | 1 SmI$_2$, THF, rt, 1 d | (42) + | 3 |
| | | (25) + | |
| | | (6) | |
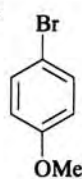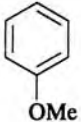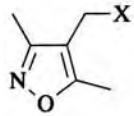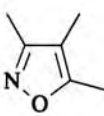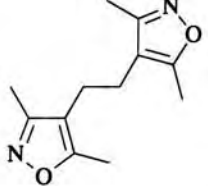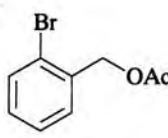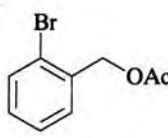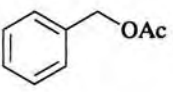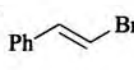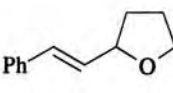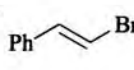
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₆ (4-bromoanisole)	2.5 SmI₂, THF, HMPA, *i*-PrOH, rt, 8 h	(anisole) (82)	24
(isoxazole-CH₂X)		I + II	
X = Cl	2 SmI₂, THF, rt, 2 d	II (54-60)	25
X = Br	2 SmI₂, THF, rt, 3 h	I (36) + II (47)	25
C₇ (2-bromobenzyl acetate)	2.5 SmI₂, THF, HMPA, rt, 2 h	(benzyl acetate) OAc (97)	24
PhCH₂Cl	1 SmI₂, THF, rt, 1.5 h	PhCH₂CH₂Ph (67)	3
PhCH₂Cl	1 SmI₂, THF, rt, 20 min	" (82	3
C₈ Ph—CH=CH—Br	SmI₂, THF	Ph—CH=CH—(tetrahydrofuran-2-yl) (22)	26
	2.5 SmI₂, THF, HMPA, rt, 20 min	Ph—CH=CH₂ (>95)	24
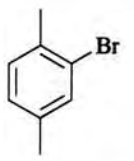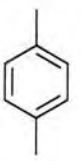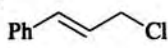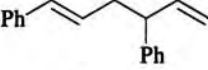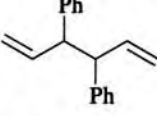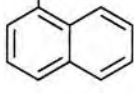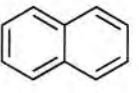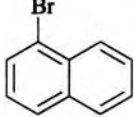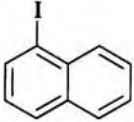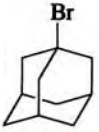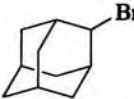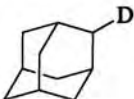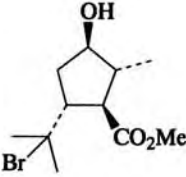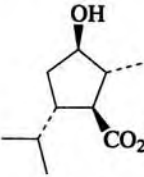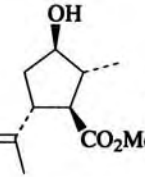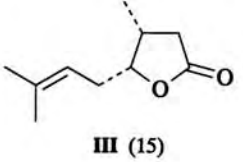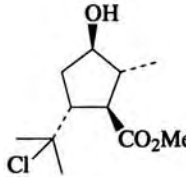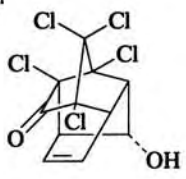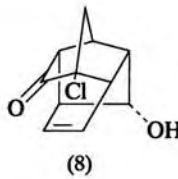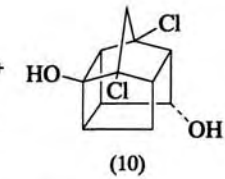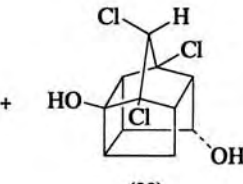
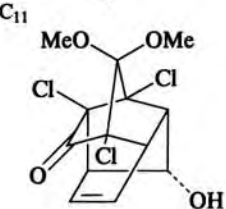| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
(2-bromo-1,4-dimethylbenzene)	2.5 SmI₂, THF, HMPA, *i*-PrOH, rt, 15 h	(*p*-xylene) (84)	24
C₉ Ph—CH=CH—CH₂Cl	SmI₂, THF, rt, 30 min	Ph—CH=CH—CH₂—CH₂—CH=CH—Ph I (51) +	3
		Ph—CH=CH—CH₂—CH(Ph)—CH=CH₂ II (23) +	
		CH₂=CH—CH(Ph)—CH(Ph)—CH=CH₂ III (7)	
Ph—CH=CH—CH₂Br	1 SmI₂, THF, rt, 5 min	I (55) + II (21) + III (6)	3
C₁₀ (1-chloronaphthalene)	2.5 SmI₂, THF, HMPA, 15 min	(naphthalene) I (>95)	24
(1-bromonaphthalene)	2.5 SmI₂, THF, HMPA, D₂O, rt, 5 min	I (98)	24

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Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
(1-iodonaphthalene)	2.5 SmI$_2$, THF, HMPA, rt, 1 min	**I** (>95)	24
(1-bromoadamantane)	2.5 SmI$_2$, MeCN, HMPA, *i*-PrOH, rt, 10 min	**I** (>95)	24
(2-bromoadamantane)	2.5 SmI$_2$, THF, HMPA, D$_2$O, rt, 10 min	**I** (20) + (2-deuterioadamantane) (80)	24
(cyclopentane with OH, Me, *i*-Pr(Br), CO$_2$Me)	2.5–4 SmI$_2$, THF, HMPA, rt	**I** (39) + **II** (17) + **III** (15)	27

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Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
(cyclopentane with OH, Me, C(CH$_3$)$_2$Cl, CO$_2$Me)	2.5–4 SmI$_2$, THF, HMPA, rt	**I** (37) + **III** (24)	27
n-C$_{10}$H$_{21}$X		*n*-C$_{10}$H$_{22}$ **I**	
X = Cl	2.5 SmI$_2$, THF, HMPA, *i*-PrOH, 60°, 8 h	**I** (>95)	24
X = Br	2.5 SmI$_2$, THF, HMPA, *i*-PrOH, rt, 10 min	**I** (>95)	24
X = I	2.5 SmI$_2$, THF, HMPA, *i*-PrOH, rt, 5 min	**I** (>95)	24
C$_{11}$ (pentachloro ketone alcohol structure)	12 SmI$_2$, THF, MeOH, -78°, 16 h	(8) + (10) + (30)	29

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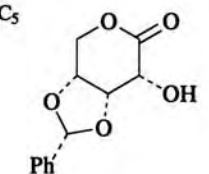| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	SmI₂, THF, HMPA, rt, 5 min	(100)	30
C₁₂	2.5 SmI₂, THF, HMPA, rt, 1 h	(>95)	24
	2.5 SmI₂, THF, HMPA, *i*-PrOH, rt, 10 min	**I** (>95)	24
	2.5 SmI₂, THF, HMPA, *i*-PrOH, rt, 10 min	**I** (>95)	24
n-C₁₂H₂₅X		*n*-C₁₂H₂₆ **I**	
X = Cl	2 SmI₂, THF, MeOH, 65°, 2 d	**I** (0)	3
X = Br	"	**I** (82)	3
X = I	2 SmI₂, THF, MeOH, 65°, 6 h	**I** (95)	3
X = OTs	2 SmI₂, THF, MeOH, 65°, 12 h	**I** (76)	3

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₅	2 SmI₂, THF, HMPA, rt, 2 h	(55) + (18) + (1)	92
C₁₆	2 SmI₂, THF, HMPA, rt, 2 h	(58) + (22) + (4)	92
	2 SmI₂, THF, HMPA, rt, 2 h	(50) + (16) + (2)	92

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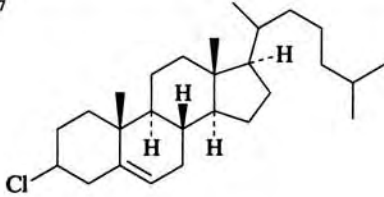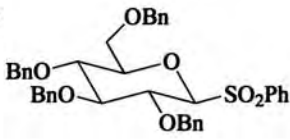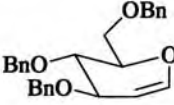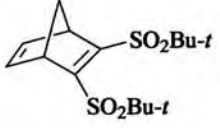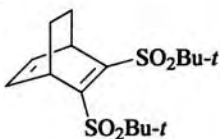
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{27}$	2.5 SmI$_2$, THF, HMPA, *i*-PrOH, rt, 3 h	(99)	24

B. Organic Sulfones

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_6$	SmI$_2$, THF, HMPA	(77) + (—)	31
C$_7$ (SO$_2$Bu-*t*)	SmI$_2$, THF, MeOH, -70°	(100)	32
C$_8$ (SO$_2$Bu-*t*)	SmI$_2$, THF, MeOH, -70°	(85)	32
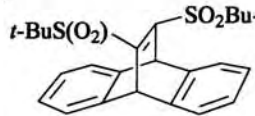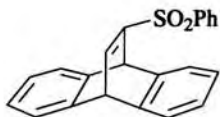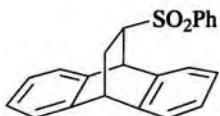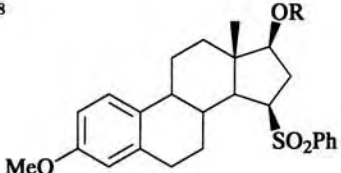
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{16}$ *t*-BuS(O$_2$)— SO$_2$Bu-*t*	SmI$_2$, THF, MeOH, -70°	*t*-BuSO$_2$ (96)	32
SO$_2$Ph	5 SmI$_2$, THF, HMPA, -20°, 30 min	(77)	33
SO$_2$Ph	5 SmI$_2$, THF, HMPA, -20°, 30 min	(74)	33
C$_{18}$ R = OH	5 SmI$_2$, THF, HMPA, 22°, 90 min	I (50)	33
R = OAc	5 SmI$_2$, THF, HMPA, -20°, 90 min	I (52)	33

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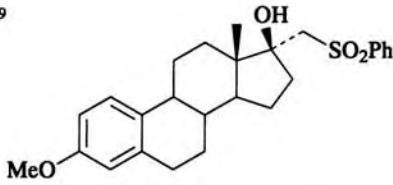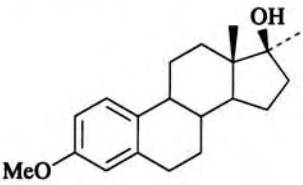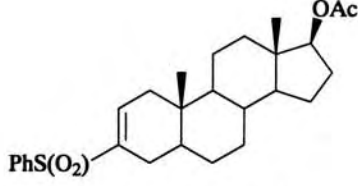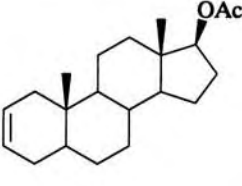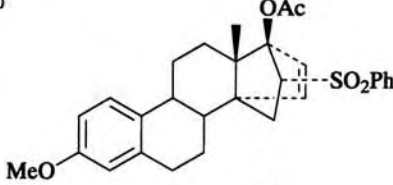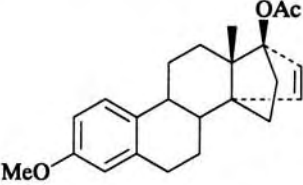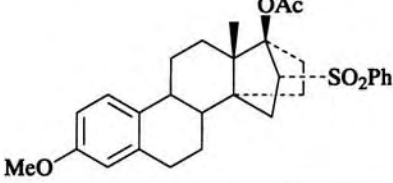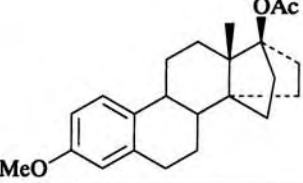
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₉			

	5 SmI$_2$, THF, HMPA, 22°, 60 min	(53)	33
	5 SmI$_2$, THF, HMPA, -20°, 90 min	(68)	33
C$_{20}$	5 SmI$_2$, THF, HMPA, -20°, 70 min	(70)	33
	5 SmI$_2$, THF, HMPA, -20°, 90 min	(87)	33

Table II. REDUCTIVE ELIMINATION/FRAGMENTATION REACTIONS
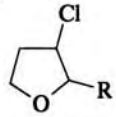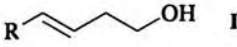
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	A. β-*Halo Ethers*		

C$_4$

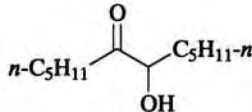| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
R = D (*cis + trans*)	SmI$_2$, THF, 65°	I 51 : 49 *Z/E*	34
R = Me (*cis*)	"	I (75-90), >95% *E*	34
R = Me (*trans*)	"	I (75-90), >95% *E*	34
R = C≡CH (*cis*)	"	I (75), >99% *E*	34
R = CH=CH$_2$ (*cis*)	"	I (84), >97% *E*	34
R = Et (66 : 34 *cis/trans*)	SmI$_2$, THF, 65°, 76 h	I (95), >98% *E*	34
	SmI$_2$, THF, HMPA, 65°, 9 h	I (92) *E*	34
	SmI$_2$, THF, DMPU, 65°, 5 h	I (96), >93% *E*	34
R = CH$_2$CH=CH$_2$ (2 : 1 *cis/trans*)	SmI$_2$, THF, 65°	I (93), >97% *E*	34
R = Ph (*trans*)	"	I (95), >97% *E*	34
R = *p*-Tol (*trans*)	"	I (100), >99% *E*	34
R = C≡CC$_5$H$_{11}$-*n* (*cis*)	SmI$_2$, THF, 65°, 22 h	I (84), >99% *E*	34
	SmI$_2$, THF, DMPU, 65°, 3 h	I (83), >94% *E*	34
R = C≡CPh (*cis*)	SmI$_2$, THF, 65°	I (75), >99% *E*	34

Table II. REDUCTIVE ELIMINATION/FRAGMENTATION REACTIONS (*Continued*)
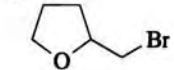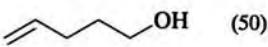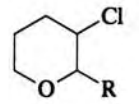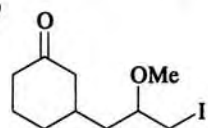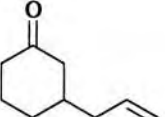
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₅	SmI₂, THF	(50)	26
		I	
R = D (74 : 26 *trans/cis*)	SmI₂, THF, 65°	**I** 53 : 47 *E/Z*	34
R = Et (*cis*)	"	**I** (85-90), 76 : 24 *Z/E*	34
R = Et (*trans*)	"	**I** (85-90), 72 : 28 *Z/E*	34
R = Et (*cis + trans*)	SmI₂, THF, DMPU, 65°	**I** 13 : 87 *Z/E*	34
R = *i*-Pr (85 : 15 *trans/cis*)	SmI₂, THF, 65°	**I** (85-90), 79 : 21 *Z/E*	34
R = C≡CPr-*n* (70 : 30 *trans/cis*)	"	**I** (79), >99% *Z*	34
R = C≡CC₅H₁₁-*n* (80 : 20 *trans/cis*)	"	**I** (93), >97% *Z*	34
R = C≡CC₅H₁₁-*n* (83 : 17 *trans/cis*)	SmI₂, THF, DMPU, 65°	**I** (90), 63 : 37 *Z/E*	34
C₉	2 SmI₂, cat. Fe(DBM)₂, THF, -78 to 0°	(69)	73

Table II. REDUCTIVE ELIMINATION/FRAGMENTATION REACTIONS (*Continued*)
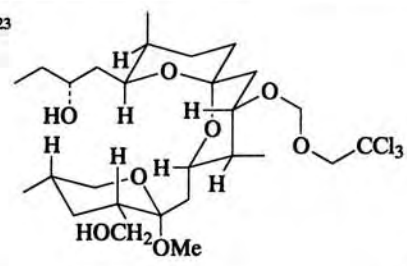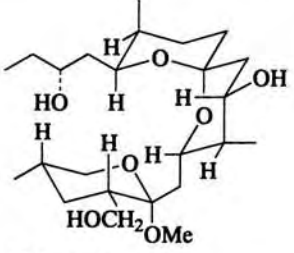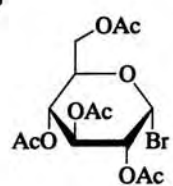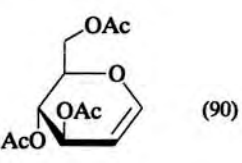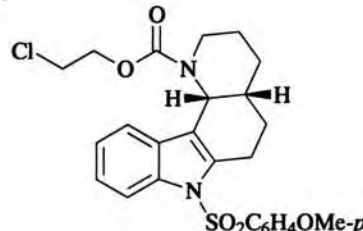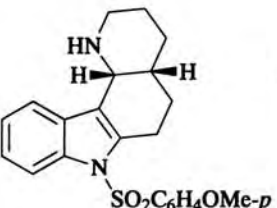
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₂₃	7 SmI₂, THF, rt, 35 min	(71)	35

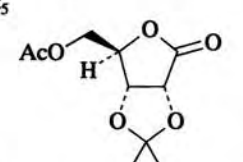*B. β-Carboalkoxy Halides and Related Substrates*

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₆	6 SmI₂, THF, rt	(90)	31
C₁₅	SmI₂, THF, 70°, 7 h	(70)	36

Table II. REDUCTIVE ELIMINATION/FRAGMENTATION REACTIONS (*Continued*)
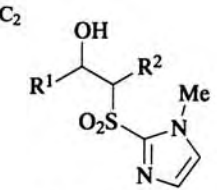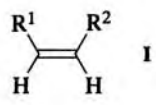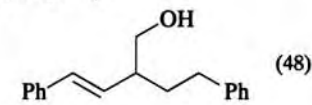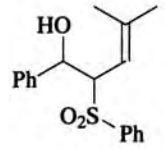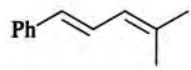
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.

C. β-Hydroxy Sulfones

C$_2$

R^1	R^2			
Ph	CH=CMe$_2$	3 SmI$_2$, THF, rt	**I** (87), 5 : 1 *E/Z*	37
(*E*)-CH=CHPh	CH=CMe$_2$	"	**I** (78), *E,E* isomer only	37
CH=CMe$_2$	(CH$_2$)$_2$Ph	"	**I** (82), 5 : 1 *E/Z*	37
Ph	(CH$_2$)$_2$Ph	3 SmI$_2$, THF, rt, 15 min	**I** (82), 8 : 1 *E/Z*	37
(CH$_2$)$_2$Ph	(CH$_2$)$_2$Ph	3 SmI$_2$, THF, rt	**I** (55), 3 : 1 *E/Z*	37
(*E*)-CH=CHPh	(CH$_2$)$_2$Ph	"	**I** (20), 9 : 2 *E/Z* +	37

	3 SmI$_2$, THF, rt, 15 min	(trace)	37

Table II. REDUCTIVE ELIMINATION/FRAGMENTATION REACTIONS (*Continued*)
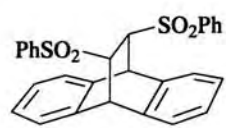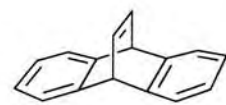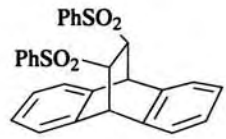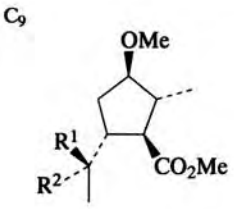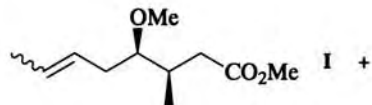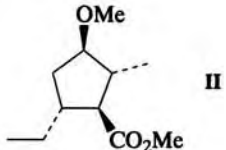
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.

D. α,β-Disulfones
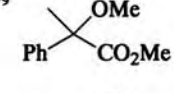
C$_{16}$

	5 SmI$_2$, THF, HMPA, -20°, 30 min	(91)	33

	5 SmI$_2$, THF, HMPA, -20°, 30 min	" (83)	33

E. γ-Halo Carbonyl Compounds and Related Substrates

C$_9$

R^1	R^2			
H	Cl	2.5-4 SmI$_2$, THF, HMPA, rt	**I** (21) + **II** (17)	27
Cl	H	"	**I** (29) + **II** (12)	27
H	Br	"	**I** (64)	27
Br	H	"	**I** (66)	27

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Table II. REDUCTIVE ELIMINATION/FRAGMENTATION REACTIONS (*Continued*)
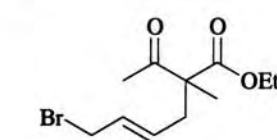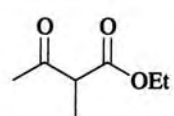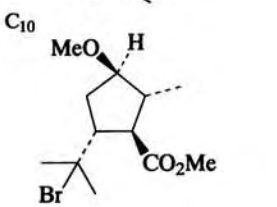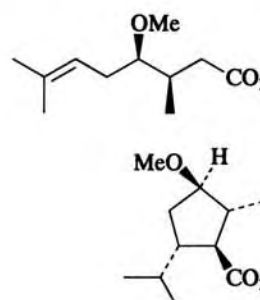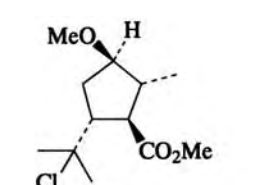
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	2 SmI$_2$, THF, -78°	(—)	38
C$_{10}$	2 SmI$_2$, THF, -78°	**I** (48) +	27
		(17) +	
		(14)	
	2 SmI$_2$, THF, -78°	**I** (77)	27

Table II. REDUCTIVE ELIMINATION/FRAGMENTATION REACTIONS (*Continued*)
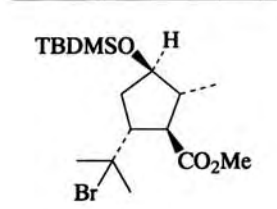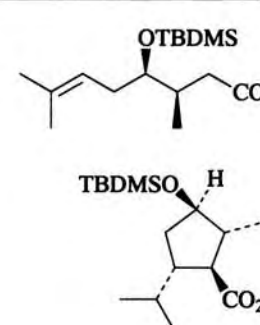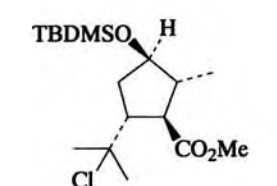
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	2 SmI$_2$, THF, -78°	**I** (55) +	27
		(17) +	
		(10)	
	2 SmI$_2$, THF, -78°	**I** (78)	27

Table II. REDUCTIVE ELIMINATION/FRAGMENTATION REACTIONS (*Continued*)
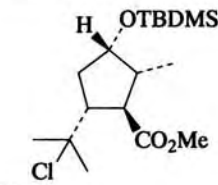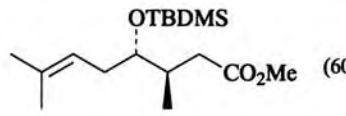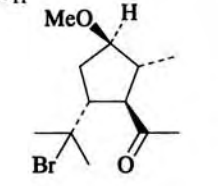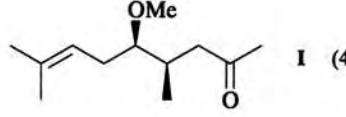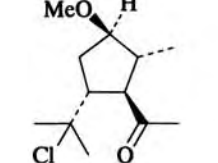
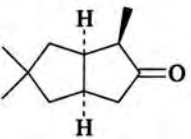| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₁ *(structure: cyclopentane with H, OTBDMS, t-Bu–Cl, CO₂Me)*	2 SmI₂, THF, -78°	*(structure)* OTBDMS, CO₂Me (60)	27
(structure: cyclopentane with MeO, H, t-Bu–Br, acetyl)	2 SmI₂, THF, -78°	*(structure)* OMe, O **I** (43)	27
(structure: cyclopentane with MeO, H, t-Bu–Cl, acetyl)	2 SmI₂, THF, -78°	**I** (18)	27

Table II. REDUCTIVE ELIMINATION/FRAGMENTATION REACTIONS (*Continued*)
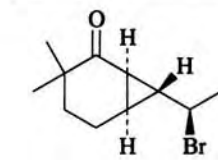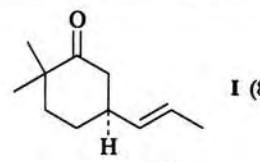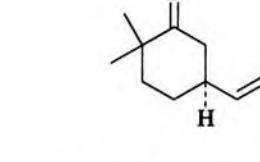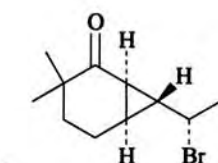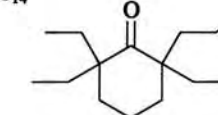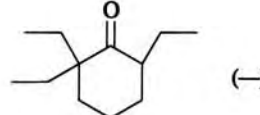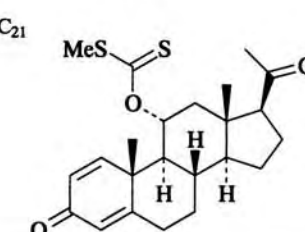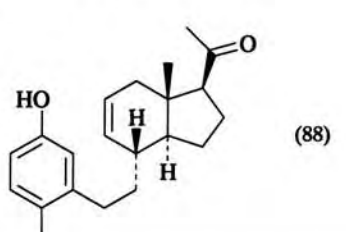
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
(bicyclic ketone structure, H, Br)	SmI₂, THF, MeOH, 25°, 2 min	*(structure)* **I** (83) + *(structure)* **II** (2)	28
C₁₄ *(bicyclic ketone structure, H, H, Br)*	SmI₂, THF, MeOH, 25°, 2 min	**I** (1) + **II** (75)	28
(cyclohexanone with ethyl groups and iodoethyl)	SmI₂, THF	*(cyclohexanone structure)* (—)	39

F. Miscellaneous

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₂₁ *(steroid with MeS–C(=S)–O at C11, acetyl)*	THF, rt, 5 min	*(aromatic HO phenol fused bicyclic structure)* (88)	36

Table III. REDUCTION OF ALDEHYDES AND KETONES

	Substrate		Conditions	Product(s) and Yield(s) (%)		Refs.

C₃
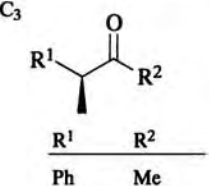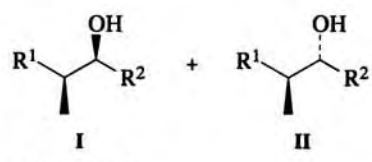
R¹	R²					
Ph	Me		SmI_2, THF, H_2O	**I** (7) + **II** (4)		40
			SmI_2, THF, HMPA, t-$BuCO_2H$, rt, 3 min	**I** (55) + **II** (35)		41
			SmI_2, THF, HMPA, MeOH, rt, 5 min	**I** (59) + **II** (23)		41
			SmI_2, THF, HMPA, n-Bu_3SnH, 65°, 2 h	**I** (17) + **II** (66)		41
C_6H_{11}	Me		SmI_2, THF, H_2O	**I** (9) + **II** (5)		40
C_6H_{11}	Et		SmI_2, THF, H_2O	**I** (25) + **II** (18)		40
Ph	t-Bu		SmI_2, THF, HMPA, t-$BuCO_2H$, rt, 3 min	**I** (16) + **II** (76)		41
Ph	t-Bu		SmI_2, THF, HMPA, n-Bu_3SnH, 65°, 4 h	**I** (7) + **II** (51)		41
Ph	$(CH_2)_2Ph$		SmI_2, THF, HMPA, t-$BuCO_2H$, rt, 3 min	**I** (53) + **II** (46)		41
Ph	$(CH_2)_2Ph$		SmI_2, THF, HMPA, n-Bu_3SnH, 65°, 2 h	**I** (19) + **II** (80)		41

Table III. REDUCTION OF ALDEHYDES AND KETONES (*Continued*)
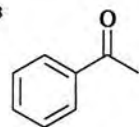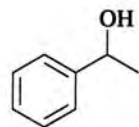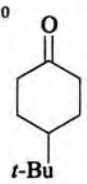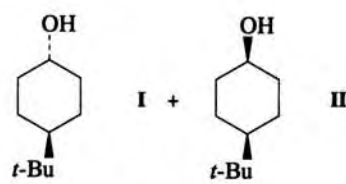
Substrate	Conditions	Product(s) and Yield(s) (%)		Refs.

C₈

	2 SmI_2, THF, MeOH, rt, 1 d	(80)		3
n-$C_7H_{15}CHO$	2 SmI_2, THF, MeOH, rt, 1 d	n-$C_7H_{15}CH_2OH$ (99)		3
n-$C_6H_{13}COMe$	2 SmI_2, THF, MeOH, rt, 1 d	n-$C_6H_{13}CHOHMe$ **I** (12)		3
	2 SmI_2, THF, H_2O, rt, 1 d	**I** (64)		3

C₁₀

	SmI_2, THF, HMPA, t-$BuCO_2H$	**I** (74) + **II** (26)		41
	SmI_2, THF, HMPA, n-Bu_3SnH	**I** (93) + **II** (7)		41

Table III. REDUCTION OF ALDEHYDES AND KETONES (*Continued*)
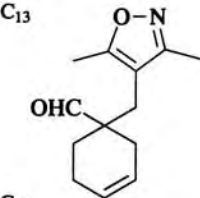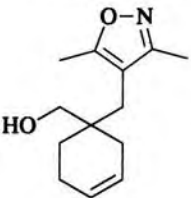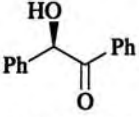
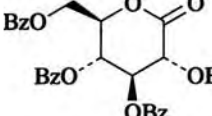| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{13}$	2 SmI$_2$, THF, rt, 24 h	(53)	25
C$_{14}$ PhCOCOPh	4 SmI$_2$, THF, MeOH, 6-8 LiNH$_2$, rt, 25 min	PhCHOHCHOHPh (10) + PhCH$_2$CHOHPh (5) + PhCH$_2$COPh (45) + PhCH$_2$OH (13)	42
	2 SmI$_2$, THF, HMPA, 2 quinidine, rt, 30 min	(77.5) 56.2 % ee	43
	2 SmI$_2$, THF, quinidine, rt	" (—) 18.8% ee	43
	2 SmI$_2$, THF, quinine, rt	" (—) 9.4% ee	43
	2 SmI$_2$, THF, cinchonidine, rt	" (—) 11.3% ee	43
	2 SmI$_2$, THF, *N*-[*N,N*-dimethyl-(*S*)-phenylalanyl]-(*S*)-1-phenylethylamine, rt	" (—) 15.7% ee	43
	2 SmI$_2$, THF, diethyl L-(+)-tartrate, rt	" (—) 7.1% ee	43

Table III. REDUCTION OF ALDEHYDES AND KETONES (*Continued*)
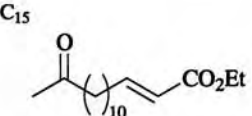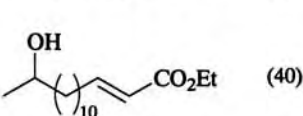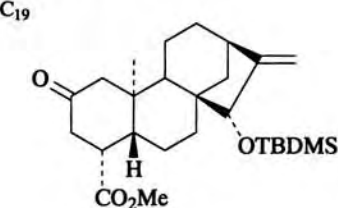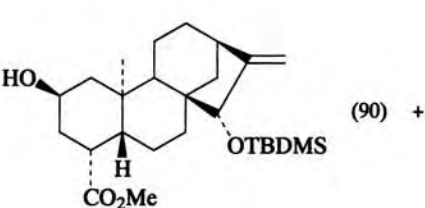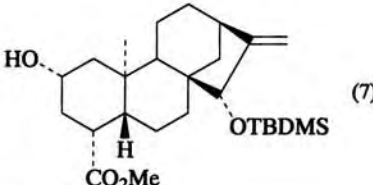
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
PhCOCHOHPh	4 SmI$_2$, THF, MeOH, 6-8 LiNH$_2$, rt, 3 s	PhCHOHCHOHPh (36) + PhCH$_2$CHOHPh (40) + PhCH$_2$COPh (tr) + PhCH$_2$OH (tr)	42
C$_{15}$	4 SmI$_2$, THF, HMPA, 65°, 1 h	(40)	44
C$_{19}$	SmI$_2$, THF, H$_2$O, rt, 10 min	(90) + (7)	45

Table IV. REDUCTION OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES
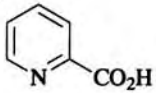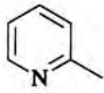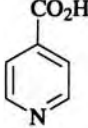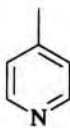
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
A. Carboxylic Acids			
C_6 (2-pyridyl)CO_2H	2 SmI_2, THF, H_3PO_4 (85%), rt, 3 s	2-methylpyridine (43)	46
4-(CO_2H)pyridine	2 SmI_2, THF, H_3PO_4 (85%), rt, 3 s	4-methylpyridine (48)	46
n-$C_5H_{11}CO_2H$	4 SmI_2, THF, H_2O, 8 NaOH, rt, 271 s	n-$C_5H_{11}CH_2OH$ (61)	47
C_7 o-$ClC_6H_4CO_2H$	4 SmI_2, THF, H_3PO_4 (85%), rt, 3 s	o-$ClC_6H_4CH_2OH$ (97)	46
m-$ClC_6H_4CO_2H$	"	m-$ClC_6H_4CH_2OH$ (96)	46
p-$ClC_6H_4CO_2H$	"	p-$ClC_6H_4CH_2OH$ (94)	46
$PhCO_2H$	4 SmI_2, THF, 10 h	$PhCH_2OH$ **I** (0)	47
	4 SmI_2, THF, H_2O, 8 NaOH, rt, 60 s	**I** (91)	47
	4 SmI_2, THF, H_2O, 10 NH_3, rt, 3 s	**I** (41)	47
	4 SmI_2, THF, H_2O, 8 $LiNH_2$, rt, 60 s	**I** (87)	47
	4 SmI_2, THF, H_3PO_4 (85%), rt, 3 s	**I** (91)	46

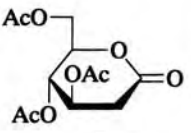Table IV. REDUCTION OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_6H_{11}CO_2H$	4 SmI_2, THF, H_2O, 8 NaOH, 58 s	$C_6H_{11}CH_2OH$ (78)	47
n-$C_6H_{13}CO_2H$	4 SmI_2, THF, H_2O, 8 NaOH, 291 s	n-$C_6H_{13}CH_2OH$ (57)	47
C_8 $PhCH_2CO_2H$	4 SmI_2, THF, H_2O, 8 NaOH, rt, 82 s	$PhCH_2CH_2OH$ (73)	47
o-$MeC_6H_4CO_2H$	4 SmI_2, THF, H_3PO_4 (85%), rt, 4 s	o-$MeC_6H_4CO_2H$ (91)	46
p-$MeC_6H_4CO_2H$	4 SmI_2, THF, H_3PO_4 (85%), rt, 4 s	p-$MeC_6H_4CO_2H$ (95)	46
n-$BuCH(Et)CO_2H$	4 SmI_2, THF, H_2O, 8 NaOH, rt, 10 s	n-$BuCH(Et)CH_2OH$ (94)	47
B. Carboxylic Acid Salts			
C_7 $PhCO_2Na$	4 SmI_2, THF, H_2O, rt, 60 s	$PhCH_2OH$ (92)	47
C. Carboxylic Acid Chlorides			
C_1 Ph_2NCOCl	2 THF, 6 H_2O, rt, 30 s	Ph_2NCHO (84)	48
C_7 $PhCOCl$	4 SmI_2, THF, H_3PO_4 (85%), rt, 3 s	$PhCH_2OH$ (31) + $PhCH_2CHOHPh$ (14) + $PhCHOHCHOHPh$ (40) + $PhCHOHCOPh$ (tr)	46
C_8 $PhCH_2COCl$	2 SmI_2, THF, 6 H_2O, rt, 30 s	$PhCH_2CH_2OH$ (22)	48

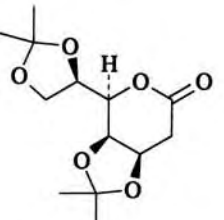Table IV. REDUCTION OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES (*Continued*)
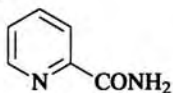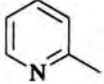
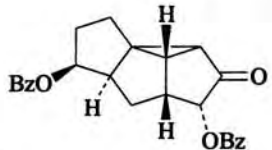|	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
		D. Carboxylic Acid Derivatives		
C_{14}				
	$(PhCO)_2O$	4 SmI$_2$, THF, MeOH, 8 LiOMe, rt, 46 min	PhCH$_2$OH **I** (12) + PhCHO **II** (38) + PhCO$_2$Me **III** (52)	42
		4 SmI$_2$, THF, MeOH, 8 KOH, rt, 7.6 min	**I** (50) + **II** (14) + **III** (16)	42
		4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 3 s	**I** (46) + **II** (13) + PhCH$_2$CHOHPh (22) + PhCHOHCHOHPh (9)	46
		E. Carboxylic Acid Esters		
C_7				
	PhCO$_2$Me	4 SmI$_2$, THF, MeOH, 12 LiNH$_2$, rt, 14 min	PhCH$_2$OH **I** (64)	42
		4 SmI$_2$, THF, MeOH, 8 LiOMe, rt, 27 min	**I** (59)	42
		4 SmI$_2$, THF, MeOH, 8 KOH, rt, 8 min	**I** (68)	42
		4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 3 s	**I** (72)	46
		F. Carboxylic Acid Amides and Derivatives		
C_6	(pyridine-2-CONH$_2$)	8 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 2 s	(2-methylpyridine) (88)	46

Table IV. REDUCTION OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES (*Continued*)
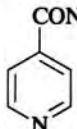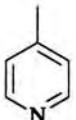
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	(4-CONH$_2$ pyridine)	8 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 3 s	(4-methylpyridine) (67)	46
C_7	o-HOC$_6$H$_4$CONH$_2$	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 3 s	o-HOC$_6$H$_4$CHO **I** (97)	46
	o-HOC$_6$H$_4$CONHOH	"	**I** (59) + o-HOC$_6$H$_4$CONH$_2$ **II** (40)	46
	o-HOC$_6$H$_4$CONHNH$_2$	4 SmI$_2$, THF, MeOH H$_3$PO$_4$ (85%), rt, 3 s	**I** (48) + **II** (50)	46
	o-ClC$_6$H$_4$CONH$_2$	"	o-ClC$_6$H$_4$CHO (>99)	46
	m-ClC$_6$H$_4$CONH$_2$	"	m-ClC$_6$H$_4$CHO (>99)	46
	p-ClC$_6$H$_4$CONH$_2$	"	p-ClC$_6$H$_4$CHO (>99)	46
	PhCONH$_2$	8 SmI$_2$, THF, H$_2$O, rt, 90 min	PhCH$_2$OH **I** (63) + PhCH$_2$NH$_2$ **II** (1)	46
		4 SmI$_2$, THF, MeOH 12 LiNH$_2$, rt, 180 s	**I** (81) + **II** (8)	42
		4 SmI$_2$, THF, MeOH 8 LiOMe, rt, 510 s	**I** (72) + **II** (4)	42
		4 SmI$_2$, THF, MeOH 8 KOH, rt, 123 s	**I** (82) + **II** (8)	42
		4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 3 s	PhCHO **I** (>99)	46
	PhCONHOH	"	**I** (91) + PhCONH$_2$ **II** (6)	46

Table IV. REDUCTION OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES (*Continued*)
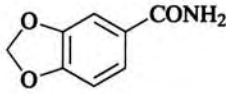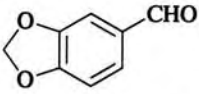
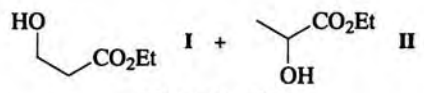| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
PhCONHNH$_2$	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 3 s	**I** (81) + **II** (17)	46
PhCONHPh	4 SmI$_2$, THF, MeOH, 12 LiNH$_2$, rt, 60 s	PhCH$_2$OH **I** (31) + PhCH$_2$NHPh **II** (20) + PhNH$_2$ **III** (28)	42
	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 3 s	**I** (4) + **II** (66) + PhCHO (23)	46

C$_8$

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
(methylenedioxy-benzamide)	"	(methylenedioxy-benzaldehyde) (>99)	46
PhCH$_2$CONH$_2$	4 SmI$_2$, THF, MeOH, H$_2$O, 6 LiNH$_2$, rt, 68 s	PhCH$_2$CH$_2$OH (56) + PhCH$_2$CH$_2$NH$_2$ (2)	42
	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 90 s	PhCH$_2$CHO (14)	46
o-MeC$_6$H$_4$CONH$_2$	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 4 s	o-MeC$_6$H$_4$CHO (90)	46
m-MeC$_6$H$_4$CONH$_2$	"	m-MeC$_6$H$_4$CHO (74)	46
p-MeC$_6$H$_4$CONH$_2$	"	p-MeC$_6$H$_4$CHO (91)	46

C$_9$

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
Ph(CH$_2$)$_2$CONH$_2$	4 SmI$_2$, THF, MeOH, H$_2$O, 6 LiNH$_2$, rt, 3 s	Ph(CH$_2$)$_3$OH (69) + Ph(CH$_2$)$_3$NH$_2$ (tr)	42
	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 4 min	Ph(CH$_2$)$_2$CHO (6)	46

Table V. REDUCTION OF CONJUGATED CARBONYL SUBSTRATES
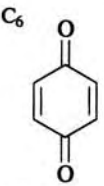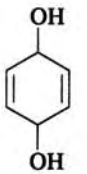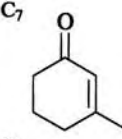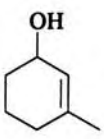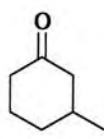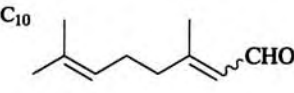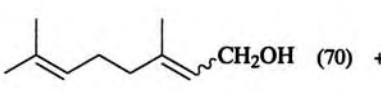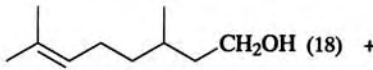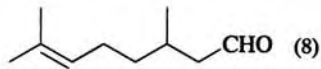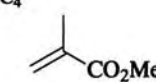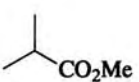
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
		A. Conjugated Aldehydes and Ketones		
C6		2 SmI₂, THF, MeOH, 65°, 5 min	(93)	49
C7		2 SmI₂, THF, MeOH, rt, 1 d	(67) + (28)	3
C9	Ph⌒CHO (trans)	"	Polymers	3
C10		"	CH₂OH (70) + CH₂OH (18) + CHO (8)	3
		B. Conjugated Esters		
C4		2 SmI₂, THF, HMPA, rt, 30 min	(67)	50

Table V. REDUCTION OF CONJUGATED CARBONYL SUBSTRATES (*Continued*)
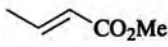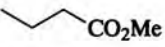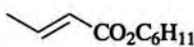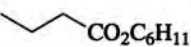
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
⟍⟍⟍CO_2Me	2 SmI_2, THF, HMPA, rt, 30 min	⟍⟍⟍CO_2Me (59)	50
⟍⟍⟍$CO_2C_6H_{11}$		⟍⟍⟍$CO_2C_6H_{11}$ **I**	
	2.5 SmI_2, THF, t-BuOH or $C_6H_{11}OH$, rt, 72 h	**I** (tr)	51
	2.5 SmI_2, THF, t-BuOH or $C_6H_{11}OH$, rt, DMF, 5 min	**I** (67)	51
	2.5 SmI_2, THF, t-BuOH or $C_6H_{11}OH$, rt, DMA, 2 min	**I** (92)	51
	2.5 SmI_2, THF, t-BuOH or $C_6H_{11}OH$, rt, TMU, 15 min	**I** (45)	51
	2.5 SmI_2, THF, t-BuOH or $C_6H_{11}OH$, rt, NMP, 15 min	**I** (10)	51
	2.5 SmI_2, THF, t-BuOH or $C_6H_{11}OH$, rt, HMPA, <1 min	**I** (7)	51
	2.5 SmI_2, THF, t-BuOH or $C_6H_{11}OH$, rt, $Me_2N(CH_2)_3NMe_2$, 6 h	**I** (82)	51
	2.5 SmI_2, THF, t-BuOH or $C_6H_{11}OH$, rt, $Me_2N(CH_2)_2NMe_2$, 24 h	**I** (61)	51
	2.5 SmI_2, THF, t-BuOH or $C_6H_{11}OH$, rt, $[Me_2N(CH_2)_2]_2NMe$, 24 h	No reaction	51

Table V. REDUCTION OF CONJUGATED CARBONYL SUBSTRATES (*Continued*)
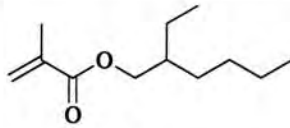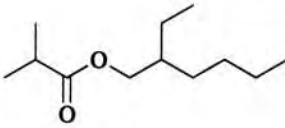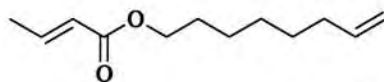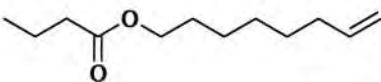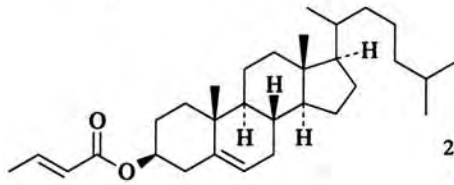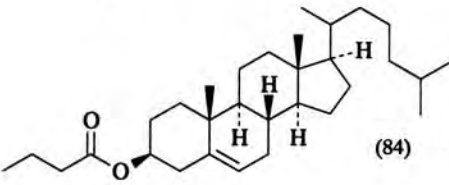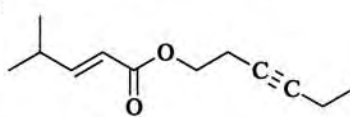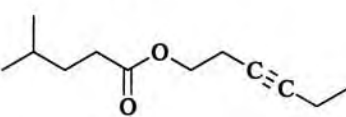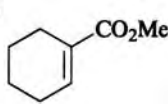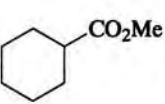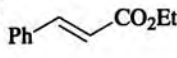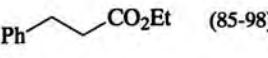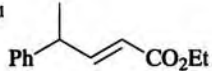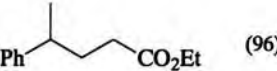
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
2-ethylhexyl methacrylate	2.5 SmI_2, THF, t-BuOH, DMA, rt, 15 min	2-ethylhexyl isobutyrate (78)	51
oct-7-enyl crotonate	2.5 SmI_2, THF, t-BuOH, DMA, rt, 2 min	oct-7-enyl butyrate (92)	51
cholesteryl crotonate	2.5 SmI_2, THF, t-BuOH, DMA, rt, 15 min	cholesteryl butyrate (84)	51
C₆ but-3-ynyl 4-methylpent-2-enoate	2.5 SmI_2, THF, t-BuOH, DMA, rt, 2 min	but-3-ynyl 4-methylpentanoate (99)	51
C₇ methyl cyclohex-1-ene-1-carboxylate CO_2Me	2 SmI_2, THF, HMPA, rt, 30 min	methyl cyclohexanecarboxylate CO_2Me (64)	50
C₉ Ph⟍CO_2Et	2 SmI_2, THF, MeOH, rt, 1 d	Ph⟍CO_2Et (85–98)	3
C₁₁ Ph⟍CO_2Et	2.5 SmI_2, THF, EtOH, DMA, rt, 12 min	Ph⟍CO_2Et (96)	51

Table V. REDUCTION OF CONJUGATED CARBONYL SUBSTRATES (*Continued*)
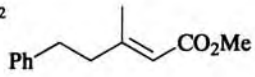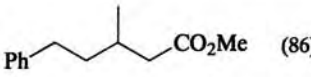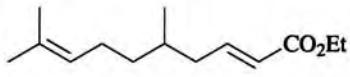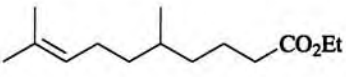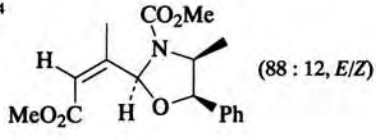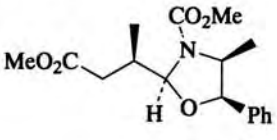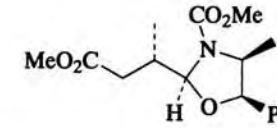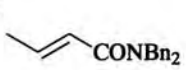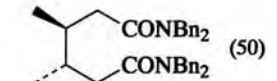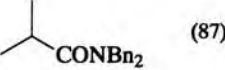
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{12}$ Ph—CH$_2$CH$_2$—C(CH$_3$)=CH—CO$_2$Me	2.5 SmI$_2$, THF, MeOH, DMA, rt, 10 min	Ph—CH$_2$CH$_2$—CH(CH$_3$)—CH$_2$CO$_2$Me (86)	51
(CH$_3$)$_2$C=CH—CH$_2$CH$_2$—CH(CH$_3$)—CH$_2$—CH=CH—CO$_2$Et	2.5 SmI$_2$, THF, EtOH, DMA, rt, 2 min	(CH$_3$)$_2$C=CH—CH$_2$CH$_2$—CH(CH$_3$)—CH$_2$CH$_2$CH$_2$CO$_2$Et (97)	51
C$_{14}$ oxazolidine substrate (88 : 12, *E/Z*)	SmI$_2$, THF, H$_2$O, rt	**I** (35) I:II = 9 + **II**	52

C. Conjugated Amides

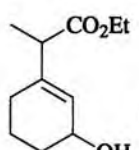| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_4$ CH$_3$CH=CH—CONBn$_2$	2.5 SmI$_2$, THF, *t*-BuOH, DMA, rt, 5 min	CH$_3$CH$_2$CH$_2$—CONBn$_2$ (30) + dimer Bn$_2$NOC—CH$_2$—CH(CH$_3$)—CH(CH$_3$)—CH$_2$—CONBn$_2$ (50)	51
CH$_2$=C(CH$_3$)—CONBn$_2$	2.5 SmI$_2$, THF, *t*-BuOH, DMA, rt, 15 min	(CH$_3$)$_2$CH—CONBn$_2$ (87)	51

Table V. REDUCTION OF CONJUGATED CARBONYL SUBSTRATES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_5$ CH$_3$CH=C(CH$_3$)—CONBn$_2$	2.5 SmI$_2$, THF, *t*-BuOH, DMA, rt, 3 min	CH$_3$CH$_2$—CH(CH$_3$)—CONBn$_2$ (99)	51
C$_9$ Ph—CH=CH—CONH$_2$	2 SmI$_2$, THF, HMPA, rt, 1 min	Ph—CH$_2$CH$_2$—CONH$_2$ (65)	50

D. Conjugated Carboxylic Acids

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_4$ HO$_2$C—CH=CH—CO$_2$H	2 SmI$_2$, THF, HMPA, rt, 5 min	HO$_2$C—CH$_2$CH$_2$—CO$_2$H (99)	50
CH$_2$=C(CH$_3$)—CO$_2$H	2 SmI$_2$, THF, HMPA, rt, 1 min	(CH$_3$)$_2$CH—CO$_2$H (80)	50
C$_5$ HO$_2$C—CH=C(CH$_3$)—CO$_2$H	2 SmI$_2$, THF, HMPA, rt, 5 min	HO$_2$C—CH$_2$—CH(CH$_3$)—CO$_2$H (88)	50
C$_6$ CH$_3$CH$_2$—CH=C(CH$_3$)—CO$_2$H	2 SmI$_2$, THF, HMPA, rt, 30 min	CH$_3$CH$_2$CH$_2$—CH(CH$_3$)—CO$_2$H (91)	50
C$_7$ (CH$_3$)C=C(CO$_2$H)(CH$_2$CO$_2$H)	2 SmI$_2$, THF, HMPA, rt, 30 min	(CH$_3$)$_2$CH—CH(CO$_2$H)—CH$_2$CO$_2$H (75)	50

304

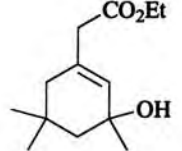305

Table V. REDUCTION OF CONJUGATED CARBONYL SUBSTRATES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
Ph⤒CO₂H	4 SmI₂, THF, H₂O, 8 NaOH, rt, 5 s	Ph⤒OH **I** (39) + Ph⤒CO₂H **II** (7)	47
	2 SmI₂, THF, MeOH, rt, 1 d	**II** (98)	3
	2 SmI₂, THF, HMPA, rt, 1 min	**II** (95)	50
CO₂H / Ph	2 SmI₂, THF, HMPA, rt, 1 min	Ph / CO₂H (60)	50
C₁₂ Ph—CO₂H / CO₂H	2 SmI₂, THF, HMPA, rt, 30 min	Ph / CO₂H / CO₂H (53)	50
E. Conjugated Anhydrides			
C₄ O⤒O⤒O	2 SmI₂, THF, HMPA, rt, 5 min	O⤒O⤒O (96)	50

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES
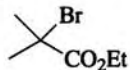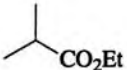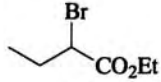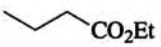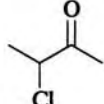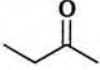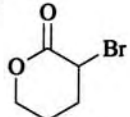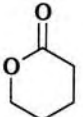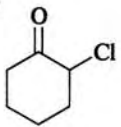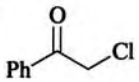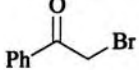
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	A. α-Halo Carbonyl Substrates		
C₄ (2-bromo-2-methylpropanoate, CO₂Et)	2 SmI₂, THF, MeOH, -78°	(isobutyrate) CO₂Et (98)	53
(2-bromobutanoate, CO₂Et)	2 Sm, 6 TMSCl, 6 NaI, MeCN, MeOH, -40°, 0.5 h	CO₂Et (73)	8
(3-chlorobutan-2-one)	"	(62)	8
C₅ (3-bromo-tetrahydropyran-2-one)	"	(δ-valerolactone) (79)	8
C₆ (2-chlorocyclohexanone)	"	**I** (88)	8
	2 SmI₂, THF, MeOH, -78°	**I** (100)	53
C₈ (Ph—CO—CH₂Cl)	2 Sm, 6 TMSCl, 6 NaI, MeCN, MeOH, -40°, 0.5 h	Ph—CO—CH₃ (80)	8
(Ph—CO—CH₂Br)	2 SmI₂, THF, MeOH, rt, 2 min	" (84)	49
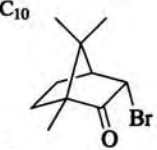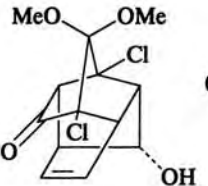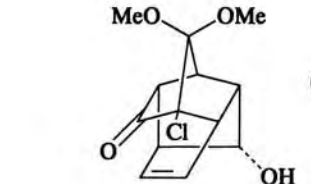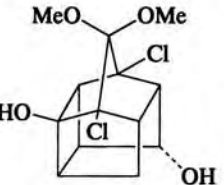
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{10}$	2 SmI$_2$, THF, MeOH, -78°	(85)	53
C$_{11}$	2.8 SmI$_2$, THF, MeOH, -78°, 1 h	(68) +	29
		(1)	
	5.5 SmI$_2$, THF, MeOH, -78°	(70)	29
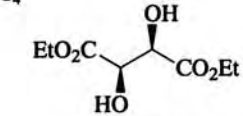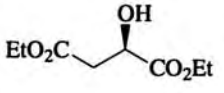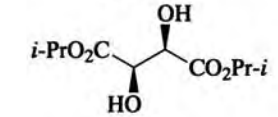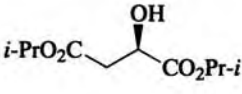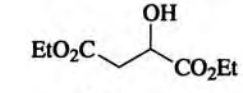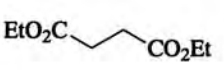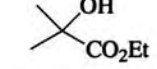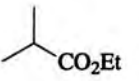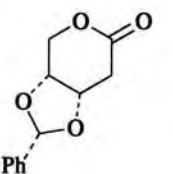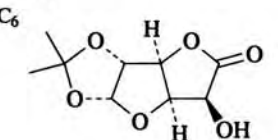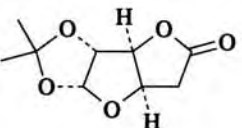
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
		B. α-Hydroxy and Vinylogous Hydroxy Carbonyl Substrates	
C$_4$	3 SmI$_2$, THF, HO(CH$_2$)$_2$OH, rt, 20 min	(72)	54
	3 SmI$_2$, THF, HO(CH$_2$)$_2$OH, rt, 1 h	(99)	54
	3 SmI$_2$, THF, HMPA, pivalic acid, 20-22°, 2-4 h	(71)	54
	"	(73)	54
C$_5$	3 SmI$_2$, THF, HMPA, HO(CH$_2$)$_2$OH, rt, 3 h	(90)	55
C$_6$	3 SmI$_2$, THF, HMPA, HO(CH$_2$)$_2$OH, rt, <1 min	(75)	55

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Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)

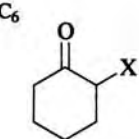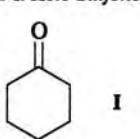| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
(OH, CO₂Et enol structure)	2 SmI₂, THF	(CO₂Et product) (90)	56
(OH, CO₂Et structure)	3 SmI₂, THF, HMPA, pivalic acid, 20–22°, 2–4 h	(CO₂Et product) (89)	54
(ketone, OH structure)	2 SmI₂, THF, Ac₂O, –78°	(ketone product) (59)	53
C₇ (acetonide lactone OH structure)	3 SmI₂, THF, HMPA, HO(CH₂)₂OH, rt, <1 min	(lactone product) (72)	55
(acetonide lactone OH structure)	3 SmI₂, THF, HMPA, HO(CH₂)₂OH, rt, <1 min	(lactone product) (99)	55

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)

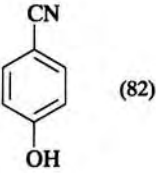| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
(acetonide lactone OH structure)	3 SmI₂, THF, HMPA, HO(CH₂)₂OH, rt, <1 min	(lactone product) (98)	55
C₈ Ph–CH(OH)–CO_2Me	3 SmI₂, THF, HMPA, pivalic acid, 20–22°, 2–4 h	Ph–CH₂–CO_2Me (75)	54
C₁₂ n-C_5H_{11}–CO–CH(OH)–C_5H_{11}-n	2 SmI₂, THF, MeOH, –78°	n-C_5H_{11}–CO–CH₂–C_5H_{11}-n (29)	53
C₂₀ (decalin ketone OH structure)	2 SmI₂, THF, t-BuOH, rt, 12 h	(decalin ketone product) (87)	57

C. α-*Alkoxy and α-Silyloxy Carbonyl Substrates*

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₂ $MeOCH_2CO_2C_8H_{17}$-n	2.5–3 SmI₂, THF, HMPA, n-$C_8H_{17}OH$, 20–22°, 3 h	$MeCO_2C_8H_{17}$-n (73)	54

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONY L AND RELATED SUBSTRATES (*Continued*)
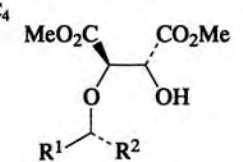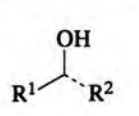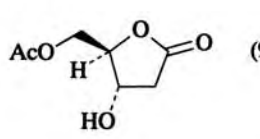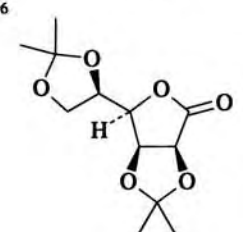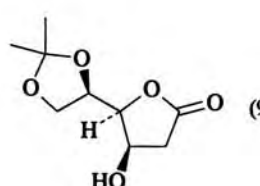
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_4$ R^1 — R^2 *n*-C$_9$H$_{19}$ — Me C$_6$H$_{11}$ — Me *i*-Pr — *n*-Bu	 SmI$_2$, THF, HMPA, MeOH " "	**I** **I** (—) **I** (—) **I** (—)	 58 58 58
C$_5$ 	4.5 SmI$_2$, THF, HO(CH$_2$)$_2$OH, rt, <1 min	(98)	55
C$_6$ 	4.5 SmI$_2$, THF, HO(CH$_2$)$_2$OH, rt, <1 min	(98)	55

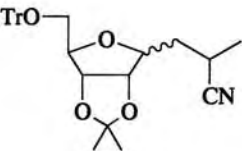Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
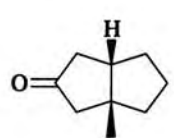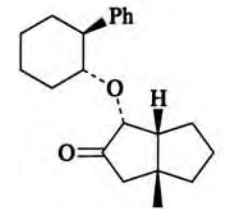
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	SmI$_2$, THF	(69)	59
C$_8$ 	2.5-3 SmI$_2$, THF, HMPA, MeOH, 20-22°, 3 h	(89)	54
C$_9$ 	2.5-3 SmI$_2$, THF, HMPA, MeOH, 20-22°, 12 h	(95)	54
	SmI$_2$, THF	**I** (90)	60
	SmI$_2$, THF	**I** (—)	60

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{11}$	2 SmI$_2$, THF, MeOH, -78°	(92)	61
	SmI$_2$, THF	(85)	60
C$_{12}$	SmI$_2$, THF	I + II (95) I:II = 3	62
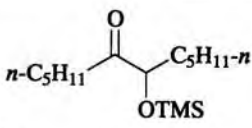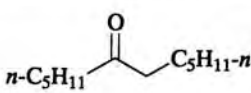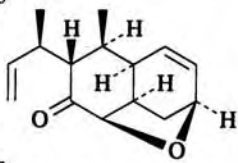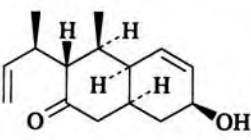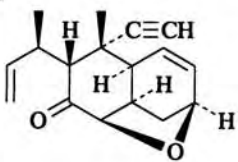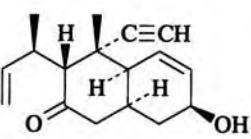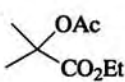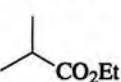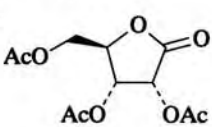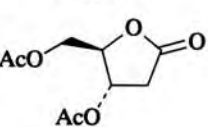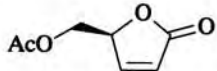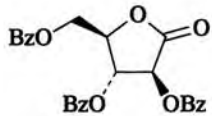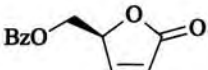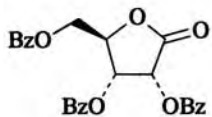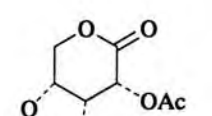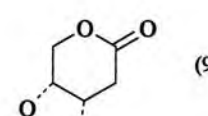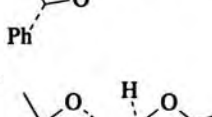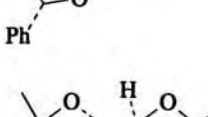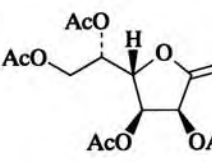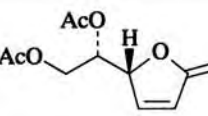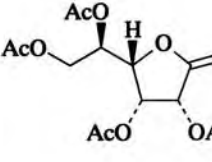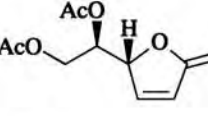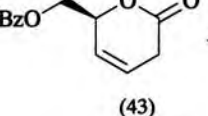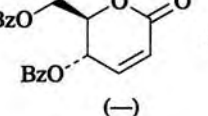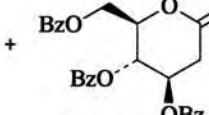
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
n-C$_5$H$_{11}$COCH(OTMS)C$_5$H$_{11}$-n	2 SmI$_2$, THF, MeOH, -78°	n-C$_5$H$_{11}$COCH$_2$C$_5$H$_{11}$-n (98)	53
C$_{15}$	2.4 SmI$_2$, THF, -78°, 0.5 h	(—)	63
C$_{17}$	2.4 SmI$_2$, THF, -78°	(—)	64

D. α-Carboalkoxy and α-Tosyloxy Carbonyl Substrates

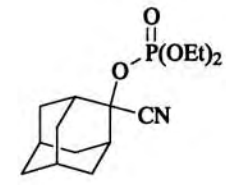| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_3$ MeCH(OAc)CO$_2$Et	2 SmI$_2$, THF, MeOH, -78°	No reaction	53
C$_4$ (CH$_3$)$_2$C(OAc)CO$_2$Et	2.5-3 SmI$_2$, THF, HMPA, EtOH, 20-22°, <5 min	(CH$_3$)$_2$CHCO$_2$Et (>95)	54
C$_5$		I + II	

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	3-4 SmI₂, THF, pivalic acid, rt, 20 min	**I** + **II** (47), **I:II** = 36:64	65
	3-4 SmI₂, THF, AcOH, rt, 20 min	**II** (30)	65
	3 SmI₂, THF, rt, 30 min	(60)	55
	"	" (55)	55
	3 SmI₂, THF, HO(CH₂)₂OH, rt, <1 min	(92)	55
C₆	"	(81)	55

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	3-4 SmI₂, THF, pivalic acid, rt, 20 min	**I** (67)	65
	3-4 SmI₂, THF, AcOH, rt, 20 min	**I** (60)	65
	3-4 SmI₂, THF, pivalic acid, rt, 20 min	**I** (58)	65
	3-4 SmI₂, THF, AcOH, rt, 20 min	**I** (60)	65
	3 SmI₂, THF, HO(CH₂)₂OH, rt	(43) + (—) + (—)	55

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
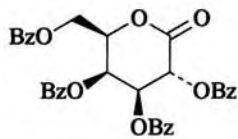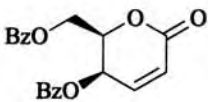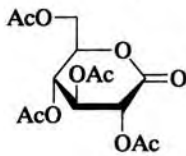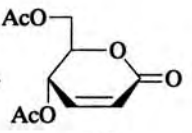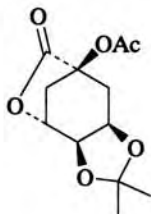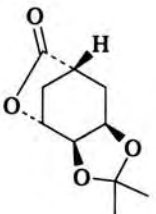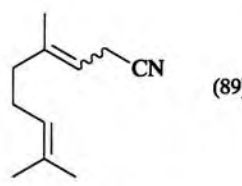
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	3 SmI$_2$, THF, rt, 30 min	(48)	55
	3-4 SmI$_2$, THF, pivalic acid, rt, 20 min	I + II (47), I:II = 1:1	65
	3-4 SmI$_2$, THF, AcOH, rt, 20 min	II (68)	65
C$_7$	3 SmI$_2$, THF, HMPA HO(CH$_2$)$_2$OH, rt, 1 h	(85)	55

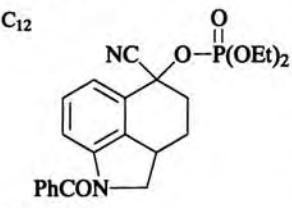Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
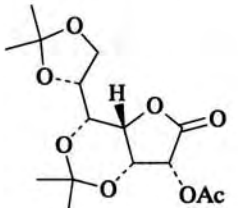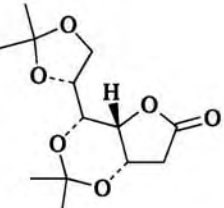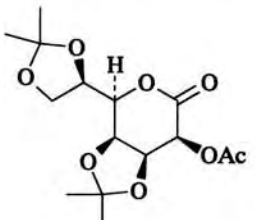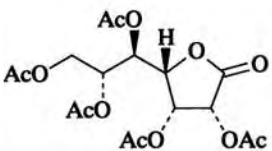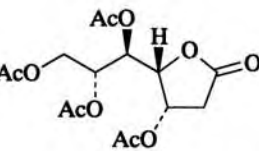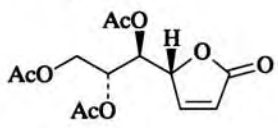
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	3 SmI$_2$, THF, HO(CH$_2$)$_2$OH, rt, <1 min	(94)	55
	3 SmI$_2$, THF, HO(CH$_2$)$_2$OH, rt, <1 min	(99)	55
		I + II	

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
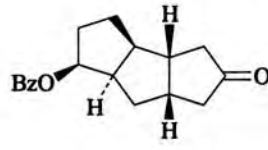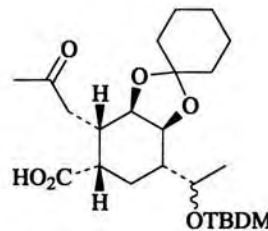
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	3-4 SmI$_2$, THF, pivalic acid, rt, 20 min	I + II (54), I:II = 42:58	65
	3-4 SmI$_2$, THF, AcOH, rt, 20 min	II (67)	65
n-C$_5$H$_{11}$CH(OAc)CO$_2$Me	2.5-3 SmI$_2$, THF, HMPA, MeOH, 20-22°, <5 min	n-C$_5$H$_{11}$CH$_2$CO$_2$Me (>95)	54
C$_8$ PhCH(OAc)CO$_2$Me	2.5-3 SmI$_2$, THF, HMPA, MeOH, 20-22°, 1 min	PhCH$_2$CO$_2$Me (96)	54
C$_{11}$ PhCOCH(OAc)(CH$_2$)$_3$I	2 SmI$_2$, THF, MeOH, -78°	PhCO(CH$_2$)$_4$I (87)	53
	2 SmI$_2$, THF, MeOH, -78 to 25241	(65)	61
C$_{12}$	2 SmI$_2$, THF, FeCl$_3$ (cat.), rt, 15 min	(84)	66
n-C$_5$H$_{11}$COCH(OAc)C$_5$H$_{11}$-n	2 SmI$_2$, THF, MeOH, -78°	n-C$_5$H$_{11}$COCH$_2$C$_5$H$_{11}$-n (75)	53
n-C$_5$H$_{11}$COCH(O$_2$CBn)C$_5$H$_{11}$-n	"	" (100)	53
n-C$_5$H$_{11}$COCH(OTs)C$_5$H$_{11}$-n	"	" (94)	53

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
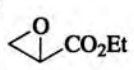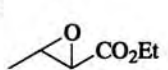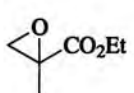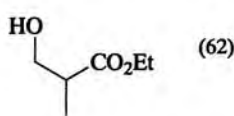
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
E. α,β-Epoxy Carbonyl Substrates			
C$_3$	2.25 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	I + II (50) I : II = 17	67
C$_4$		I + II	
	2.5 SmI$_2$, THF, rt, 1 h	I + II (5)	67
	2.5 SmI$_2$, THF, HMPA, rt, 1 min	I + II (19)	67
	2.5 SmI$_2$, THF, HMPA, i-PrOH, rt, 1 min	I + II (34), I:II = 10	67
	2.5 SmI$_2$, THF, DMAE, rt, 30 min	I + II (60), I:II = 20	67
	2.5 SmI$_2$, THF, HMPA, TMEDA, i-PrOH, rt, 1 min	I + II (46), I:II = 200	67
	2.5 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	I + II (68), I:II = >200	67
	2.5 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	(62)	67

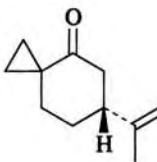Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_5$ (epoxide with CO$_2$Me, NBn$_2$)	2 SmI$_2$, THF, -78 to 0°, 2 h	(OH, CO$_2$Me, NBn$_2$) (70)	68
C$_6$ (cyclohexanone epoxide)	2 SmI$_2$, THF, MeOH, -90°	(cyclohexanone, OH) (74)	69
(epoxide CO$_2$Et)	2.25 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	(HO, CO$_2$Et) (62)	67
(ketone epoxide dimethyl)	2 SmI$_2$, THF, MeOH, -90°	(ketone, OH) (79)	69
C$_7$ n-Bu (epoxide ketone)	2 SmI$_2$, THF, MeOH, -90°	n-Bu (ketone, OH) (97)	69
C$_8$ (cyclohexane epoxide acetyl)	2 SmI$_2$, THF, MeOH, -90°	(acetyl cyclohexanol) (79)	69

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_9$ (spiro epoxide CO$_2$Et)	2.25 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	(OH, CO$_2$Et) (76)	67
(cyclohexyl epoxide CO$_2$Et) >98% ee	2.25 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	(OH, CO$_2$Et) (—), >98% ee	67
(dimethyl cyclohexanone epoxide)	2 SmI$_2$, THF, MeOH, -90°	(dimethyl cyclohexanone, OH) (82)	69
(ketone epoxide C$_5$H$_{11}$-n)	2 SmI$_2$, THF, MeOH, -90°	(ketone, OH, C$_5$H$_{11}$-n) (81)	69
(ketone epoxide C$_5$H$_{11}$-n) 95% ee	2 SmI$_2$, THF, MeOH, -90°	(ketone, OH, C$_5$H$_{11}$-n) (94), 90% ee	69
C$_{10}$ (epoxide ketone isopropenyl)	2 SmI$_2$, THF, MeOH, -90°	(epoxide ketone isopropenyl) (34)	69

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
  1.7 : 1 mixture of diastereomers	2.25 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	(68) 3.8 : 1 mixture of diastereomers	67
	2 SmI$_2$, THF, MeOH, -90°	(79)	69
C$_{11}$ 	2 SmI$_2$, THF, -78 to 0°, 2 h	(70)	68
	2 SmI$_2$, THF, MeOH, -90°	(76)	69

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
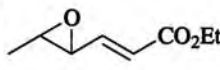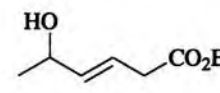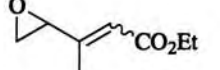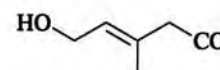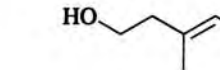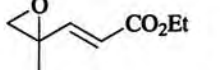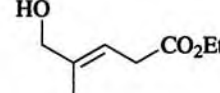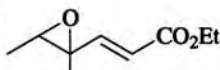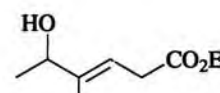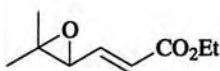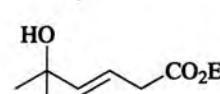
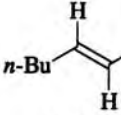| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
F. Vinylogous Epoxy Carbonyl and Related Substrates			
C$_6$ 	2.1 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	(73)	67
	2 SmI$_2$, THF, EtOH, -98°	(77) + (4)	70
	2.1 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	(74)	67
C$_7$ 	2.1 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	(80)	67
	2.1 SmI$_2$, THF, HMPA, DMAE, rt, 1 min	(90)	67
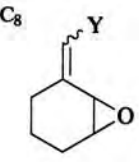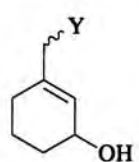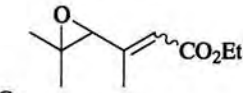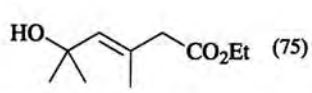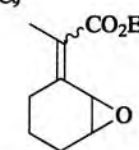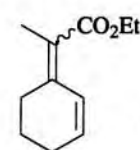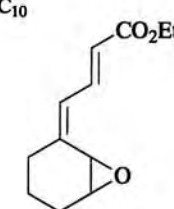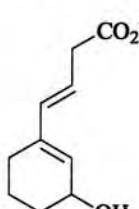
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_8$ (epoxide with =Y group)		I (hydroxy cyclohexene with Y)	
Y = CO$_2$Et	2 SmI$_2$, THF, MeOH or EtOH, -90°	I (68)	70
Y = CN	"	I (71)	70
Y = COMe	"	I (69)	70
(epoxide, =C(Me)CO$_2$Et)	2 SmI$_2$, THF, EtOH, -98°	HO—...CO$_2$Et (75)	70
C$_9$ (=CHCO$_2$Et epoxide)	2 SmI$_2$, THF, EtOH, -98°	(CO$_2$Et cyclohexenol) (78) + (CO$_2$Et cyclohexadiene) (9)	70
C$_{10}$ (dienoate epoxide, CO$_2$Et)	2 SmI$_2$, THF, EtOH, -90°	(CO$_2$Et dienol) (65)	70

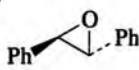| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
(CO$_2$Et epoxide bicyclic)	2 SmI$_2$, THF, EtOH, -98°	(lactone) (43) + (cyclohexanol CO$_2$Et) (44)	70
n-C$_5$H$_{11}$ epoxide, 95% ee, CO$_2$Et	2 SmI$_2$, THF, EtOH, -98°	HO n-C$_5$H$_{11}$...CO$_2$Et (84), 95% ee	70
C$_{11}$ (CO$_2$Et dimethyl epoxide)	2 SmI$_2$, THF, EtOH, -98°	(CO$_2$Et cyclohexenol) (81)	70
(epoxide with =CH—Y)		I (OH diene with Y)	
Y = COSEt	2 SmI$_2$, THF, MeOH or EtOH, -90°	I (80)	70
Y = S(O$_2$)Ph	"	I (82) + (OH ...S(O$_2$)Ph) (5)	70
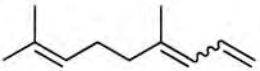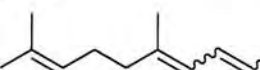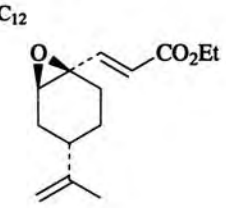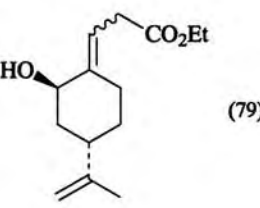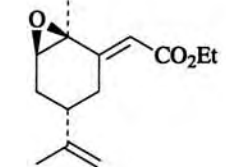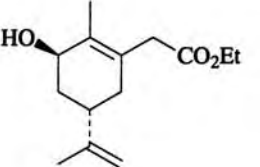
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
$Y = PO(OEt)_2$	2 SmI$_2$, THF, MeOH or EtOH, -90°	**I** (84)	70
$Y = H$	2 SmI$_2$, THF, MeOH or EtOH, rt	**I** (69) + (9)	70
$Y = Me$	2 SmI$_2$, THF, MeOH or EtOH, 0°	**I** (42) + (32)	70
$Y = SPh$	"	**I** 54)	70
C$_{12}$	2 SmI$_2$, THF, EtOH, -98°	(79)	70
	2 SmI$_2$, THF, EtOH, -98°	(81)	70
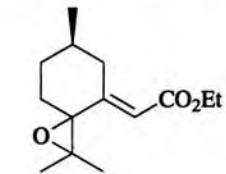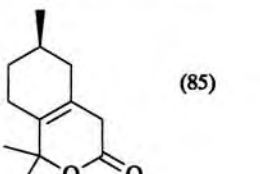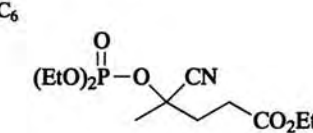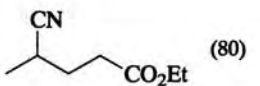
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	2 SmI$_2$, THF, EtOH, -98°	(85)	70

G. α-Keto Sulfides, α-Keto Sulfoxides, and α-Keto Sulfones

C$_6$		**I**	
$X = SPh$	2 SmI$_2$, THF, MeOH, -78°	**I** (76)	53
$X = S(O)Ph$	"	**I** (64)	53
$X = S(O_2)Ph$	"	**I** (88)	53

H. α-Cyano Phosphates

| C$_6$ | 3 SmI$_2$, THF, *t*-BuOH, rt, 2 h | (80) | 71 |

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
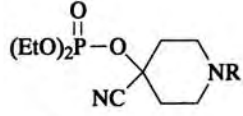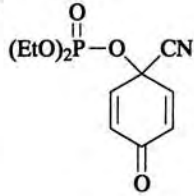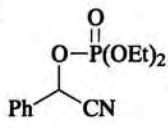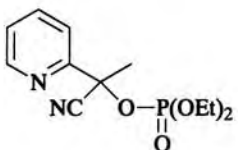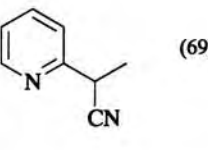
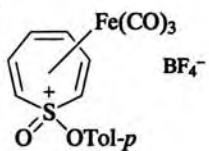| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
(EtO)$_2$P(O)—O—[piperidine with NC and NR]		NC—[piperidine]—NR **I**	
R = Bn	3 SmI$_2$, THF, *t*-BuOH, rt, 2 h	**I** (79)	71
R = CO$_2$CH=CH$_2$	3 SmI$_2$, THF, *t*-BuOH, rt, 1 h	**I** (92)	71
R = Ts	3 SmI$_2$, THF, *t*-BuOH, rt, 15 min	**I** (92)	72
C$_7$ (EtO)$_2$P(O)—O—[cyclohexadienone with CN]	3 SmI$_2$, THF, *t*-BuOH, rt, 12 min	[phenol with CN] (82)	72
C$_8$ O—P(OEt)$_2$, Ph, CN	3 SmI$_2$, THF, *t*-BuOH, rt, 2 h	Ph—CN (85)	71
[pyridine]—C(Me)(CN)—O—P(OEt)$_2$	3 SmI$_2$, THF, *t*-BuOH, rt, 10 min	[pyridine]—CH(Me)(CN) (69)	71

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
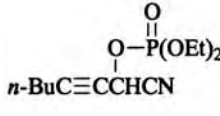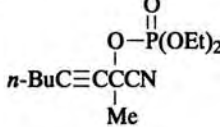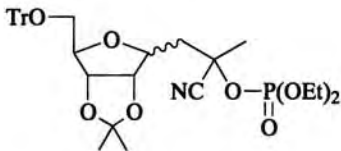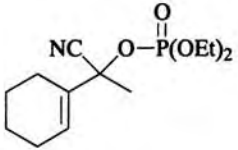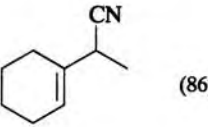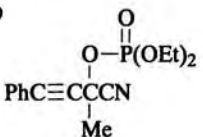
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
n-BuC≡CCHCN—O—P(OEt)$_2$	3 SmI$_2$, THF, *t*-BuOH, rt, 10 min	*n*-BuC≡CCH$_2$CN (60)	7 2
C$_9$ *n*-BuC≡CCCN(Me)—O—P(OEt)$_2$	3 SmI$_2$, THF, *t*-BuOH, rt, 30 min	*n*-BuC≡CCH(Me)CN (98)	72
TrO—[furanose with NC, O-P(OEt)$_2$, isopropylidene]	3 SmI$_2$, THF, *t*-BuOH, rt, 3 h	TrO—[furanose with CN, isopropylidene] (61)	72
NC—C(Me)—O—P(OEt)$_2$ [cyclohexene]	3 SmI$_2$, THF, *t*-BuOH, rt, 15 min	[cyclohexene]—CH(Me)(CN) (86)	71
C$_{10}$ PhC≡CCCN(Me)—O—P(OEt)$_2$	3 SmI$_2$, THF, *t*-BuOH, rt, 30 min	PhC≡CCH(Me)CN (85)	72

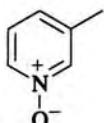Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
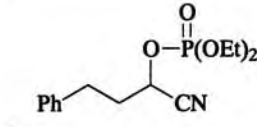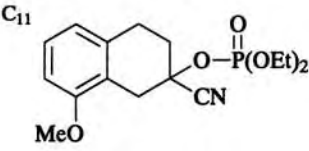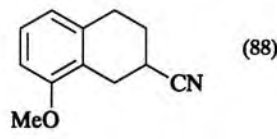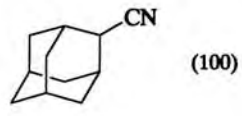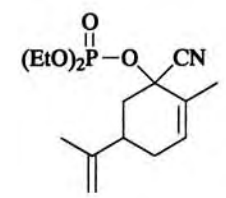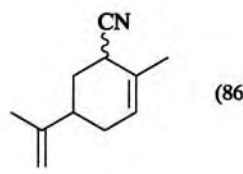
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	3 SmI$_2$, THF, *t*-BuOH, rt, 3 h	(82)	71
C$_{11}$	3 SmI$_2$, THF, *t*-BuOH, rt, 4 h	(88)	72
	3 SmI$_2$, THF, *t*-BuOH, rt, 4 h	(100)	71
	3 SmI$_2$, THF, *t*-BuOH, rt, 30 min	(86)	71

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)
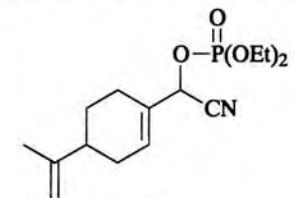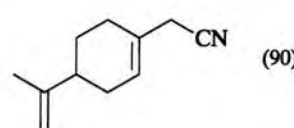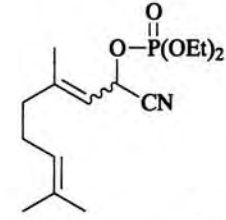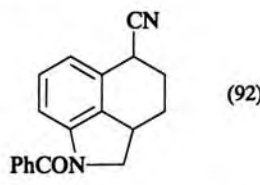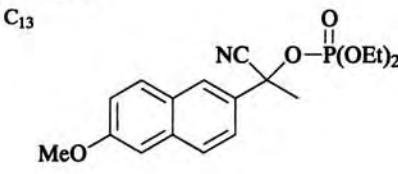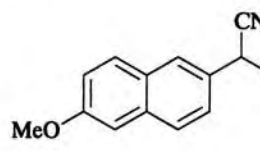
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	3 SmI$_2$, THF, *t*-BuOH, rt, 30 min	(90)	72
	3 SmI$_2$, THF, *t*-BuOH, rt, 2 h	(89)	71
C$_{12}$	3 SmI$_2$, THF, *t*-BuOH, rt, 30 min	(92)	72
C$_{13}$	3 SmI$_2$, THF, *t*-BuOH, rt, 10 min	(96)	71

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{14}$	3 SmI$_2$, THF, *t*-BuOH, rt, 10 min	(94)	71
	3 SmI$_2$, THF, *t*-BuOH, rt, 10 min	(90)	71
C$_{17}$	3 SmI$_2$, THF, *t*-BuOH, rt, 10 min	(97)	71
	3 SmI$_2$, THF, *t*-BuOH, rt, 3 h	(97)	71

Table VI. REDUCTIVE CLEAVAGE OF α-HETEROSUBSTITUTED CARBONYL AND RELATED SUBSTRATES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{20}$		I	
R = C$_8$H$_{17}$	3 SmI$_2$, THF, *t*-BuOH, rt, 3 h	I (83), 3α:3β = 3:2	71
R = OMOM	3 SmI$_2$, THF, *t*-BuOH, rt, 3 h	I (84), 3α:3β = 3:2	71
R = OH	3 SmI$_2$, THF, *t*-BuOH, rt, 4 h	I (92), 3α:3β = 4:1	71
C$_{21}$	3 SmI$_2$, THF, *t*-BuOH, rt, 15 min	(93)	72
C$_{28}$	3 SmI$_2$, THF, *t*-BuOH, rt, 10 min	(76)	71

I. Miscellaneous Substrates

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_6$	2 SmI$_2$, THF, MeOH, -78°	(94)	53

Table VII. REDUCTIVE CLEAVAGE OF CYCLOPROPYL KETONES
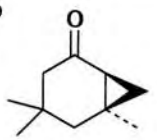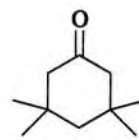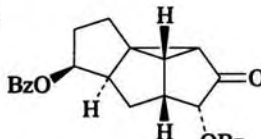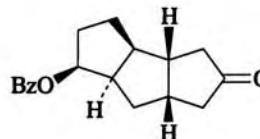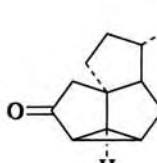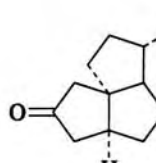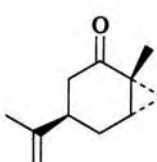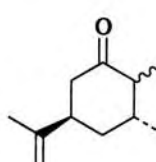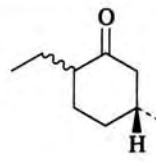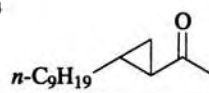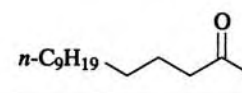
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{10}$	SmI$_2$, THF, DMPU, rt, 5 min	(39)	74
C$_{11}$	2 SmI$_2$, THF, MeOH, -78 to 25°	(65)	61
	2 SmI$_2$, THF, MeOH, 25°	(86)	61
	SmI$_2$, THF, DMPU, rt, 5 min	(34)	74

Table VII. REDUCTIVE CLEAVAGE OF CYCLOPROPYL KETONES (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	2 SmI$_2$, Fe(DBM)$_3$ (cat.), THF, *t*-BuOH	(81)	73
C$_{14}$ n-C$_9$H$_{19}$	SmI$_2$, THF, DMPU, rt, 5 min	n-C$_9$H$_{19}$ (49)	74

Table VIII. DEOXYGENATION REACTIONS
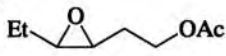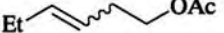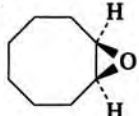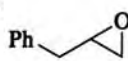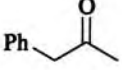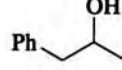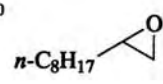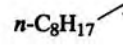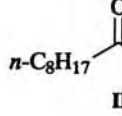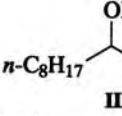
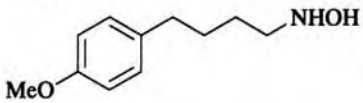| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
A. Epoxides			
C$_6$ Et—(epoxide)—OAc	2 SmI$_2$, THF, HMPA, DMAE, rt, 2.5 h	Et—CH=CH—CH$_2$CH$_2$—OAc (88), *E:Z* = 3:1	75
C$_8$ (cyclooctene oxide, *cis*, H, O, H)	2 SmI$_2$, THF, *t*-BuOH, rt, 24 h	(cyclooctene) **I** (65)	3
	2 SmI$_2$, THF, *t*-BuOH, 65°, 2 h	**I** (95)	3
C$_9$ Ph—CH$_2$—(epoxide)	2 SmI$_2$, THF, 65°, 4 d	**I** (92)	3
	2 SmI$_2$, THF, *t*-BuOH, rt, 24 h	Ph—CH$_2$—CH=CH$_2$ **I** (82) +	3
		Ph—CH$_2$—CO—CH$_3$ **II** + Ph—CH$_2$—CH(OH)—CH$_3$ **III**	
		II + III (18)	
C$_{10}$ *n*-C$_8$H$_{17}$—(epoxide)	4 SmI$_2$, THF, *t*-BuOH, rt, 2 d	*n*-C$_8$H$_{17}$—CH=CH$_2$ **I** (92) +	3
		n-C$_8$H$_{17}$—CO—CH$_3$ **II** + *n*-C$_8$H$_{17}$—CH(OH)—CH$_3$ **III**	
		II + III (6)	

Table VIII. DEOXYGENATION REACTIONS (*Continued*)
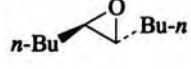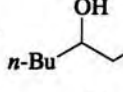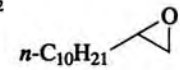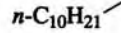
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
n-Bu—(epoxide)—Bu-*n*	2 SmI$_2$, THF, *t*-BuOH, rt, 3 h	*n*-Bu—CH=CH—*n*-Bu + *n*-Bu—CH(OH)—CH$_2$—*n*-Bu	3
		I (76) (17)	
	4 SmI$_2$, THF, *t*-BuOH, rt, 2 d	**I** (96)	3
	2 SmI$_2$, THF, HMPA, DMAE, rt, 24 h	**I** (95) *E:Z* = 3:1	75
	2 SmI$_2$, THF, HMPA, glutaric anhydride, rt, 1 h	**I** (69) *E:Z* = 3:1	75
C$_{12}$ *n*-C$_{10}$H$_{21}$—(epoxide)		*n*-C$_{10}$H$_{21}$—CH=CH$_2$ **I**	
	1.2 SmI$_2$, THF, HMPA, rt, 2 h	**I** (37)	75
	2 SmI$_2$, THF, DMAE, rt, 24 h	**I** (88)	75
	2 SmI$_2$, THF, HMPA, DMAE, rt, 1.5 h	**I** (95)	75
	2 SmI$_2$, THF, HMPA, glutaric anhydride, rt, 1 h	**I** (90)	75

Table VIII. DEOXYGENATION REACTIONS (*Continued*)
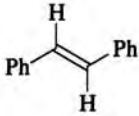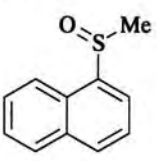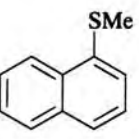
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{14}$	2 SmI$_2$, THF, *t*-BuOH, rt, 30 min	**I** (94), *trans:cis* = 2:1	3
	2 SmI$_2$, THF, *t*-BuOH, 65°, 5 min	**I** (98), *trans:cis* = 2:1	3
B. Sulfoxides			
C$_7$ Ph(Me)SO	2.2 SmI$_2$, THF, HMPA, 20°, 1 min	PhSMe (93)	41,75
C$_8$ Bu$_2$SO	2.2 SmI$_2$, THF, HMPA, 20°, 1 min	Bu$_2$S (99)	41,75
	2.2 SmI$_2$, THF, 20°, 24 h	" (71)	41,75
C$_9$ *p*-Tol(Et)SO	2 SmI$_2$, THF, 65°, 4 h	*p*-TolSEt (77)	3
C$_{11}$	2 SmI$_2$, THF, 65°, 1 h	(90)	3
C$_{12}$ Ph$_2$SO	2.2 SmI$_2$, THF, HMPA, 20°, 1 min	Ph$_2$S (94)	41,75
	2.5 SmI$_2$, THF, rt, 2 d	" (95)	3
	2 SmI$_2$, THF, 65°, 2 h	" (90)	3

Table VIII. DEOXYGENATION REACTIONS (*Continued*)
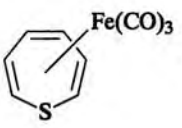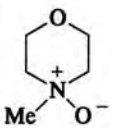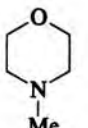
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C. Sulfones and Related Substrates			
C$_6$	15 SmI$_2$, THF, 0°	(38)	77
C$_7$ Ph(Me)SO$_2$	4.4 SmI$_2$, TH F, HMPA, 20°, 10 min	PhSMe (99)	41,75
	4.4 SmI$_2$, THF, 20°, 24 h	" (0)	41,75
C$_8$ Bu$_2$SO$_2$	4.4 SmI$_2$, THF, HMPA, 65°, 8 h	Bu$_2$S (26)	41,75
C$_{12}$ Ph$_2$SO$_2$	4.4 SmI$_2$, THF, HMPA, 20°, 1 min	Ph$_2$S (93)	41,75
	4.4 SmI$_2$, THF, 20°, 24 h	" (0)	41,75
D. N-Oxides			
C$_4$	2.2 SmI$_2$, THF, HMPA, 20°, 1 min	(98)	76

Table VIII. DEOXYGENATION REACTIONS (*Continued*)
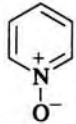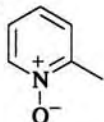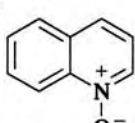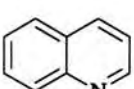
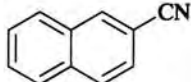| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5	2 SmI_2, THF, 65°, 10 min	(80)	49
C_6	2 SmI_2, THF, rt, <5 min	(83)	49
	2 SmI_2, THF, rt, 15-20 min	(80)	49
C_9	2.2 SmI_2, THF, HMPA, 20°, 1 min	(96)	41,75
C_{24} $(C_8H_{17})_3NO$	2 SmI_2, THF, 65°, 10 min	$(C_8H_{17})_3N$ (79)	49
	E. Phosphine Oxides		
C_{18} Ph_3PO	2.2 SmI_2, THF, HMPA, 65°, 16 h	Ph_3P (75)	41,75
	2.2 SmI_2, THF, 65°, 24 h	" (0)	41,75

Table VIII. DEOXYGENATION REACTIONS (*Continued*)

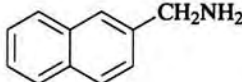| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	F. Arsine Oxides		
C_{18} Ph_3AsO	2 SmI_2, THF, 65°, 5 min	Ph_3As (82)	49
	G. Miscellaneous Deoxygenations and Desulfurizations		
C_4 *n*-BuNCS	SmI_2, THF, HMPA, rt, 0.5 h	*n*-BuNC (79)	78
C_6 PhNCS	SmI_2, THF, HMPA, rt, 0.5 h	PhNC (83)	78
C_7 *p*-TolNCS	SmI_2, THF, HMPA, rt, 0.5 h	*p*-TolNC (81)	78
C_{12} $(Bu_3Sn)_2O$	2.2 SmI_2, THF, HMPA, 20°, 1 min	$(Bu_3Sn)_2$ (92)	41,75
	2.2 SmI_2, THF, 20°	" (0)	41,75

Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
		A. Nitro Compounds		
C_2	(EtO)$_2$CH-CH$_2$NO$_2$	4 SmI$_2$, THF, MeOH, rt, 3 min	(EtO)$_2$CH-CH$_2$NHOH (58)	79
		1. 6 SmI$_2$, THF, MeOH, rt, 8 h 2. *p*-PhC$_6$H$_4$COCl, CH$_2$Cl$_2$, Et$_3$N, rt, 16 h	Complex mixture	79
	TBDPSO-CH$_2$CH$_2$NO$_2$	4 SmI$_2$, THF, MeOH, rt, 3 min	TBDPSO-CH$_2$CH$_2$NHOH (79)	79
		1. 6 SmI$_2$, THF, MeOH, rt, 8 h 2. *p*-PhC$_6$H$_4$COCl, CH$_2$Cl$_2$, Et$_3$N, rt, 16 h	TBDPSO-CH$_2$CH$_2$NHCOC$_6$H$_4$Ph-*p* (80)	79
C_3	TBDPSO-CH$_2$CH$_2$CH$_2$NO$_2$	4 SmI$_2$, THF, MeOH, rt, 3 min	TBDPSO-CH$_2$CH$_2$CH$_2$NHOH (83)	79
		1. 6 SmI$_2$, THF, MeOH, rt, 8 h 2. *p*-PhC$_6$H$_4$COCl, CH$_2$Cl$_2$, Et$_3$N, rt, 16 h	TBDPSO-CH$_2$CH$_2$CH$_2$NHCOC$_6$H$_4$Ph-*p* (76)	79
	TBDPSO-CH$_2$CH(CH$_3$)NO$_2$	4 SmI$_2$, THF, MeOH, rt, 3 min	TBDPSO-CH$_2$CH(CH$_3$)NHOH (85)	79
		1. 6 SmI$_2$, THF, MeOH, rt, 8 h 2. *p*-PhC$_6$H$_4$COCl, CH$_2$Cl$_2$, Et$_3$N, rt, 16 h	TBDPSO-CH$_2$CH(CH$_3$)NHCOC$_6$H$_4$Ph-*p* (79)	79

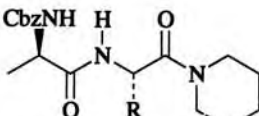## Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS (*Continued*)

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4	MeO$_2$C-CH$_2$CH$_2$CH$_2$NO$_2$	4 SmI$_2$, THF, MeOH, rt, 3 min	MeO$_2$C-CH$_2$CH$_2$CH$_2$NHOH (complex mixture)	79
	TBDPSO-CH$_2$C(CH$_3$)$_2$NO$_2$		TBDPSO-CH$_2$C(CH$_3$)$_2$NHOH (93)	79
		1. 6 SmI$_2$, THF, MeOH, rt, 8 h 2. *p*-PhC$_6$H$_4$COCl, CH$_2$Cl$_2$, Et$_3$N, rt, 16 h	TBDPSO-CH$_2$C(CH$_3$)$_2$NHCOC$_6$H$_4$Ph-*p* (93)	79
C_6	PhNO$_2$	8 SmI$_2$, THF, MeOH, rt, 5 min	PhNH$_2$ **I** (85)	49
		"	**I** (25) + PhN=NPh (25)	80
	p-nitroaniline (4-O$_2$N-C$_6$H$_4$-NH$_2$)	8 SmI$_2$, THF, MeOH, rt, 5 min	*p*-phenylenediamine (4-H$_2$N-C$_6$H$_4$-NH$_2$) (89)	49
	1-nitro-cyclohexanone ethylene ketal	4 SmI$_2$, THF, MeOH, rt, 3 min	1-(N-hydroxyamino)-cyclohexanone ethylene ketal, NHOH (42)	79

344

345
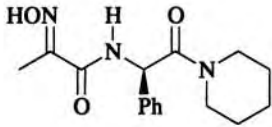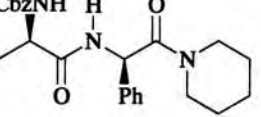
Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS (*Continued*)
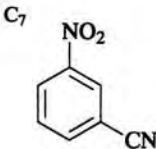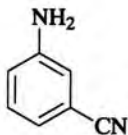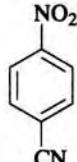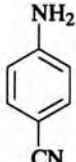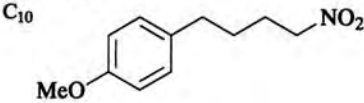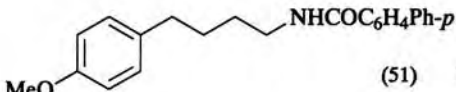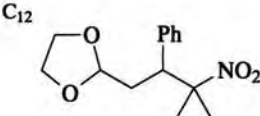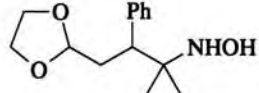
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. 6 SmI$_2$, THF, MeOH, rt, 8 h 2. *p*-PhC$_6$H$_4$COCl, CH$_2$Cl$_2$, Et$_3$N, rt, 16 h	Complex mixture	79
C$_7$	6 SmI$_2$, THF, MeOH, 5 min	(95)	80
	6 SmI$_2$, THF, MeOH, rt, 5 min	(84)	80
C$_{10}$	4 SmI$_2$, THF, MeOH, rt, 3 min	(72)	79
	1. 6 SmI$_2$, THF, MeOH, rt, 8 h 2. *p*-PhC$_6$H$_4$COCl, CH$_2$Cl$_2$, Et$_3$N, rt, 16 h	(51)	79
C$_{12}$	4 SmI$_2$, THF, MeOH, rt, 3 min	(88)	79

Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS (*Continued*)
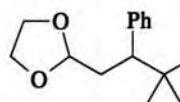
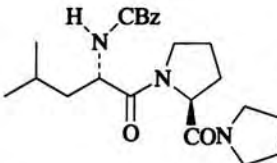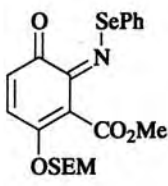| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. 6 SmI$_2$, THF, MeOH, rt, 8 h 2. *p*-PhC$_6$H$_4$COCl, CH$_2$Cl$_2$, Et$_3$N, rt, 16 h	(81)	79
	B. Nitriles		
C$_7$ PhCN	4 SmI$_2$, THF, MeOH, rt	No reaction	80
	8 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 6 min	PhCH$_2$NH$_2$ (99)	46
	8 SmI$_2$, THF, KOH (50%), rt, 25 min	" (91)	46
o-ClC$_6$H$_4$CN	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 5 s	*o*-ClC$_6$H$_4$CH$_2$NH$_2$ **I** (76)	46
	4 SmI$_2$, THF, KOH (50%), rt, 3 min	**I** (26) + PhCH$_2$NH$_2$ **II** (40)	46
	8 SmI$_2$, THF, KOH (50%), rt, 4 min	**I** (6) + **II** (77)	46
p-ClC$_6$H$_4$CN	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 10 s	*p*-ClC$_6$H$_4$CH$_2$NH$_2$ **I** (83)	46
	4 SmI$_2$, THF, KOH (50%), rt, 5 min	**I** (39) + PhCH$_2$NH$_2$ **II** (24)	46
	8 SmI$_2$, THF, KOH (50%), rt, 3 min	**I** (12) + **II** (56)	46

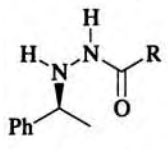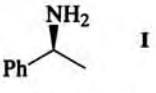Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS (*Continued*)

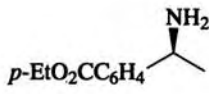|	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	o-HOC$_6$H$_4$CN	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 30 s	o-HOC$_6$H$_4$CH$_2$NH$_2$ (90)	46
		8 SmI$_2$, THF, KOH (50%), rt, 9 min	" (88)	46
	p-HOC$_6$H$_4$CN	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 30 s	p-HOC$_6$H$_4$CH$_2$NH$_2$ (72)	46
		8 SmI$_2$, THF, KOH (50%), rt, 10 min	" (81)	46
C$_8$	o-MeC$_6$H$_4$CN	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 35 s	o-MeC$_6$H$_4$CH$_2$NH$_2$ **I** (52) + (o-MeC$_6$H$_4$CH$_2$)$_2$NH **II** (10)	46
		4 SmI$_2$, THF, KOH (50%), rt, 2 min	**I** (58) + **II** (8)	46
		8 SmI$_2$, THF, KOH (50%), rt, 12 min	**I** (70) + **II** (16)	46
	p-MeC$_6$H$_4$CN	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 10 s	p-MeC$_6$H$_4$CH$_2$NH$_2$ **I** (55) + (p-MeC$_6$H$_4$CH$_2$)$_2$NH **II** (14)	46
		4 SmI$_2$, THF, KOH (50%), rt, 6 min	**I** (64)	46
		8 SmI$_2$, THF, KOH (50%), rt, 12 min	**I** (83) + **II** (2)	46
	PhCH$_2$CN	4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 50 s	Ph(CH$_2$)$_2$CN (48)	46
		4 SmI$_2$, THF, KOH (50%), rt, 35 min	" (58)	46

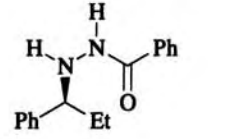Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS (*Continued*)
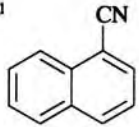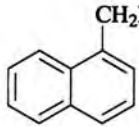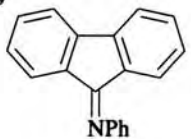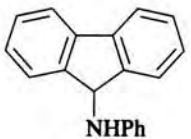
	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{11}$		4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 10 s	(71)	46
		4 SmI$_2$, THF, KOH (50%), rt, 5 min	" (83)	46
		4 SmI$_2$, THF, H$_3$PO$_4$ (85%), rt, 5 s	(84)	46
		4 SmI$_2$, THF, KOH (50%), rt, 4 min	" (86)	46
C$_{12}$	n-C$_{11}$H$_{23}$CN	4 SmI$_2$, THF, rt, 2 MeOH	No reaction	80

<p style="text-align:center">C. Imines</p>

	Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{13}$	PhCH=NPh	2.5 SmI$_2$, THF, MeOH, rt, 24 h	PhCH$_2$NHPh (80)	80
C$_{19}$		2 SmI$_2$, THF, 65°, 1 h	(97)	81
	Ph$_2$C=NPh	2 SmI$_2$, THF, 65°, 1 h	Ph$_2$CHNHPh (98)	81

Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS (*Continued*)
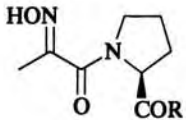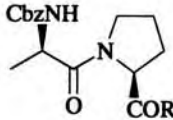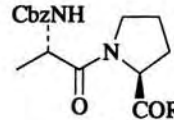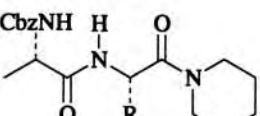
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
		D. Oximes and Related Substrates	

C₃

	Conditions	Product(s)	Refs.
R = OMe	1. 5 SmI₂, THF, MeOH, -40°, 1 h 2. CbzCl, pyridine	**I** (54) + **II** (10)	82
R = OBu-*t*	"	**I** (60) + **II** (7)	82
R = —N(pyrrolidine)	"	**I** (81) + **II** (1)	

R = Me	"	**I** (56) + **II** (14)	82
R = *i*-Pr		**I** (69) + **II** (8)	82
R = *t*-Bu		**I** (66) + **II** (7)	82

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.

C₄

Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₆	1. 5 SmI$_2$, THF, MeOH, -40° 2. CbzCl, pyridine	(69) + (6)	82
C₇ PhCH=NOH	4 SmI$_2$, THF, MeOH, 8 LiNH$_2$, rt, 3 s	PhCH$_2$NH$_2$ (45) + PhCH$_2$OH (3)	42
	4 SmI$_2$, THF, 4 MeOH, rt, 5 min	PhCH(NH$_2$)CH$_2$Ph (75) + PhCH$_2$NHCH$_2$Ph (25)	80
	SmI$_2$, THF, MeOH, -10°	(74)	83

E. *Azo Compounds*

C₁₂ PhN=NPh	2 SmI$_2$, THF, MeOH, rt, 5 min	PhNHNHPh (95)	49

Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS (*Continued*)
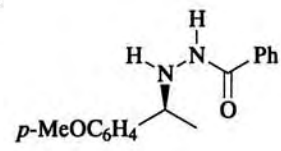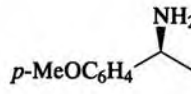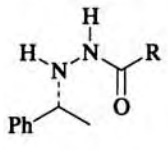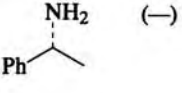
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	8 SmI$_2$, THF, MeOH, rt, 24 h	PhNH$_2$ (50)	80

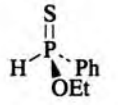F. *Hydrazines and Related Substrates*

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₈	2.2 SmI$_2$, THF, MeOH, rt, 0.5 h	(—)	84
		I	
R = Ph, 89% ee	"	**I** (72), 89% ee	84
R = *p*-MeOC$_6$H$_4$	"	**I** (—)	84
R = *p*-Me$_2$NC$_6$H$_4$	"	**I** (—)	84
	"	(—)	84

Table IX. REDUCTION OF NITROGEN-BASED FUNCTIONAL GROUPS (*Continued*)
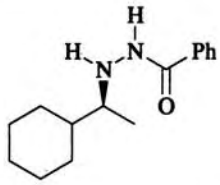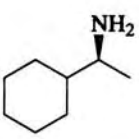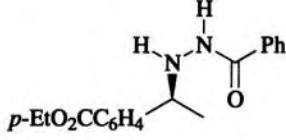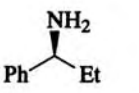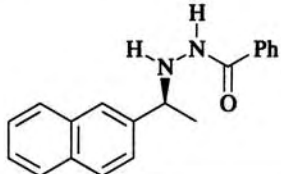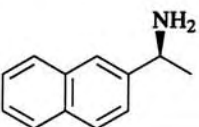
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
 C$_9$	2.2 SmI$_2$, THF, MeOH, rt, 0.5 h	(—)	84
	"	(—)	84
 C$_{12}$	"	(—)	84
PhNHNHPh	2 SmI$_2$, THF, rt, 4 d	PhNH$_2$ (55)	80
	2.2 SmI$_2$, THF, MeOH, rt, 0.5 h	(—)	84

Table X. REDUCTION OF MISCELLANEOUS FUNCTIONAL GROUPS
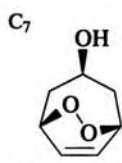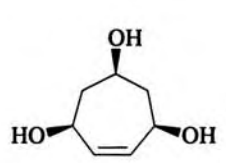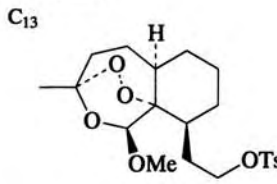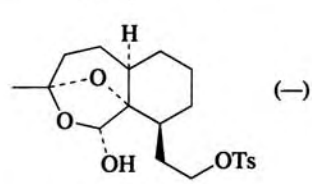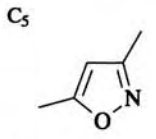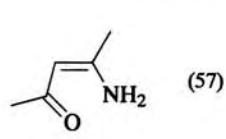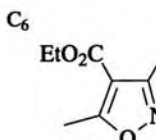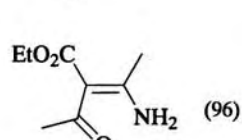
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
A. Peroxides			
C$_7$	SmI$_2$, THF	(77)	85
C$_{13}$	SmI$_2$, THF, 25°	(—)	86
B. Isoxazoles			
C$_5$	2 SmI$_2$, THF, rt, 1 h	(57)	25
C$_6$	2 SmI$_2$, THF, rt, 1 h	(96)	25

Table X. REDUCTION OF MISCELLANEOUS FUNCTIONAL GROUPS (*Continued*)
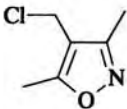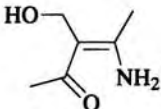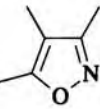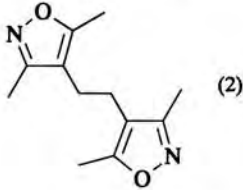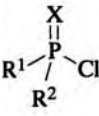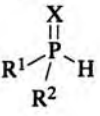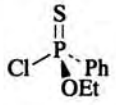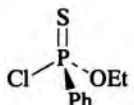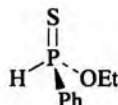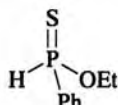
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	2 SmI$_2$, THF, 1 h		25

C. Halo Phosphine Oxides and Sulfides

R^1	R^2	X			
OEt	OEt	O	2 SmI$_2$, THF, 65°, 3 h	I (10)	87
OEt	OEt	S	2 SmI$_2$, THF, rt, 7 d	I (20)	87
Ph	OEt	O	2 SmI$_2$, THF, rt, 7 d	I (0)	87
Ph	OEt	S	2 SmI$_2$, THF, rt, 48 h	I (91)	87
Ph	Ph	O	2 SmI$_2$, THF, rt, 35 min	I (75) + Ph$_2$P(O)P(O)Ph$_2$ (7)	87
Ph	Ph	S	2 SmI$_2$, THF, rt, 40 min	I (89)	87

Table X. REDUCTION OF MISCELLANEOUS FUNCTIONAL GROUPS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
90% ee	2 SmI$_2$, THF, rt, 48 h	(83), 20% ee	87
90% ee	2 SmI$_2$, THF, rt, 60 h	" (83), 4.5% ee	87
88% ee	2 SmI$_2$, THF, rt, 48 h	(80), 19% ee	87
91% ee	2 SmI$_2$, THF, rt, 60 h	(85), racemic	87

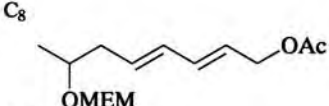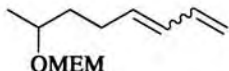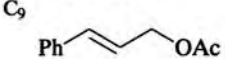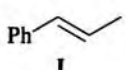*D. Pd-Catalyzed Reduction of Allylic and Propargylic Carboxylates*
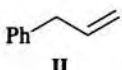
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_8$	2 SmI$_2$, Pd(PPh$_3$)$_4$ (1 mol%), THF, *i*-PrOH, rt, 2 h	(79)	88
C$_9$	2 SmI$_2$, Pd(PPh$_3$)$_4$ (1 mol%), THF, *i*-PrOH, rt, 1 h	Ph⌣ (20) + Ph⌣ (80) I II	88
	2 SmI$_2$, PdCl$_2$ (1 mol%), PPh$_3$ (4 mol%), THF, *i*-PrOH, rt, 1 h	I (20) + II (80)	88

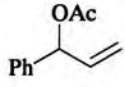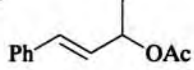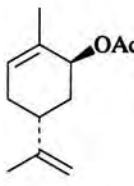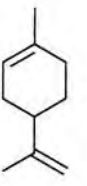Table X. REDUCTION OF MISCELLANEOUS FUNCTIONAL GROUPS (*Continued*)
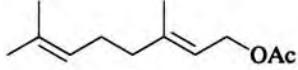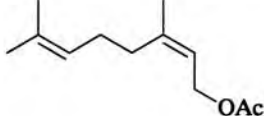
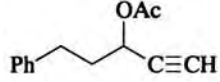| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
OAc, Ph (1-phenylallyl acetate)	2 SmI$_2$, Pd(PPh$_3$)$_4$ (1 mol%), THF, *i*-PrOH, rt, 1 h	**I** (20) + **II** (80)	88
C$_{10}$ Ph ⟶ OAc (crotyl-type acetate)	2 SmI$_2$, Pd(PPh$_3$)$_4$ (1 mol%), THF, *i*-PrOH, rt, 1 h	Ph ⟶ (67) + Ph ⟶ (14)	88
OAc (cyclohexenyl acetate, enantiomerically enriched)	2 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrOH, 65°, 8 h	(81), racemic	88
OAc (geranyl/neryl acetate)	2 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrOH, 65°, 2 h	**I** (81) + **II** (4) + **III** (6)	88
OAc	2 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrOH, 65°, 2 h	**I** (9) + **II** (72) + **III** (14)	88

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{11}$ OAc, Ph ⟶ (phenyl dienyl acetate)	2 SmI$_2$, Pd(PPh$_3$)$_4$ (1 mol%), THF, *i*-PrOH, rt, 1 h	Ph ⟶ (44) + Ph ⟶ (38) + Ph ⟶ (6)	88
OAc, Ph ⟶ C≡CH	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrCHOHPr-*i*, 40°, 2 h	Ph ⟶ C=C=CH$_2$ (H) (71) + Ph ⟶ C≡CH (4)	89
OAc, Ph ⟶ C≡CTMS	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrCHOHPr-*i*, 40°, 2 h	Ph ⟶ C=C=C(H)(TMS) (54) + Ph ⟶ C≡CTMS (22)	89
C$_{12}$ OAc, Ph ⟶ C≡CTMS (methyl)	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrCHOHPr-*i*, 40°, 2 h	Ph ⟶ C(Me)=C=C(H)(TMS) (70) + Ph ⟶ C≡CTMS (12)	89
C$_{13}$ OAc, *n*-BuC≡C ⟶ C$_6$H$_{13}$-*n*	2 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrOH, 40°, 2 h	*n*-Bu(H)C=C=C(C$_6$H$_{13}$-*n*)(H) (83) + *n*-BuC≡C ⟶ C$_6$H$_{13}$-*n* (8)	89

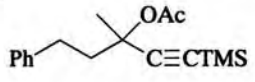Table X. REDUCTION OF MISCELLANEOUS FUNCTIONAL GROUPS (*Continued*)
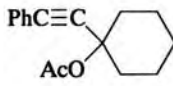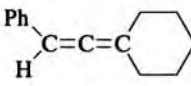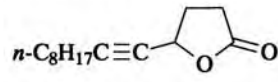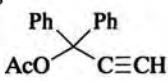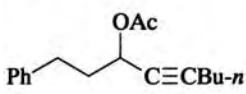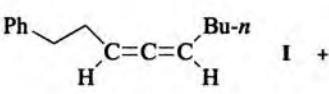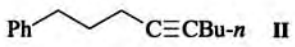
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{14}$	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (2 mol%), THF, *i*-PrOH, rt, 2 h	(90)	89
	1. 2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrCHOHPr-*i*, 40°, 2 h 2. CH$_2$N$_2$	(66)	89
C$_{15}$	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (1 mol%), THF, *i*-PrOH, rt, 2 min	(95)	89
	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, Y, 40°, 2 h	**I** + **II**	89

Y	I + II	I:II
i-PrOH	(74) + (11)	6.7:1
H$_2$O	(—)	1:1.5
MeOH	(—)	2:1
i-PrCO$_2$H	(—)	3:1
PhOH	(—)	9:1
t-BuOH	(—)	15:1
Ph$_3$COH	(—)	17:1
i-PrCHOHPr-*i*	(—)	20:1

360

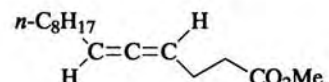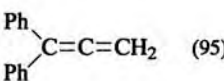Table X. REDUCTION OF MISCELLANEOUS FUNCTIONAL GROUPS (*Continued*)
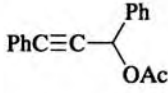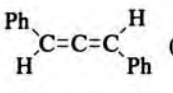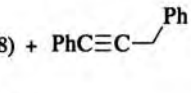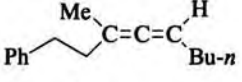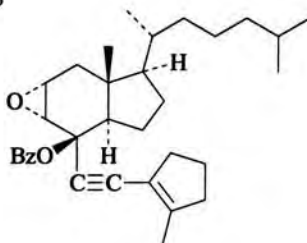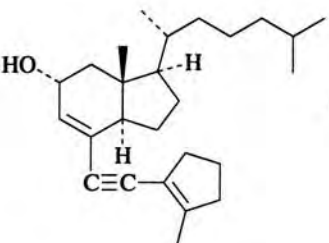
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (2 mol%), THF, *i*-PrOH, rt, 0.5 h	(88) + PhC≡C⟨⟩Ph (5)	89
C$_{16}$	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrCHOHPr-*i*, 40°, 2 h	(96)	89
C$_{21}$ *n*-C$_{18}$H$_{37}$C≡CCH$_2$OAc	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrOH, 65°, 1 h	**I** (38) + *n*-C$_{18}$H$_{37}$C≡CMe **II** (50)	89
	2.5 SmI$_2$, Pd(PPh$_3$)$_4$ (5 mol%), THF, *i*-PrCHOHPr-*i*, 40°, 2 h	**I** (22) + **II** (66)	89
C$_{26}$	5 SmI$_2$, Pd(PPh$_3$)$_4$ (3 mol%), THF, rt, 1 h	(89)	90

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Table X. REDUCTION OF MISCELLANEOUS FUNCTIONAL GROUPS (*Continued*)
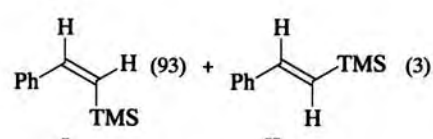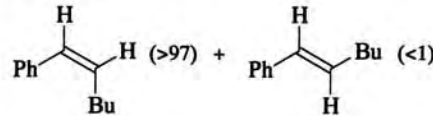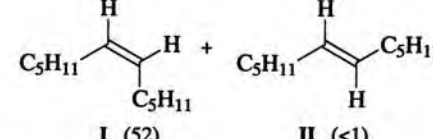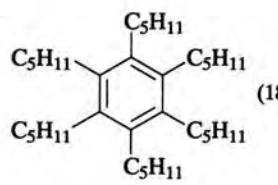
Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.

E. Transition Metal Catalyzed Reduction of Alkynes

Table X. REDUCTION OF MISCELLANEOUS FUNCTIONAL GROUPS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.

Table X. REDUCTION OF MISCELLANEOUS FUNCTIONAL GROUPS (*Continued*)

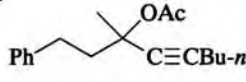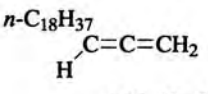| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	2 SmI$_2$, CoCl$_2$•(H$_2$O)$_x$ (3 mol%), THF, rt, 2 h	**I** (65) + **II** (18) + **III** (1)	91
	2 SmI$_2$, CoCl$_2$•4PPh$_3$ (3 mol%), THF, *i*-PrOH, rt, 2 h	**I** (59) + **II** (1)	91
	2 SmI$_2$, CoCl$_2$•4PPh$_3$ (3 mol%), THF, EtOH, rt, 1 h	**I** (77) + **II** (1)	91
	2 SmI$_2$, CoCl$_2$•4PPh$_3$ (3 mol%), THF, MeOH, rt, 0.5 h	**I** (95) + **II** (4)	91
	2 SmI$_2$, CoCl$_2$•4PPh$_3$ (3 mol%), THF, AcOH, rt, 0.5 h	**I** (>99) + **II** (<1)	91
	2 SmI$_2$, CoCl$_2$•4PPh$_3$ (3 mol%), THF, *t*-BuOH, rt, 8 h	**I** (54) + **II** (2)	91
	2 SmI$_2$, CoCl$_2$•4PPh$_3$ (3 mol%), THF, HMPA, *i*-PrOH, rt, 0.5 h	**I** (12) + **II** (70) + **III** (5)	91
	2 SmI$_2$, NiCl$_2$•(H$_2$O)$_x$ (3 mol%), THF, rt, 2 h	**I** (59) + **II** (15) + **III** (6)	91
	2 SmI$_2$, NiCl$_2$•4PPh$_3$ (3 mol%), THF, *i*-PrOH, rt, 2 h	**I** (62) + **II** (6)	91
	2 SmI$_2$, NiCl$_2$•4PPh$_3$ (3 mol%), THF, HMPA, *i*-PrOH, rt, 2 h	**I** (1) + **II** (80) + **III** (8)	91
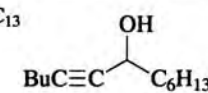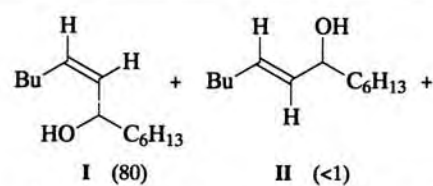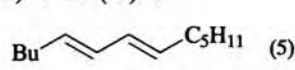
8. Acknowledgements

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The [2,3]-Wittig Rearrangement

Takeshl Nakal, Tokyo Institute of Technology, Meguro, Tokyo 152, Japan

Koichl Mikaml, Tokyo Institute of Technology, Meguro, Tokyo 152, Japan

1. Introduction

The [2,3]-sigmatropic rearrangement, generalized by Eq. 1, constitutes a versatile type of bond reorganization which encompasses a number of variations in


$$(1)$$

terms of both the atom pair (X,Y) and the type of electron pair on Y (anions, nonbonding electron pairs, or ylides). The Sommelet–Hauser rearrangement is representative. (1)

This chapter focuses on the special class of [2,3]-sigmatropic rearrangement that involves an oxycarbanion (X = oxygen, Y = carbanion) as the migrating terminus (Eq. 2). This type of rearrangement is now termed the [2,3]-Wittig (sigmatropic)


$$(2)$$
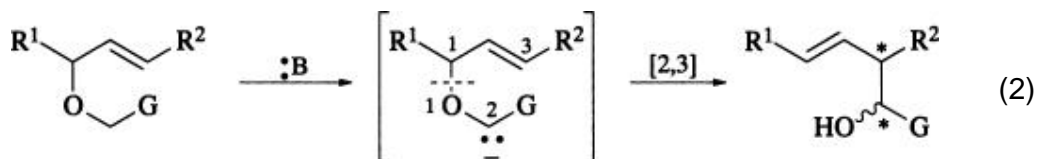
rearrangement. The reaction name clearly originates from the fact that this rearrangement formally represents a [2,3]-sigmatropic version of the classic Wittig rearrangement, (2, 3) a well-known 1,2-alkyl shift of oxycarbanions (Eq. 3).

$$(3)$$
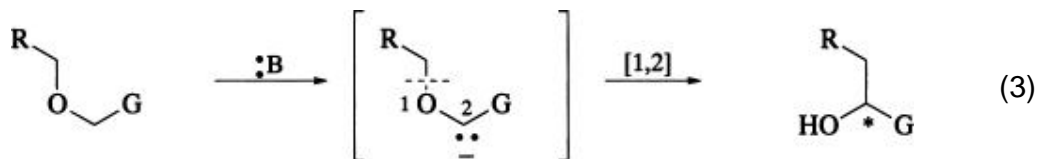
The [2,3]-Wittig rearrangement has a rather recent history. Perhaps the first observation of the [2,3]-Wittig shift is the rearrangement of the allyl fluorenyl

ether **1** (Eq. 4), (4-7) which was made in 1960 in the context of mechanistic studies on the Wittig rearrangement.


$$ (4) $$
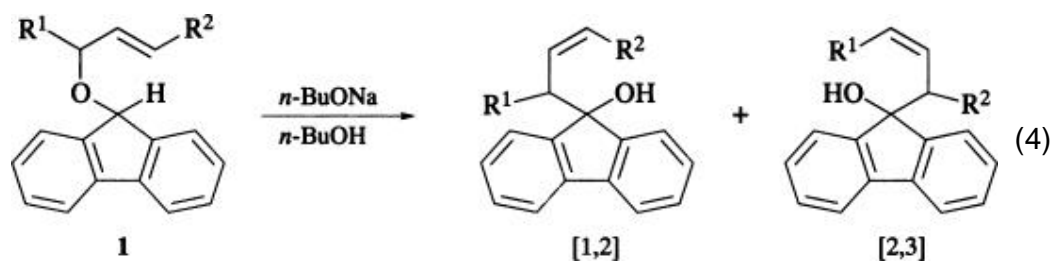
The period of the 1960s to the early 1970s witnessed slow progress with a focus on mechanistic studies mainly of allyl benzyl ether systems. (8-10) The synthetic power of this carbanion rearrangement as a general method was recognized when Still (1978) (11) and Nakai (1981) (12) established the highly stereoselective variants of the genuine [2,3]-Wittig rearrangement. In recent years the [2,3]-Wittig rearrangement has enjoyed widespread application in many facets of organic synthesis. Various aspects of the reaction have been reviewed. (13-17)

This chapter deals with the mechanism, scope and limitation, stereochemistry, and synthetic applications of the [2,3]-Wittig rearrangement with emphasis on the stereochemical aspects and the synthetic utility. Other hetero [2,3]-Wittig rearrangements such as thio-[2,3]-Wittig variants are not covered.

2. Mechanism

2.1. [2,3] Shift vs. [1,2] Shift

The competition and mechanistic distinction of the [1,2] and [2,3] shift in the carbanion rearrangement concerned was the subject of early mechanistic studies. (8-10) As exemplified in Eq. 4, the [1,2] shift often competes with the [2,3] shift to an extent that depends markedly on the substrate structure and the reaction temperature. For instance, the rearrangement of benzyl ether **2** affords a mixture of the [1,2] and [2,3] products, with the ratio varying with the temperature. (18)

2

n-BuLi
THF

[2,3]

[1,2]

-25°, 7.5:1
23°, 6:1
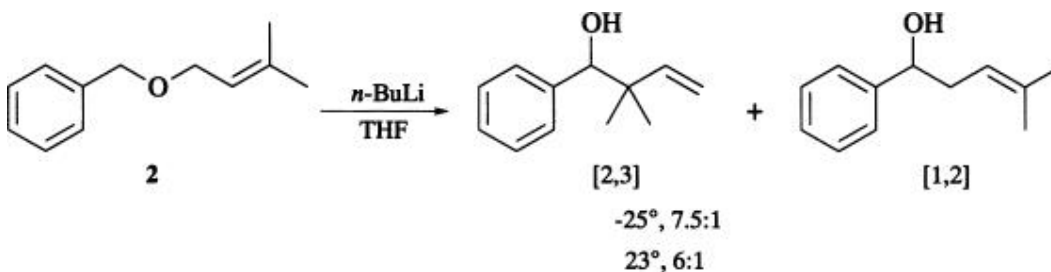
However, it is now generally recognized that concurrence of the [1,2] shift can be minimized and often suppressed completely when the reaction is carried out at the proper temperature.

Moreover, it is now widely accepted that the [1,2]-Wittig rearrangement proceeds via a radical dissociation–recombination mechanism, (8-10) whereas the [2,3]-Wittig rearrangement is a concerted, thermally allowed sigmatropic reaction following the Woodward–Hoffman rules (19) or Fukui's frontier orbital theory. (20) Thus the [2,3]-Wittig rearrangement is a concerted reaction that proceeds through a six-electron, five-membered transition state in a suprafacial fashion along the allylic array as depicted in A or B. Theoretically, it is thus evident that

A   B
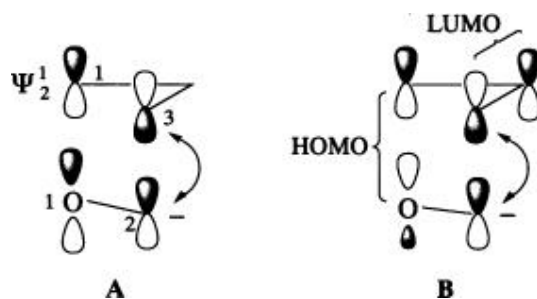
the smaller the energy gap between the HOMO (carbanion) and the LUMO (allyl), the more readily the rearrangement occurs. This means roughly that the less stable the carbanion involved, the faster the rearrangement.

## 2.2. [2,3] Shift vs. [1,4] Shift

An additional problem of periselectivity arises in the carbanion rearrangement of the bis(allyl) ether system. In this case, both the [1s,4s] and [2s,3s] shifts are allowed by orbital symmetry (Eq. 5), together with the nonconcerted [1,2] and

$$ (5) $$
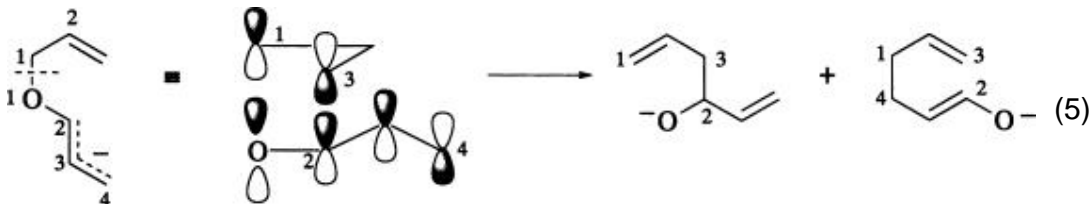
[3,4] shifts. (8-10) In fact, the rearrangement of bis(prenyl) ether affords 8% of the [1,4] product, along with 67% of the [2,3], 14% of the [1,2], and 10% of the [3,4] products. (18) The exact mechanism of the [1,4] shift (concerted vs. dissociation–recombination) is still controversial. (8-10, 21) The problem of periselectivity for the [2,3] vs. [1,4] shifts becomes more serious with certain cyclic ether substrates.

2.3. Transition State Conformation

To understand the stereochemistry of the [2,3]-Wittig rearrangement, the conformation of the five-membered transition state needs to be determined. That is an extremely difficult task. (22) Even given the reasonable postulate that the [2,3] shift proceeds via a "folded envelope" conformation, there are still the three options **A–C**.
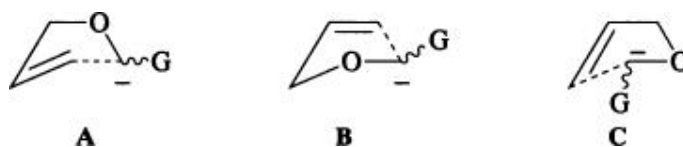
While conformers **A** and **B** are often used to explain the stereochemistry of [2,3]-sigmatropic processes, (8-10, 18, 23) conformer **C** has been proposed by the authors of this review as the preferable conformation for the transition state of the [2,3]-Wittig process. (24) While molecular mechanics (MM2) calculations have led to conflicting results, (25, 26) a recent ab initio molecular orbital calculation has shown that the transition state conformation quite similar to conformer **A** is located by the 3-21G and 6-31 + G basis set levels. (27) In the literature, however, both conformers **A** and **C** have often been used. It appears that the basic conformers **A** and **C** work equally well to explain the stereochemical outcome in most [2,3]-Wittig processes. Thus the basic conformer of type **C**, more familiar to the authors of this chapter, is used as a working hypothesis throughout this review *only* for the sake of consistency.

3. Scope and Limitations

Generally speaking, the [2,3]-Wittig rearrangement can be achieved with any α -(allyloxy)carbanions with different substituents (G) on the migrating terminus. Thus its synthetic utility is determined principally by the availability of methods for generating the oxycarbanions at temperatures low enough to minimize the undesirable [1,2] shift. Nonetheless, the [2,3]-Wittig rearrangement has limitations in the range of applicable substrates, especially for some cyclic substrates.

3.1. Acyclic Substrates

The [2,3]-Wittig rearrangement of acyclic ethers can usually be achieved in a highly periselective manner as long as carbanion generation and rearrangement can be carried out at temperatures ranging from –60 to –85°. The most popular method for carbanion generation is direct lithiation (deprotonation) with butyllithium or lithium diisopropylamide (LDA). A standard procedure is illustrated in Eq. 6. (28, 29) The deprotonation method is widely applicable to various types of substrates, including bis(allyl) ethers, allyl benzyl ethers, allyl propargyl ethers,

$$\text{(6)}\quad (74\%)$$
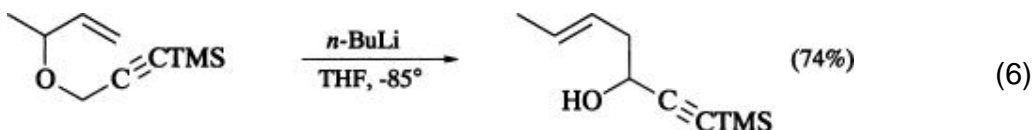
and α -allyloxy carbonyl compounds. Of course, the applicability of this method is restricted to those compounds possessing relatively acidic α hydrogens. This limitation can be overcome by transmetalation methods such as the tin–lithium exchange reaction (Eq. 7) (11) or reductive lithiations of O,S-acetals (Eq. 8). (30, 31) The

$$\text{(7)}\quad (>95\%)$$

$$\text{(8)}\quad (67\text{-}77\%)$$
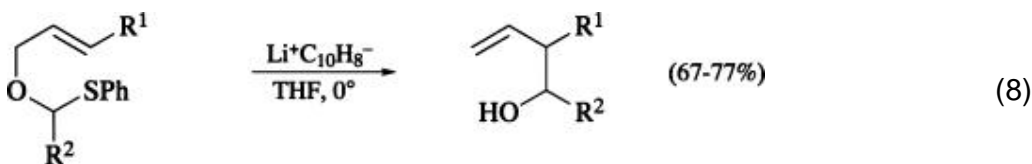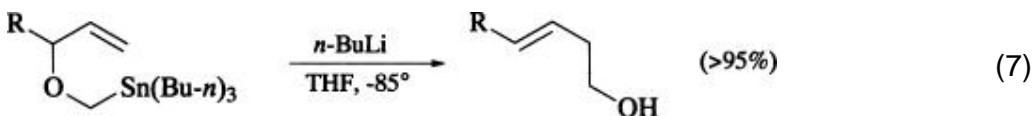
use of the tin–lithium exchange procedure by Still and Mitra was significant in the history of the [2,3]-Wittig rearrangement, since it uncovered the great

synthetic potential of this type of rearrangement.

Particularly notable is the [2,3]-Wittig rearrangement of unsymmetrical bis(allylic) ethers, another important variant which considerably enhanced the synthetic potential of the [2,3]-Wittig rearrangement. (12) In this reaction, an addα' lithiation. A general regioselection rule has now been established from systematic studies of
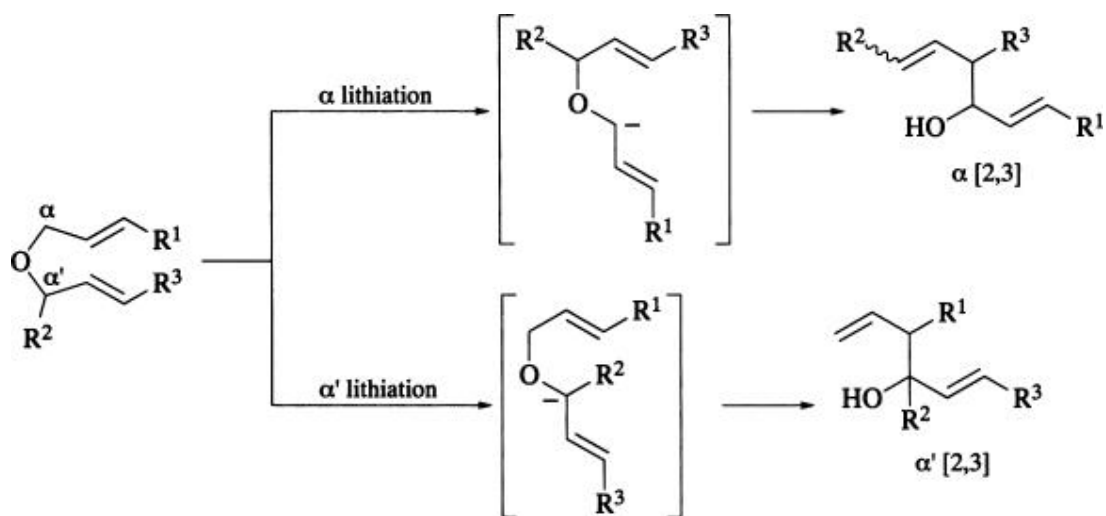

the rearrangement of a variety of bis(allylic) ethers under standard conditions (butyllithium, tetrahydrofuran, –85°). (12) In the rearrangements of unsymmetrical substrates with different substitution patterns at the α and γ positions of the two allylic moieties, lithiation takes place exclusively on the less-substituted allylic moiety, thus leading to the exclusive formation of the α -[2,3] Wittig product as the single regioisomer. Thus **3** provides the single regioisomer **4**, while **5** affords a 1:2 mixture of the α - and α '-[2,3] products. The β -alkyl substitution has little effect. Thus **6** provides a 3:4 mixture of the regioisomers, whereas **7** affords only the α -[2,3] product.

5

6, R = H
7, R = Me
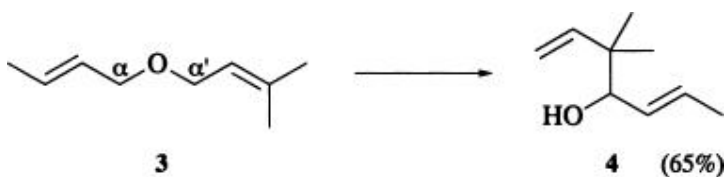
However, no problem with regioselectivity arises when a carbanion-stabilizing group such as methylthio or trimethylsilyl is at the γ position of one allyl moiety; both **8** (32) and **9** (33) provide the α -[2,3] product exclusively, independent of the

8

9
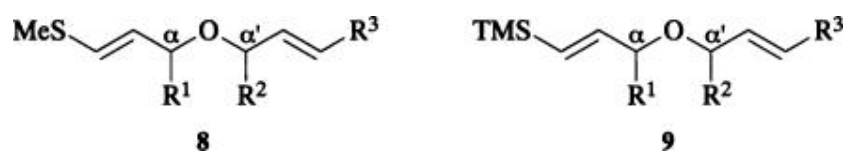
substitution pattern. Such positional ambiguities are not present in the rearrangements of allyl propargyl ethers since lithiation occurs exclusively on the propargylic moiety. (12)

Replacement of the allylic migrating group by a propargylic group constitutes another general class of [2,3]-Wittig variants that afford allenic alcohols (Eq. 9). (34-37) While the yields are only modest because of the strained allenic

$$G = CN, C\equiv CMe \qquad (50\text{-}64\%) \qquad (9)$$
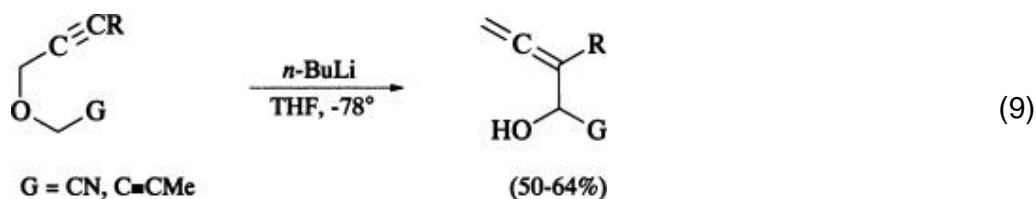
transition state, Still's variant (G = SnR_3) and the carboxylic acid variant (G = CO_2H) have been reported to give allenic products in respectable yields. (38, 39)

3.2. Cyclic Substrates

The [2,3]-Wittig rearrangement is also applicable to a wide variety of cyclic substrates. These variants are classified according to Ziegler's convention originally proposed for the cyclic Claisen variants. (40) In this convention the carbons to which the tether bridging the pericyclic array is attached are expressed in the form {m,n}. The twelve types shown in Fig. 1 are conceptually possible. The subscripts *endo* and *exo* designate the presence of substituent G as a part of the tether in the ring, and as a substituent on the ring, respectively.

Figure 1.

4

3

5

2 O

1

G

{1,1}

HO G

{1,3} exo

HO G

{1,3} endo

OH

3

O

1

G

{1,4} exo

HO G

{1,4} endo

OH

5

{1,5} exo

HO G

{1,5} endo

HO G

{3,3}

HO G

{3,4}

HO G

3

5

{3,5}

HO G

{4,5}

HO G

5

{5,5}

HO G
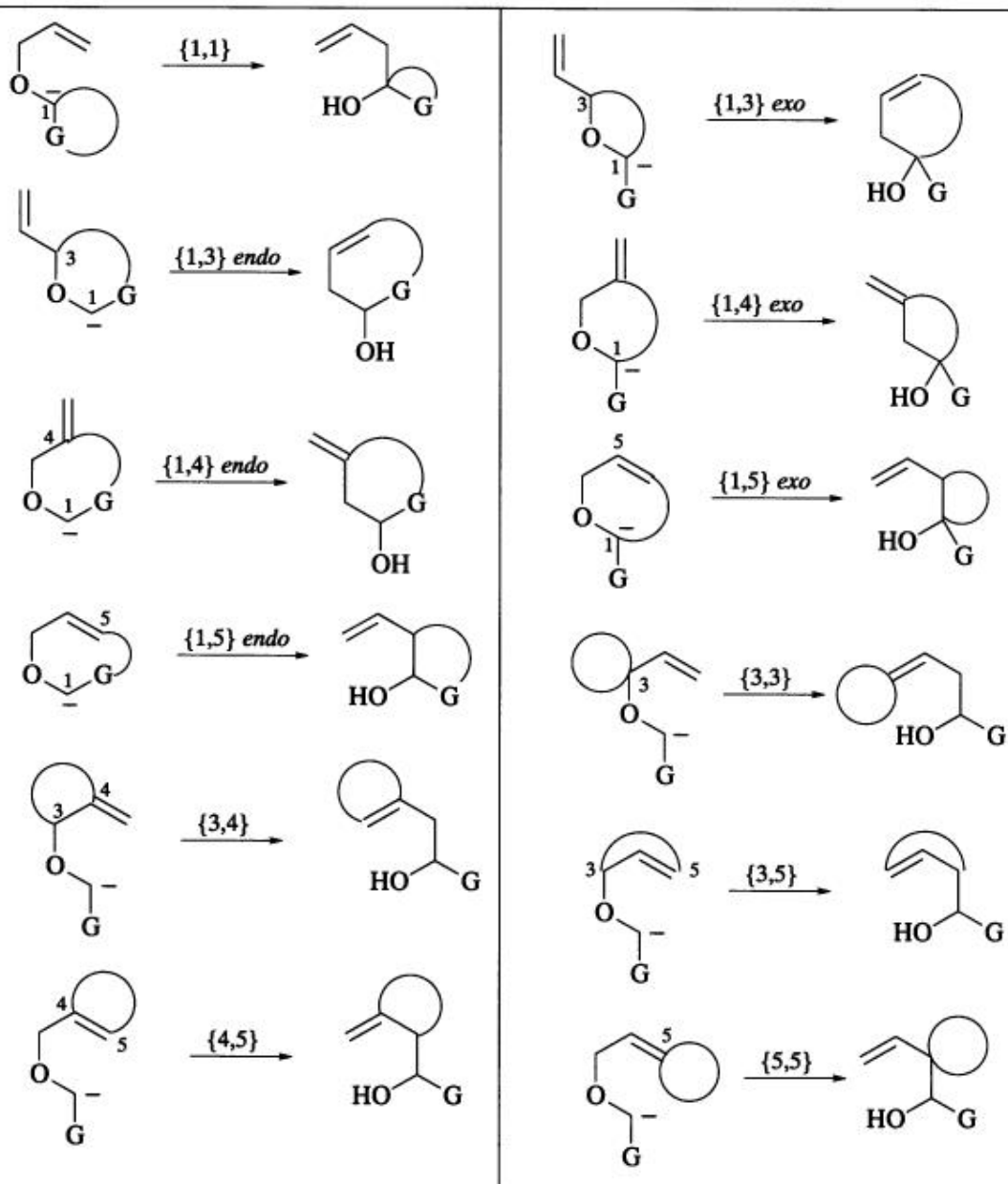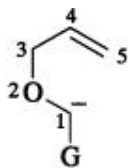
Each of these cyclic variants provides a different synthetic consequence, namely, ring enlargement for {1,3} rearrangement, ring contraction for {1,4} and {1,5} rearrangements, introduction of a new side chain onto the ring for {1,1}, {3,4}, {3,5}, and {4,5} rearrangements, and creation of a quaternary center on the ring for {5,5} rearrangement. Despite their great potential, however, only a limited number of cyclic rearrangements have been exploited thus far.

The {1,5}-[2,3]-Wittig rearrangement is relatively well studied in the context of synthesis of medium and large ring natural products. The rearrangements of the 13-membered bis(allyl) ether **10** (25, 41) and the 17-membered allyl propargyl ether **11** (42, 43) are the first reported prototypes of this group. The stereochemical features of this type of ring contraction and its application in natural product synthesis are described later. It should be noted here that the rearrangement of cyclic bis(allyl) ethers no longer obeys the regioselection rule mentioned above for acyclic substrates. In fact, **10** provides a 1:3 mixture of the α - and α '-[2,3] products (41) and **12** affords only the α′-[2,3] product via exclusive lithiation on the more substituted moiety. (44)
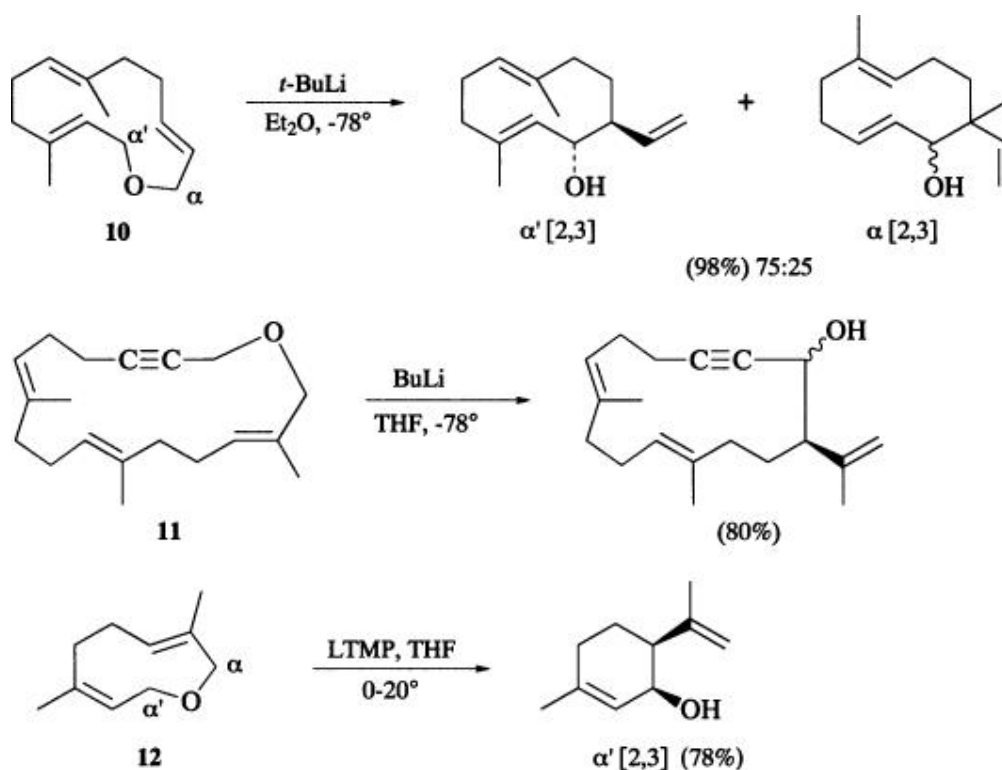
There are several examples of {3,4}-[2,3]-Wittig rearrangements, particularly in steroid side chain synthesis. The earliest examples are shown in Eq. 10. (45-47) The stereochemical features and synthetic applications of this methodology are the subject of a subsequent section.

$$(10)$$

G = Sn(Bu-n)$_3$, C≡CX (X = H, TMS)   (75 to >95%)
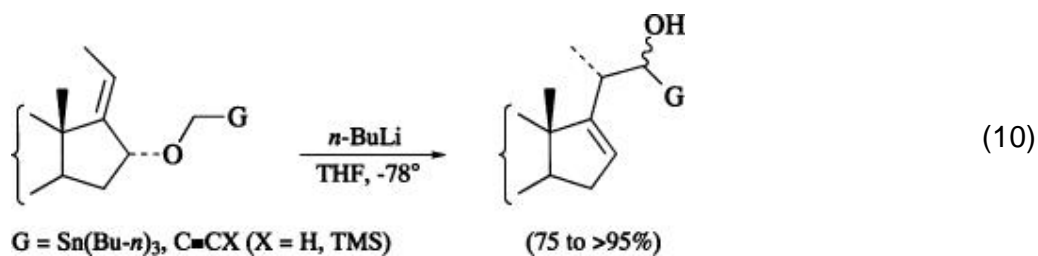
The {3,5} rearrangement was also relatively well studied. However, this type of cyclic variant often suffers the serious drawback that the undesired [1,2] shift competes seriously with it (Eq. 11). (48) Of special interest are the allyl cyclohexenyl

[2,3]   [1,2]   (11)

G = C≡CH, 38:62
G = Ph, 37:63
G = CO$_2$H, 67:33
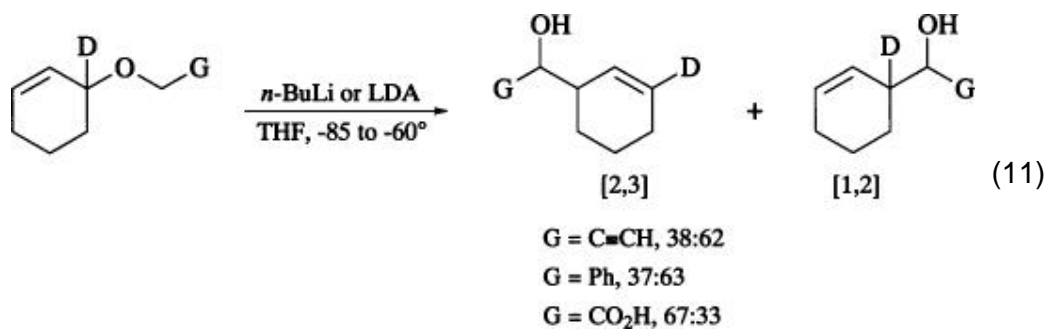
ethers **13** (49) where the [1,4] product is also formed, with the ratio dependent on the substitution pattern on the ring; a conformational effect is suggested to explain the variation in periselectivity. Interestingly, however, the [2,3] product is obtained mainly with the {3,5} prototype of the cyclohexenyl (Eq. 12) (50, 51) and dihydrofuryl substrates (Eq. 13). (52-54)

Eq. (12) scheme:

Compound **13** → (n-BuLi, THF, -78°) → [1,4] product (CHO) + [2,3] product (OH, vinyl)

R¹	R²	[1,4] : [2,3] : [1,2]
H	H	12 : 24 : 64
H	Me	18 : 54 : 28
Me	C(Me)=CH₂	48 : 6 : 46

(12)

Eq. scheme: Bu-i bicyclic, R_3SiO, $Sn(Bu-n)_3$ → (n-BuLi, C_6H_{14}, -78°) → HO, Bu-i product, R_3SiO (34%)

Eq. (13) scheme: furanyl-O-CH₂-C≡CTMS → (n-BuLi, THF) → furanyl, HO, C≡CTMS product (73%) (13)
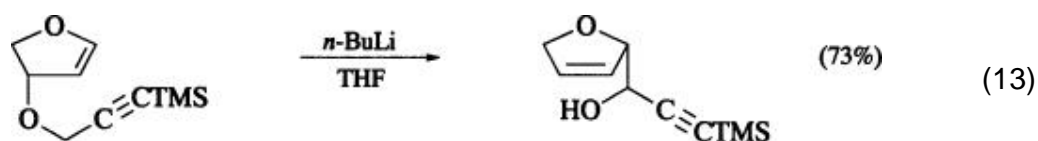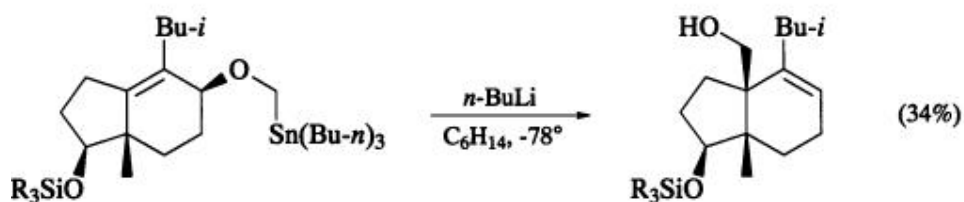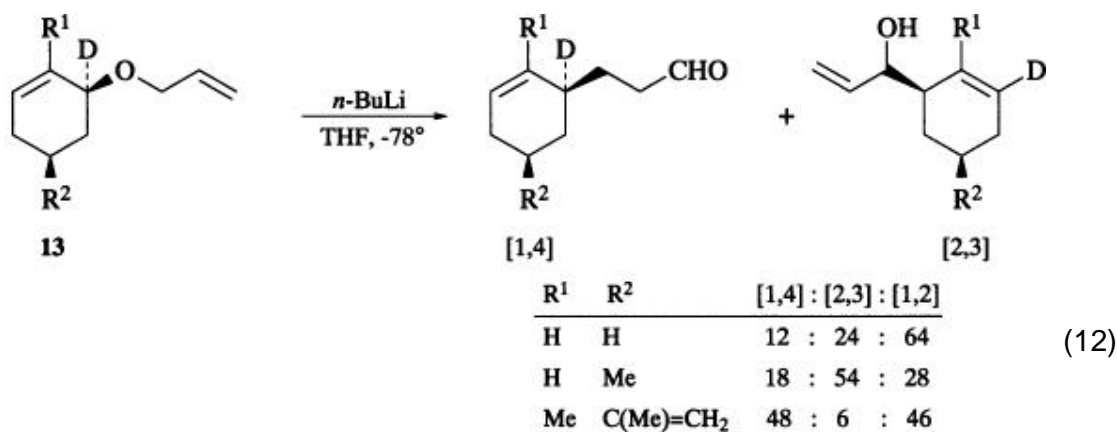
Examples of other types of {m,n} rearrangement are quite rare. An example of the {1,1} type is given in Eq. 4. A single example was reported for the {1,3}*exo*(six-membered ring with G = COMe), (55) the {3,3} (tetrahydrofuran ring with G = CO_2H), (56) the {4,5} (cyclohexane ring with G = C ≡ CMe), (57) and the {5,5} (cyclohexane ring with G = CO_2H). (68) No examples were reported of the {1,3}*endo*, {1,4}*exo*, and {1,5}*exo* rearrangements.

3.3. Competing Reactions
The enolate rearrangement of α -allyloxy carbonyl systems **14** deserves special comment since two competing modes of sigmatropic processes, the [2,3]-Wittig rearrangement and the [3,3]-Claisen rearrangement, are conceivable.
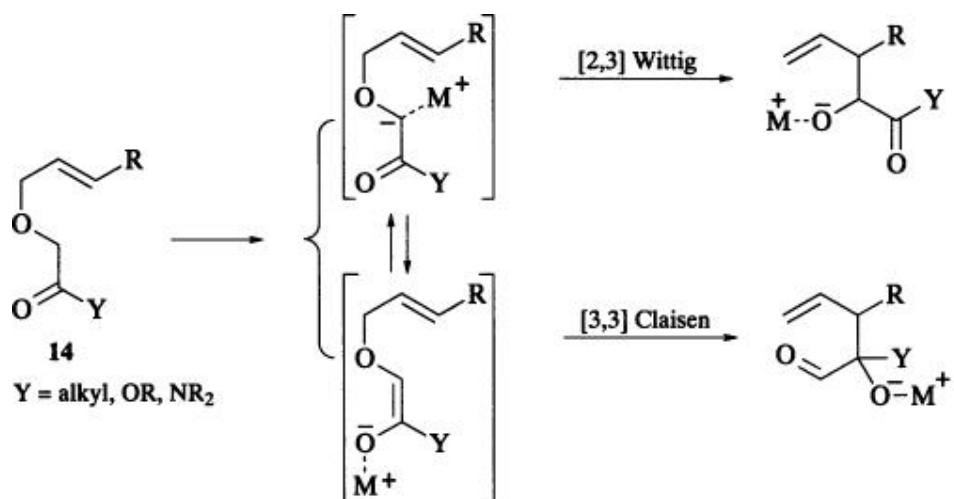
Conflicting observations have been reported for the allyloxy ketone system. Treatment of ketone **15** with potassium *tert*-butoxide (55) and of ketone **16a** with LDA in a mixture of hexamethylphosphoramide (HMPA) and tetrahydrofuran (59) affords the [2,3]-Wittig product exclusively, whereas treatment of ketone **16b** with potassium hydride (or sodium hydride) produces the [3,3]-Claisen product predominantly. (60)
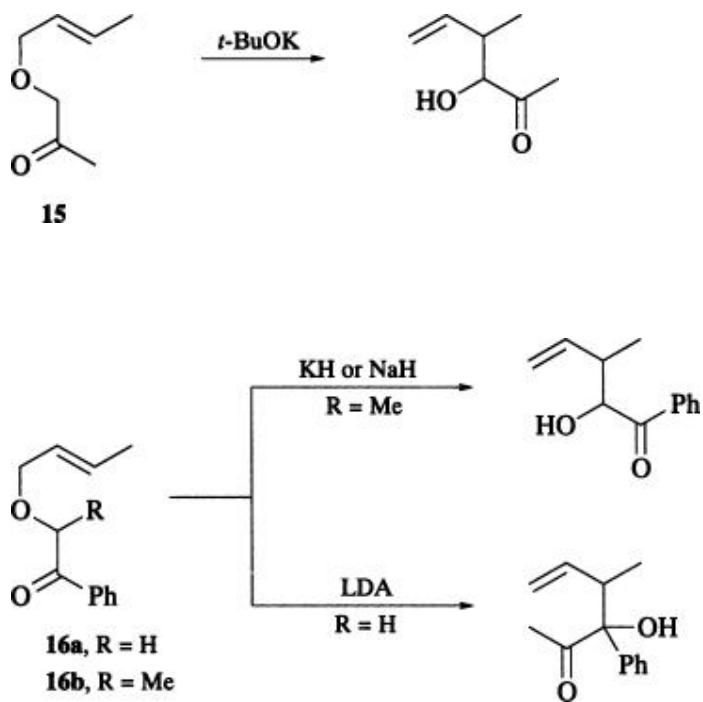
Interesting rearrangements were also reported for the acid **17**, the ester **18**, the amide **19**, and the silylated derivatives **20** and **21**. When the lithium enolate is generated with LDA in tetrahydrofuran, both acid **17** (58) and amide **19** (61) undergo the [2,3]-Wittig rearrangement at ca. –80°, whereas ester **18** does not. (62) In contrast, the lithium enolate of **18** generated in HMPA–tetrahydrofuran undergoes the [2,3]-Wittig shift at –70°. (62) Heating of **20** at 80° affords the [3,3]-Claisen product quantitatively, (62-64) whereas transmetalation of **20** with tin(IV) chloride or titanium(IV) chloride at –50° leads to the exclusive formation of the [2,3]-Wittig product. (65) On treatment with tetrabutylammonium fluoride at –70°, **21** affords the [2,3]-Wittig product quantitatively, while **20** does not rearrange under the same conditions. (62)

17, Y = OH
18, Y = OMe
19, Y = N(CH₂)₄

[2,3] Wittig

21

20

[3,3] Claisen
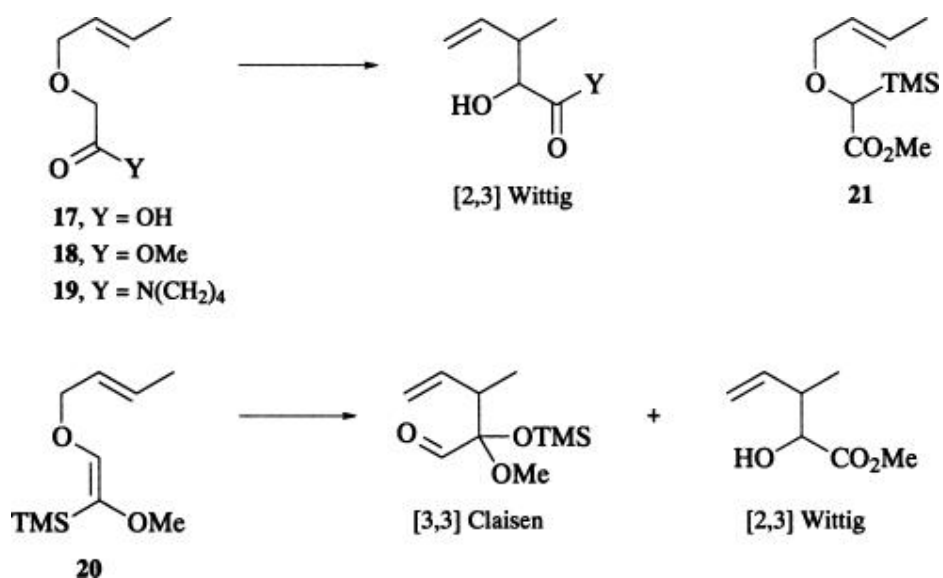
[2,3] Wittig

4. Stereochemical Control

The [2,3]-Wittig rearrangement usually proceeds through a highly ordered cyclic transition state to create a new C-C double bond and a new C-C single bond. Consequently, this type of rearrangement should allow stereochemical control, including stereoselective generation of an olefinic bond, with both internal and relative asymmetric induction, and chirality transfer along the pericyclic array. While studies on olefinic stereoselection began simultaneously with the initial mechanistic studies, stereocontrol over the newly created chiral centers is the subject of recent investigations, mainly because the [2,3]-sigmatropic rearrangement was believed to show only modest levels of asymmetric induction (66) except for a single example. (18) Over the past decade, however, remarkable progress has been made in the development of stereoregulated [2,3]-Wittig variants, hence the [2,3]-Wittig technology is now increasingly utilized to great advantage in stereocontrolled organic synthesis. This section deals with the stereochemical principles that govern the [2,3]-Wittig rearrangement.

4.1. Olefinic Stereoselection

The rearrangement of ethers derived from secondary allylic alcohols affords the E and Z products. Examination of the transition-state conformations suggests that the R group should prefer the *exo* orientation, thus leading to preferential formation of the E isomer (Eq. 14). The E preference is amply confirmed and widely recognized as a general attribute of the [2,3]-Wittig rearrangement.
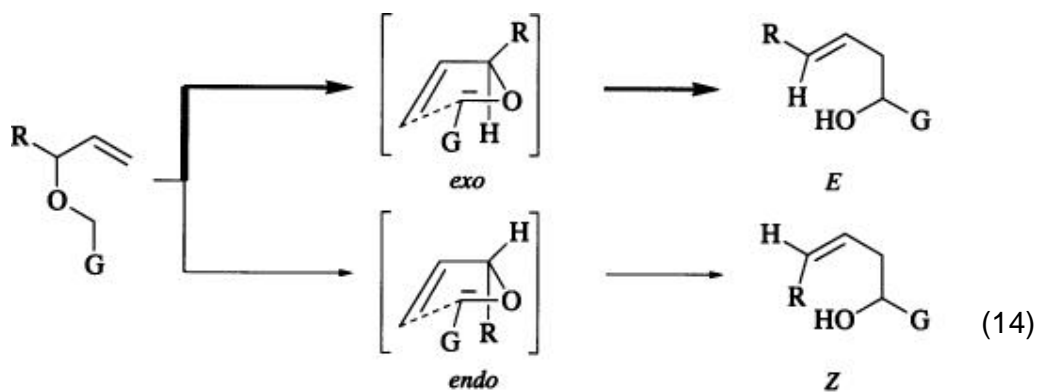
R	G	
Me	$C(R')=CH_2$ (R' = H, Me)[12]	98-100% E
Me	$C \equiv CR'$ (R' = H, TMS)[67]	93-98% E
Me	Ph[18]	100% E
Me	CO_2H[12]	>75% E
Me	CO_2Me[59]	75% E

Two notable exceptions to this *E* selectivity were reported. One is the rearrangement of the tin-substituted ethers **22** which affords the *Z* product predominantly. (11) This unusual *Z* selectivity was applied to the synthesis of the Cecropia juvenile hormone. (68) The other exception is the zirconium enolate rearrangement of allyloxy ester **23** which gives the *Z* product exclusively. (69) It is also notable that the introduction of a bulky group such as trimethylsilyl at the β position of the allyl group results in decreased *E* selectivity because of the destabilization of the generally preferred *exo* transition state by the additional interaction of β -Me₃Si with

R¹	R²	
n-C₇H₁₅	H	60% Z
n-Bu	Me	100% Z

100% Z

23   R = Me, *i*-Pr, *n*-Bu
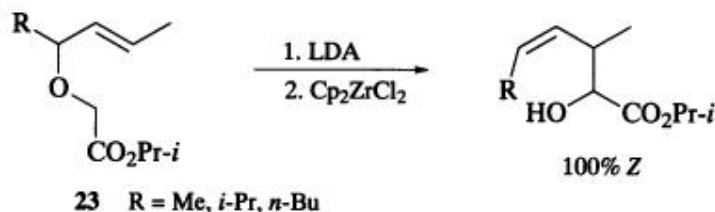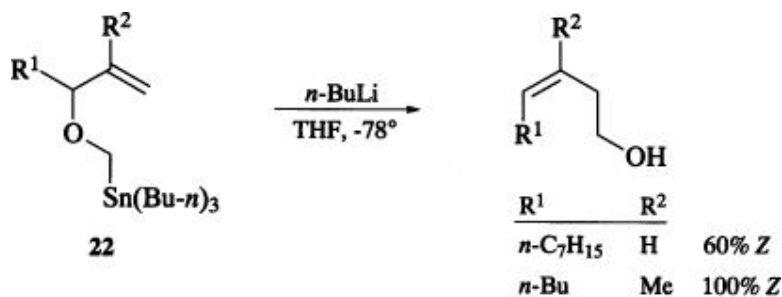
R. (70) The rearrangement of **24**, which proceeds with 80% *E* selectivity, is particularly interesting, leading eventually to the *Z* olefin in a leukotriene synthesis. (71)

24   R = *n*-C₅H₁₁
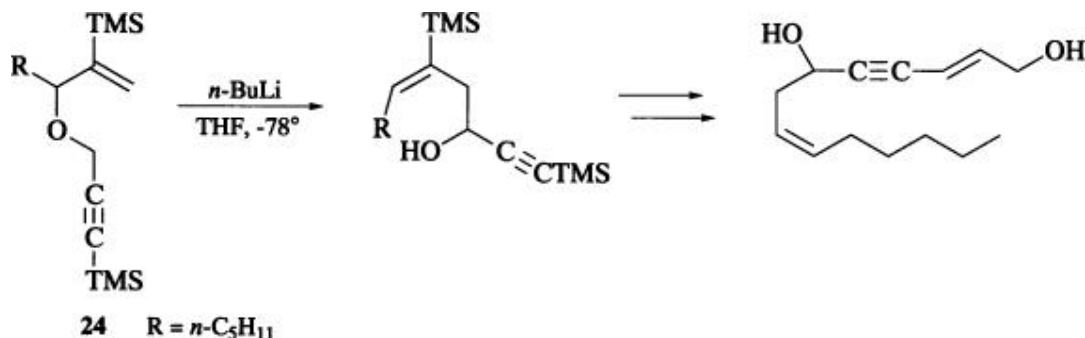
The rearrangement of ethers derived from tertiary allylic alcohols (Eq. 15)

would not be expected to show high *E* selectivity, because of the small difference

$$(15)$$
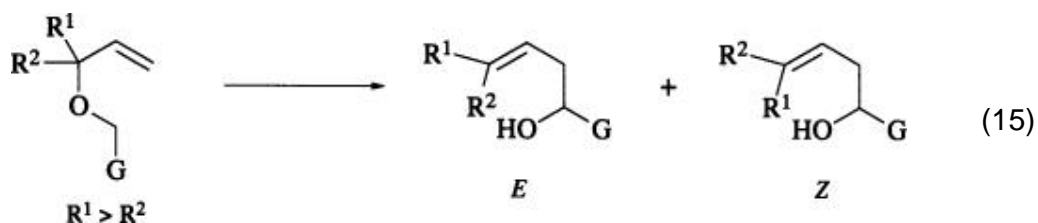
in energy between the two transition states. However, exclusive formation of the *E* trisubstituted olefin was reported in the rearrangement of **25** (Eq. 16), (72) where the methoxymethoxy (MOMO) group plays a key role in defining the transition state geometry. Of special interest is the {3,4} rearrangement of **26**, which affords varying amounts of the *E* and *Z* products, depending on the reaction conditions (Eq. 17). (73)

$$(16)$$

$$(17)$$
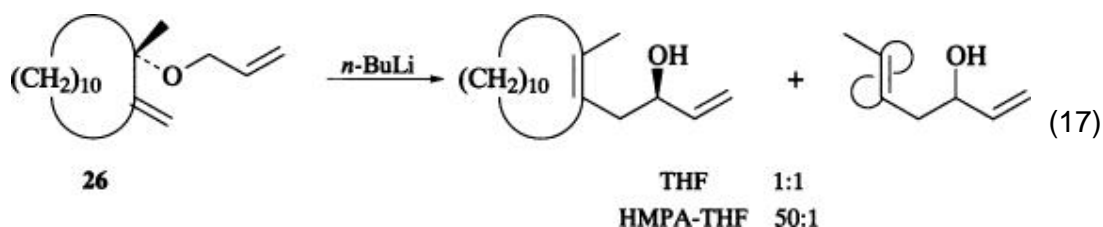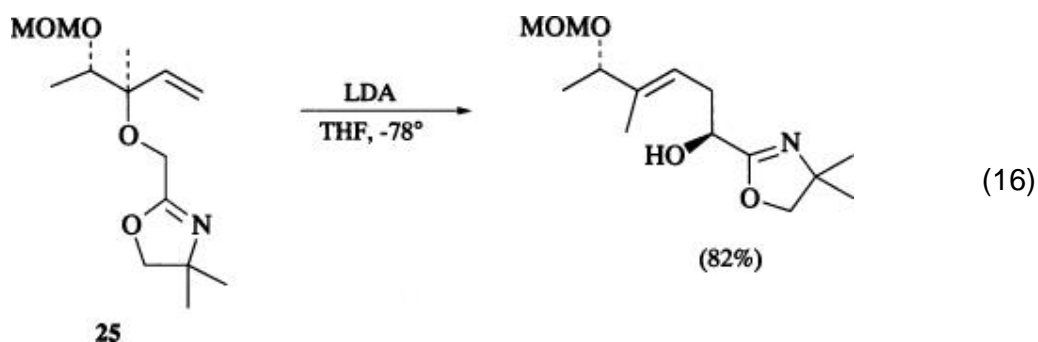
4.2. Diastereoselection

4.2.1.1. Transition-State Model

Of the stereoselections achievable with the [2,3]-Wittig rearrangement, diastereoselection (internal 1,2 asymmetric induction) with respect to the newly created vicinal chiral centers is the most important from the standpoint of stereocontrol. The rearrangement of γ -substituted allyl ethers provides the two racemic diastereomers through the two pairs of transition states (Fig. 2). Thus

the *E* substrate can proceed through transition states T_1 and T_2 which lead to the *threo* and *erythro* products, respectively. Similarly, the *Z* substrate affords the *threo* and *erythro* products via T_3 and T_4, respectively. The two transition states (T_1 vs. T_2 or T_3 vs. T_4) are unequal in energy, and the *threolerythro* ratio reflects the transition state geometry.

Figure 2.
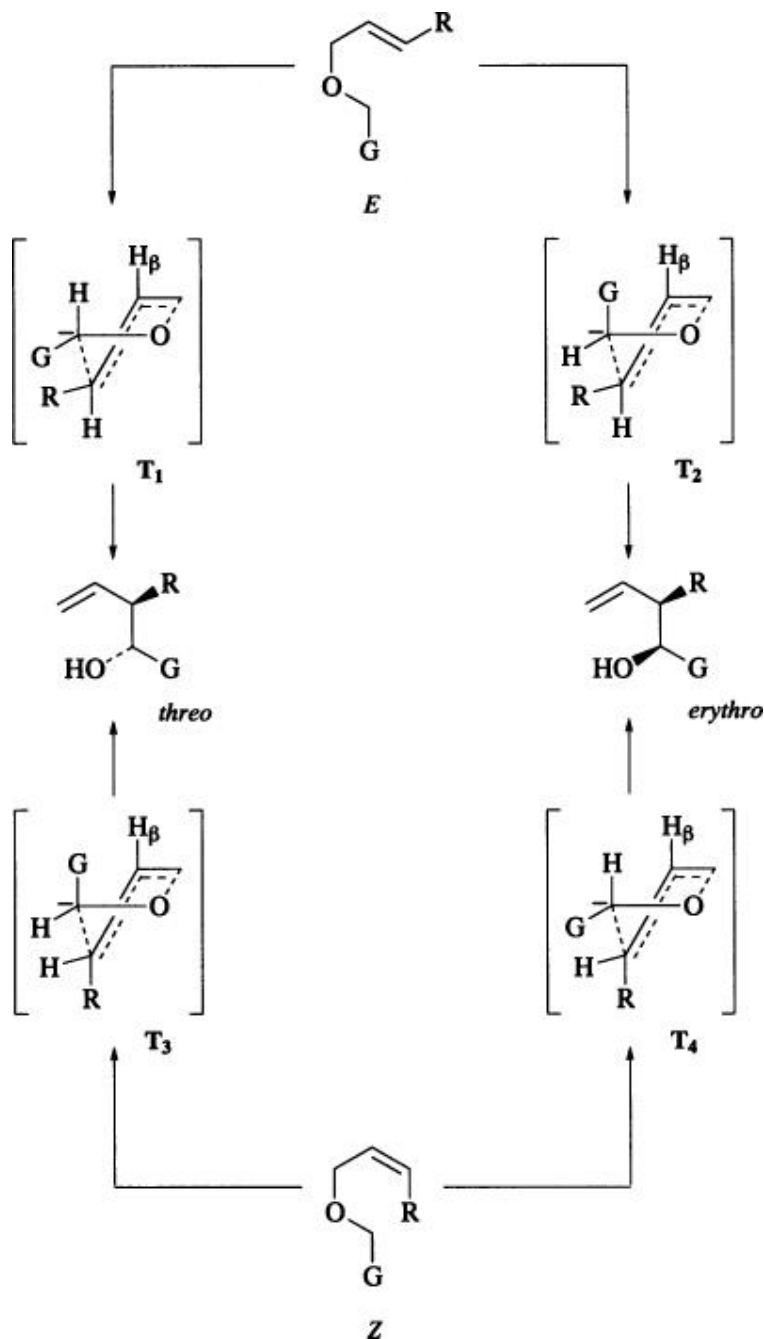
A detailed study of the rearrangements of a variety of the geometric pairs of crotyl ethers with different G groups revealed significant trends of diastereoselection. These results led to the proposal of the transition state model depicted below, which provides a logical basis for explaining and

predicting the diastereoselection of a wide range of [2,3]-Wittig rearrangements. (24) The essentials are as follows: (1) The sense of diastereoselection is dictated primarily by the olefin geometry of the substrate, and the degree is determined critically by the nature of the G group on the migrating terminus. (2) As a general rule, an E substrate exhibits *threo* selection, whereas a Z substrate shows *erythro* selection. The general selection is rationalized in terms of the pseudo-1,3-diaxial interaction of G with H_β in T_2 and T_3. For instance, the Z to *erythro* selection occurs because T_3 is sterically less favorable than T_4. (3) The *erythro* selectivity observed for the Z series is in the order: G = Ph (100%) > $C(CH_3) = CH_2$ > $CH = CH_2$ > $C \equiv CH$ (90%), whereas the *threo* selectivity observed for the E series is in the opposite order: G = $C \equiv CH$ (99%) > $CH = CH_2$ > $C(CH_3) = CH_2$ (70%) > Ph (53%). While this order of *erythro* selection is consistent with the expected order of the 1,3 repulsion concerned, the order of *threo* selection is best explained by assuming an additional gauche interaction of G with R in the preferred T_1, which operates to diminish the *threo* selectivity. (4) A notable exception to this general selection rule is the enolate [2,3]-Wittig family including G = CO_2H, CO_2R, and $CONR_2$, (58, 61-65) where a relatively high degree of E to *erythro* selection is generally observed, while the Z substrates show a low level of either *threo* or *erythro* selection. The unusual E to *erythro* selection reflects the fact that the gauche interaction in T_1 prevails overwhelmingly over the 1,3 repulsion in T_2. This transition state model is further strengthened by many other examples and also by theoretical calculations, (26) thus providing a logical basis for developing highly diastereoselective variants described below. It should be noted, however, that a different transition state model has recently been proposed. (27)

4.2.1.2. Highly Selective Variants
Among the variants described so far, only two (G = Ph for Z to *erythro* and G = $C \equiv CH$ for E to *threo*) provide a synthetically useful level (>98%) of diastereoselection. However, other variants have been developed that exhibit >98% for either *threo* or *erythro* selection. Equations 18 and 19 summarize the highly E to *threo* and Z to *erythro* selective variants, respectively. (28, 29) It should be noted that the G group leading to an enhanced E to *threo*

$$G = C \equiv CH \quad 99\% \; threo$$
$$G = C \equiv CMe \quad 99\% \; threo$$

(18)

threo
72-74%

$$G = Ph \quad\quad >99\% \ erythro$$
$$G = C\equiv CMe \quad 100\% \ erythro$$
$$G = C\equiv CTMS \quad 100\% \ erythro \quad (19)$$
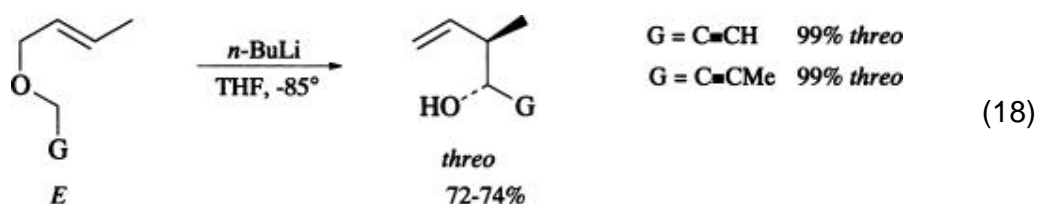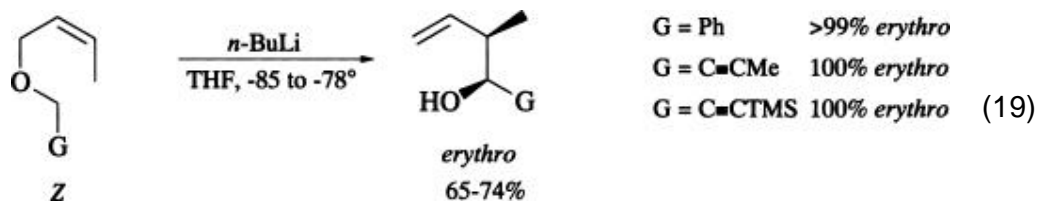
erythro
65-74%

selectivity does not provide an increased *Z* to *erythro* selectivity and vice versa, except for the pair of G = C ≡ CMe.

Of special interest is the case of G = C ≡ CSiMe$_3$, in which the *Z* substrate exhibits an extremely high *erythro* selectivity that surprisingly exceeds the geometric purity of the substrate used, whereas the *E* counterpart also shows *erythro* selection, although the degree is moderate (73%). (28, 29) From the synthetic point of view, the propargylic variants thus developed possess particular advantages; they can provide an extremely high level of either diastereoselection by the proper choice of crotyl geometry and ethynyl group, and the rearrangement product possesses unique multifunctionality which readily allows a variety of further transformations, as demonstrated in the formal total synthesis of (+)-oudemansin. (28, 29)

On the other hand, two highly *E* to *erythro* selective variants were also developed which afford α -hydroxy- β -alkyl carboxylic acid derivatives of synthetic value (Eq. 20). (61, 74) In these cases, the *Z* counterparts show a much lower *erythro* selectivity. Of further interest is that the rearrangement of (*E*)-**27a** shows a high *erythro* selectivity, whereas (*E*)-**27b** provides a high *threo* selectivity. (75, 76) Another notable exception is the rearrangement of an *E/Z* mixture of **28** where both the *E* and *Z* substrates show extremely high *threo* selectivity. (77)

100% *erythro*

G = CON(CH$_2$)$_4$ 98% *erythro*   (20)

erythro
86-92%

(E)-27a, R = H   97:3   (85-97%)
(E)-27b, R = Me   3:97

28 E/Z = 35:65

(79%) 98% *threo*
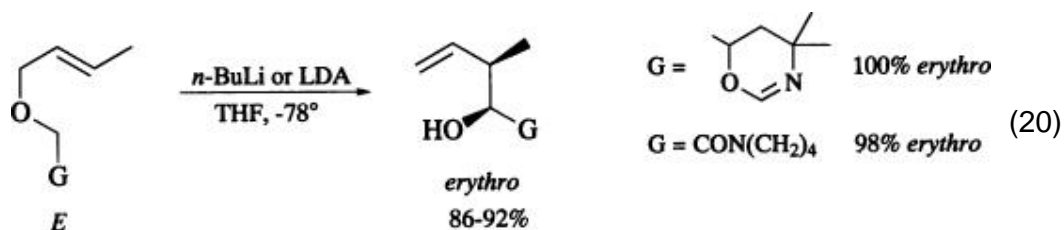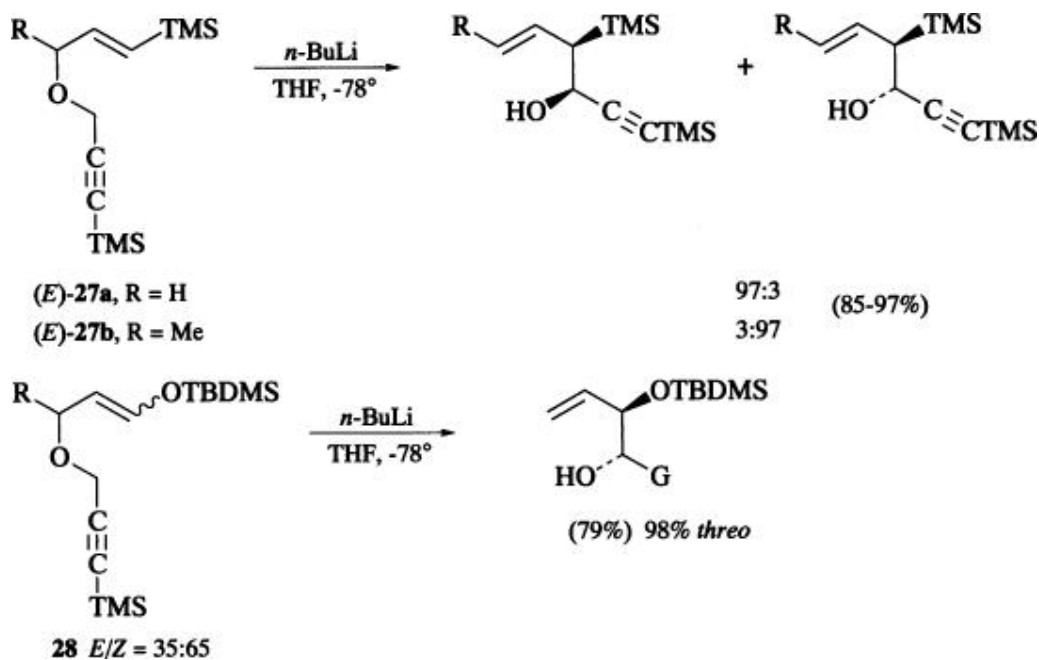
4.2.1.3. Cyclic Variants

The diastereoselection in cyclic variants is different from that in the acyclic counterparts discussed so far, since the proximity of the reacting centers enforced by bridging is expected to profoundly influence the transition state geometry. The diastereoselection in ring contraction via the {1,5} rearrangement is relatively well studied. For instance, the rearrangement of the 13 membered bis(allyl) ether **29** provides an entirely different selection from that of the acyclic counterpart. (41) Both the *E, E* and *Z, Z* substrates show *threo* (*trans*) selectivity to afford (E)-*trans*-**30** and (Z)-*trans*-**31** as single products, respectively,

29   30   31

(94-96%)
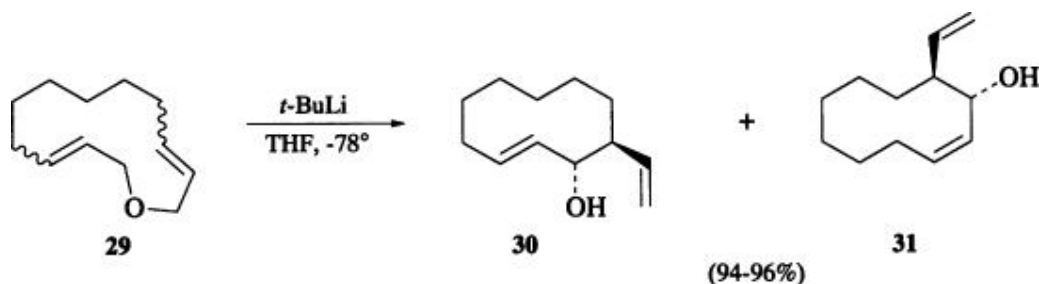
while the *E, Z* substrate produces a complex isomeric mixture. In contrast, rearrangement of the 13-membered allyl propargyl system **32** follows the general selection rule. (78, 79) The *E* substrate provides the *threo* (*trans*) product **33** exclusively, whereas the *Z* substrate affords the *erythro* (*cis*)

product **34** exclusively. Reasonable mechanistic grounds were advanced for these diastereoselections. For instance,
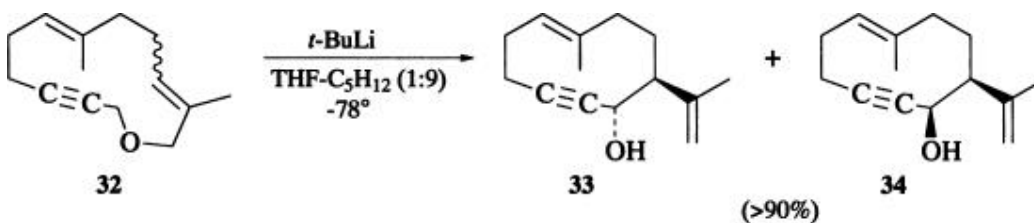
the high *E* to *threo* (*trans*) selection reflects the fact that conformer **C** is sterically less congested, since conformer **D** suffers from the steric interaction

C ⟶ *threo* (*trans*)   **D** ⟶ *erythro* (*cis*)
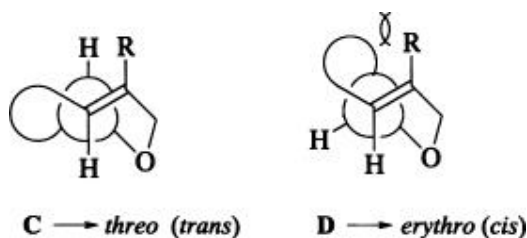
indicated. (25, 42, 43) Interestingly, diastereoselection in the rearrangement of the 17-membered ether **11** depends markedly upon the solvent used; hexane–tetrahydrofuran
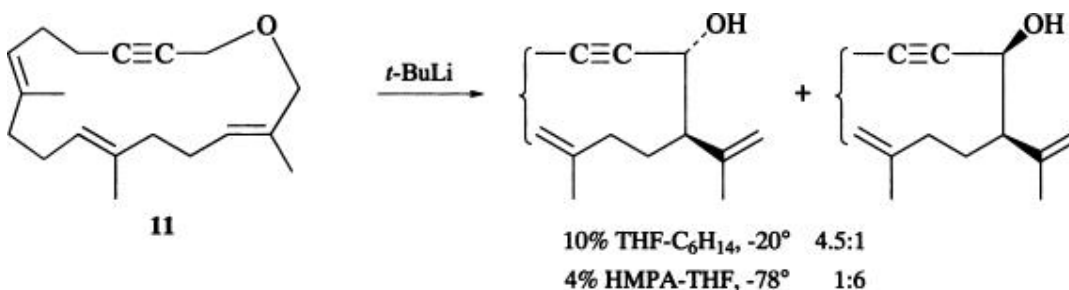
affords the *threo* (*trans*) product predominantly, whereas HMPA–tetrahydrofuran produces the *erythro* (*cis*) isomer as the major product. (42, 43) These observations suggest that ring size of the substrate and/or the nature of the base used are additional factors in determining diastereoselectivity in the [2,3]-Wittig ring contractions.

4.3. Asymmetric Synthesis

In principle, the asymmetric versions of the [2,3]-Wittig rearrangement leading to optically active products can be classified into four types in terms of the key stereoselection involved. The first is the so-called "asymmetric transition type" that employs a chiral substrate derived from an *enantiomerically enriched* allylic alcohol and hence involves asymmetric transmission (chirality transfer)

along the allylic array. The second is the "asymmetric induction type," which employs a substrate having a *chiral* substituent somewhere on the pericyclic array; hence the problem of diastereofacial selection (relative asymmetric induction) arises between the preexisting stereocenter and the newly created chiral center(s). The third is the "chiral base-induced type," which is an enantioselective reaction of an achiral substrate with a chiral *nonracemic* base. The fourth is the "configurationally defined carbanion type," which involves a diastereo- or enantiomerically defined lithium-bearing terminus, wherein the steric course of inversion vs. retention at the migrating terminus is the key issue.

4.3.1.1. Asymmetric Transmission Type

The most synthetically valuable feature of the [2,3]-Wittig rearrangement is its ability to transmit the chirality at C-1 of the allylic moiety into the newly created chiral centers at C-3 and C-4 as generalized in Eq. 21. This type of asymmetric rearrangement destroys the original chirality

(21)
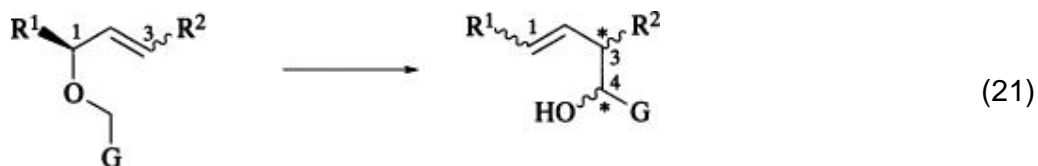
while simultaneously creating new ones, and hence there is conservation of optical purity. The asymmetric transmission technology is widely applicable to both acyclic and cyclic substrates, thus providing an efficient tool for concurrent control of absolute and relative stereochemistry with considerable stereopredictability.

Guided by the transition state model advanced above, one can readily predict both the olefinic geometry and the absolute and relative stereochemistry of the product from the three variables in the substrates: the absolute configuration, the double bond geometry, and the nature of the G group. In an asymmetric version of the highly (Z to *erythro*)-selective variants shown in Eq. 19, for instance, (S)-(Z)-**35** would rearrange predominantly to (E)-($3S$, $4S$)-**36** through the transition

(Z)-(S)-**35**

(E)-($3S,4S$)-**36**
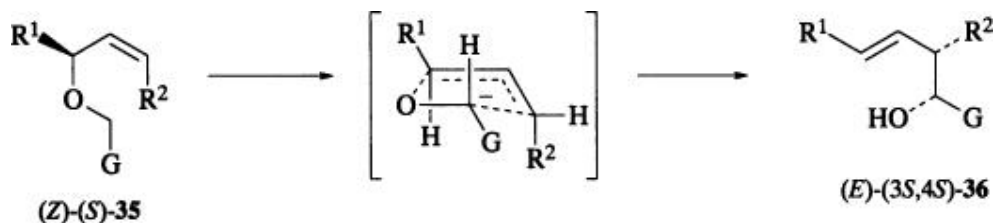
state with *exo*-R^1 and *equatorial*-G. The key to success is the proper choice of the combination of olefin geometry and G group.

The first success of such asymmetric transmission was in the rearrangement of (S)-(Z)-**35a**, which attains complete chirality transfer along with practically 100% of both *E* and *erythro* selectivity, as predicted, to eventually afford insect pheromone **37** of the same optical purity as that of the substrate. (80) Essentially

>98% *E*, >98% de

36a (64%)

37, 98% ee

35a, 98% ee
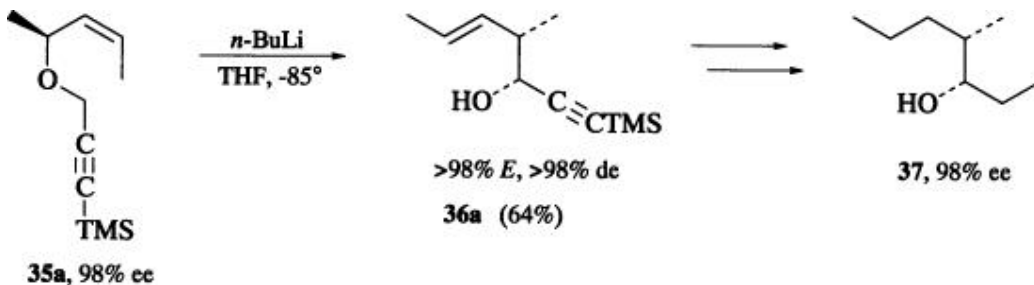
complete chirality transfer (>95%) has also been achieved in other (*Z* to *erythro*)-selective variants with different G groups such as CH = CH$_2$ (81) and C$_6$H$_5$ (81, 82) (Eqs. 22 and 23).

100% chirality transfer

(22)

R = *i*-Pr, 86% de, 97% chirality transfer
R = *i*-Bu, ~100% de, 94% chirality transfer

(23)
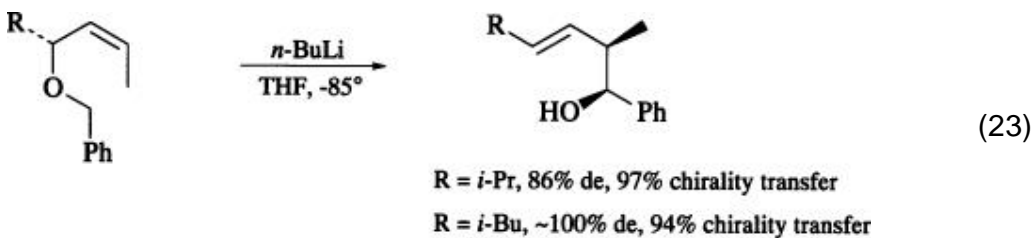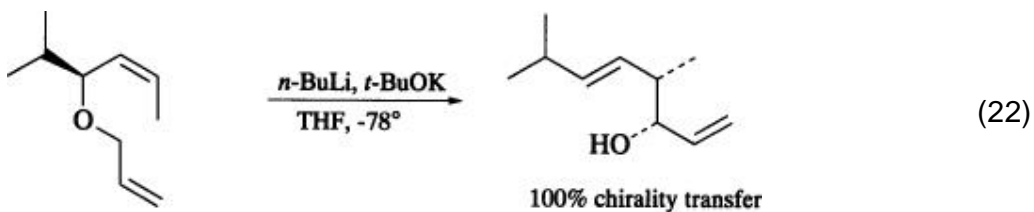
This asymmetric transmission technology is also applicable to the rather unusual (*E* to *erythro*)-selective variants. The Zr–enolate rearrangement of **38** gives (*Z*)-**39** with >96% chirality transfer, (69) whereas the Ti–enolate rearrangement of **40** produces (*E*)-**41** with complete chirality transfer. (63)

Effective asymmetric transmission is also feasible in rearrangements of tertiary allylic ethers, if they

(Z)-39   (53%)

(E)-41   (62%)
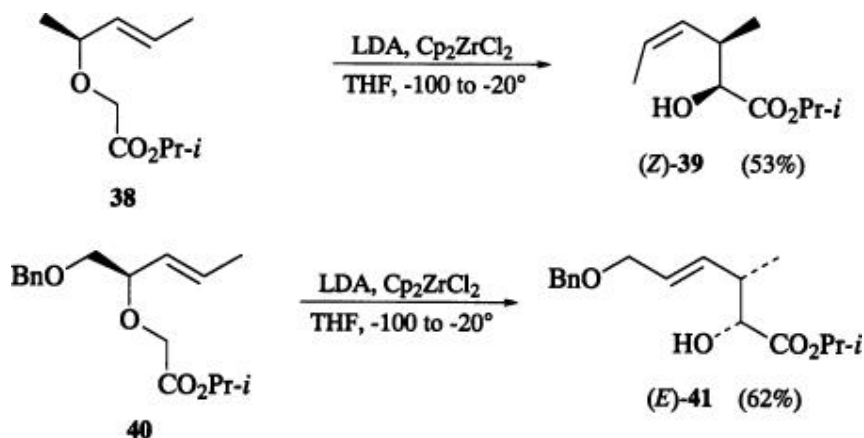
are well suited for the exclusive formation of a single olefinic geometry. The rearrangements of (E)- and (Z)-**42** afford exclusively (E)-*erythro*- and (E)-*threo*-**43**,

erythro-(E)-**43**

threo-(E)-**43**

(E)- or (Z)-**42**
R = Me, BnOCH₂
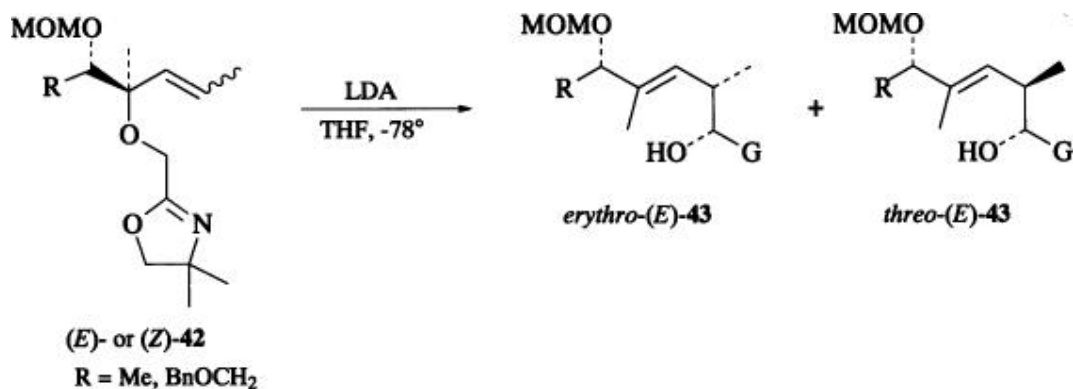
respectively, whereas the epimers at the tertiary stereogenic center produce a stereoisomeric mixture. (72, 84)

The asymmetric transmissions via cyclic [2,3]-Wittig rearrangements are also known, although they are relatively small in number. Equation 24 shows an example

(24)
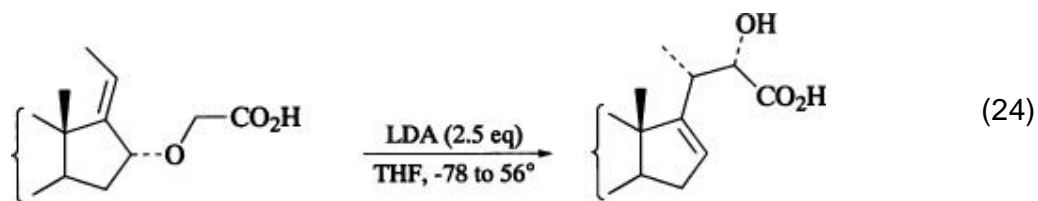
of {3,4} rearrangement in the steroid side chain synthesis. ([85], [86]) More applications of this type of rearrangement to steroid side chain synthesis will be described later. Equation [25] illustrates an example of {3,5} rearrangement. ([54]) Another

$$(25)$$
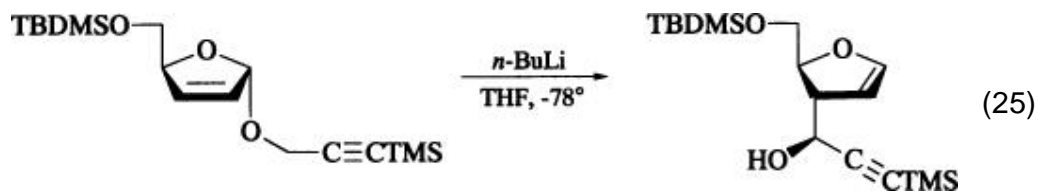
interesting example is the dianion {3,3} rearrangement on the carbohydrate template (Eq. [26]), where (E)- and (Z)-**44** afford *threo*- and *erythro*-**45**, respectively. ([56])

$$(26)$$
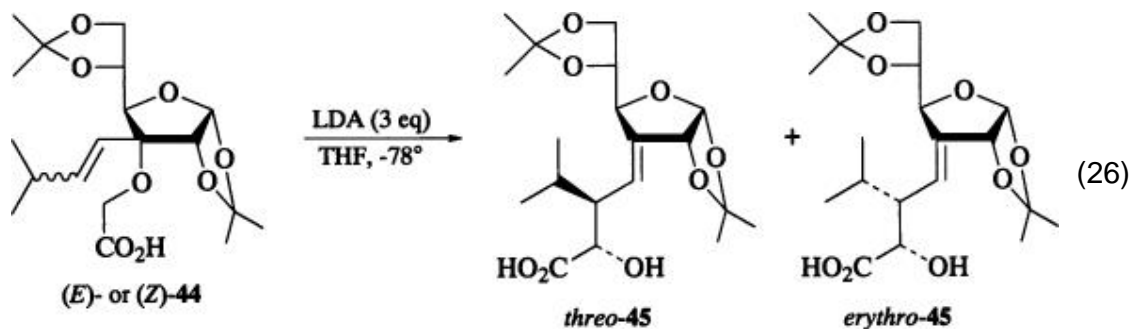
It is noted that the senses of diastereoselection in Eqs. [24] and [26] are opposite to those observed with the acyclic counterparts.

While the asymmetric transmission processes discussed so far involve chirality transfer from C-1 to both C-3 and C-4, the C-1 chirality can, of course, be transferred to either C-3 or C-4 when one employs an enantiomerically enriched substrate where G = H and R^2 ¹ H or G ¹ H and R^2 = H, respectively (cf. Eq. [21]).

Such 1,3-chirality transfer has been achieved via the Wittig–Still variant within acyclic and cyclic frameworks. The simplest example is the rearrangement of (Z)-(S)-**46** that affords (E)-(R)-**47** exclusively, while (E)-(S)-**46** provides a 1:1 mixture of (E)-(S)- and (Z)-(R)-**47**. This 1,3-chirality transfer technology has been widely utilized in cyclic frameworks to effect a suprafacial hydroxymethylation. ([50], [51], [87-90])

(Z)-(S)-**46**　　　　　　　　　　　　　　　　　　(E)-(S)-**47**

(77%)

R = H, *i*-Pr　　　　　　　　　　　　(34-45%)
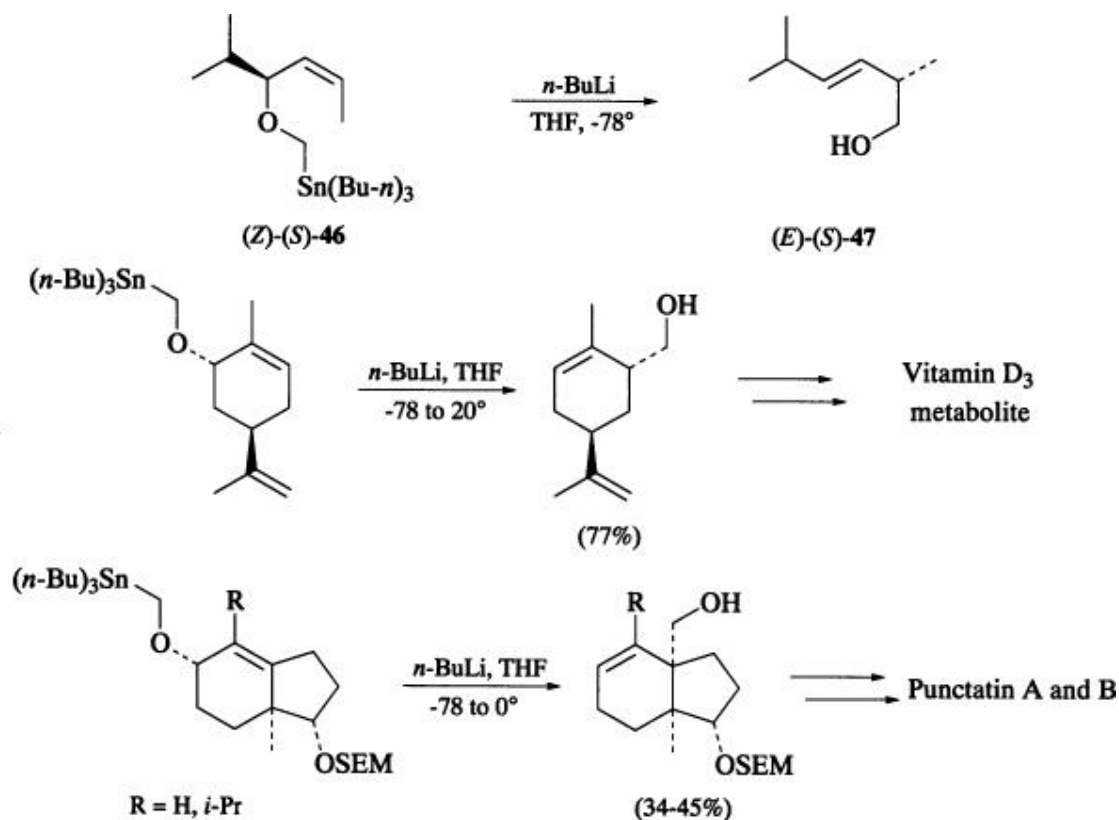
1,3-Chirality transfer from a tertiary stereocenter is also known. The rearrangements of (E)- and (Z)-**48** afford (E)-(S)- and (E)-(R)-**49** respectively. Again, the epimers at the tertiary stereocenter produce an E/Z mixture. (91-93)

(E)- or (Z)-**48**　　　　　　　　(E)-(S)-**49**　　　　　　　(E)-(R)-**49**
R = CH(Me)Pr-*n*
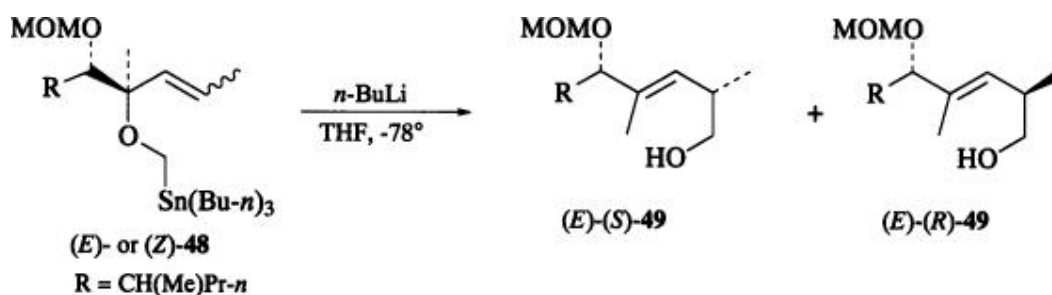
Chirality transfer from C-1 to C-4 has been reported in different variants. Again, the minimum requirement for complete 1,4-chirality transfer is the exclusive formation of only one double-bond geometry. Equation 27 shows acyclic examples

(27)

X = H, Me, TMS
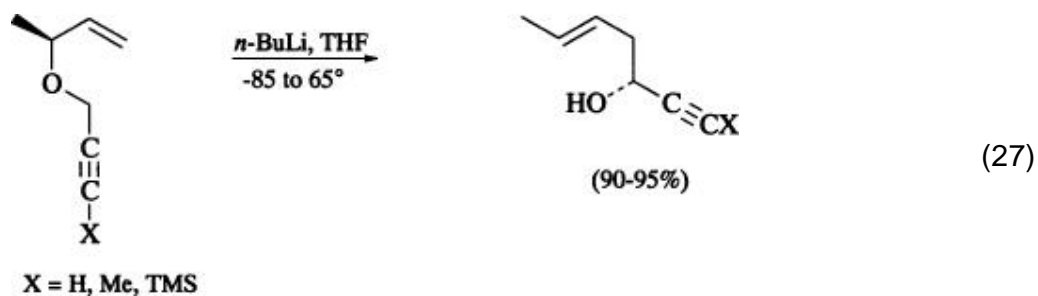
which attain 81–98% of chirality transfer together with 93–98% *E* selectivity.
(67) An example of complete 1,4-chirality transfer from a tertiary stereocenter
is already shown in Eq. 16. An example of the {3,4}-rearrangement is given in
Eq. 28. (94)
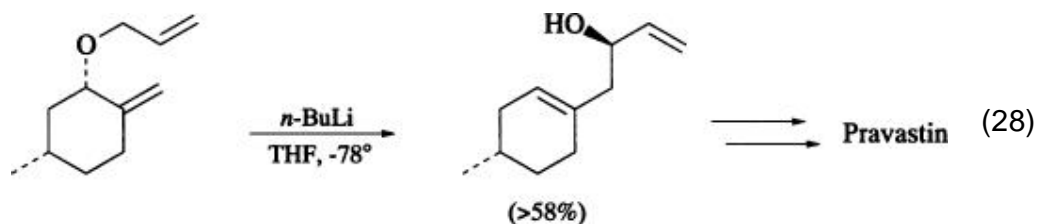
4.3.1.2. Asymmetric Induction Type
This type of rearrangement can be divided into the three types **A–C** in terms of
the location of a chiral substituent (G_c^* or R_c^*) in the substrate.
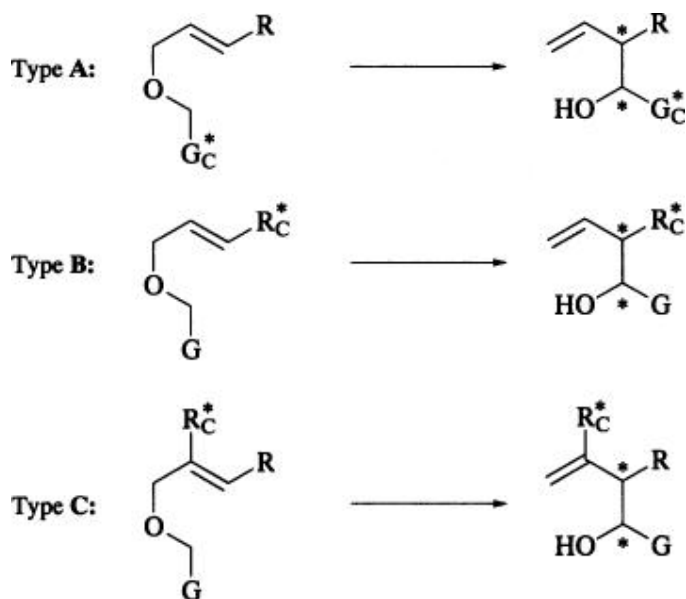
The rearrangement of type **A** has been well studied using various chiral enolates as the migrating terminus, despite the potential competition posed by the [3,3]-Claisen process. The first example reported, **50a**, employed the chiral 2-oxazoline ring as the G_C^* to provide a reasonably high level of both diastereofacial selection (% de) and *erythro* selection (Eq. 29). (95) However, a similar reaction of

50a R = Me

(29)
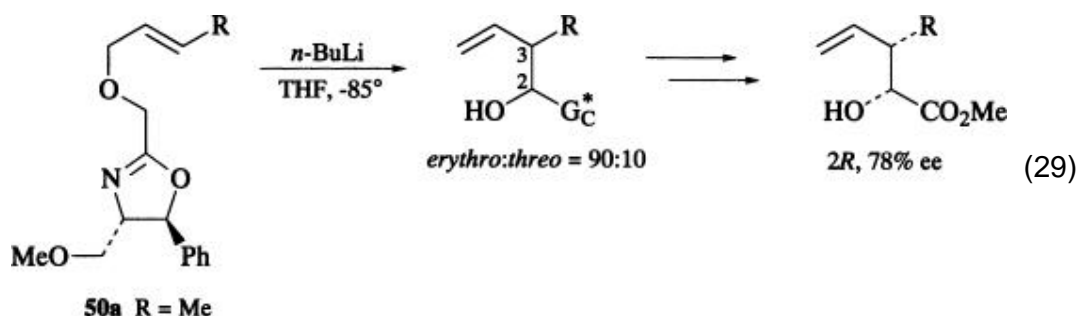
50b (R = H) shows only 38% de (2*R*). Interestingly, the dianion rearrangement of **51** with potassium hydride shows the opposite sense of π-facial selection to give (2*S*)-**52** in 84% de, whereas the KH-induced process in the presence of 18-crown-6 exhibits a further reversal in π-facial selection to afford (2*R*)-**52** in 96% de. (96) It should be noted that similar KH-induced rearrangements of the (*E*)-crotyl analog of **51** provided an extremely low level of *erythro* selection.

	(2*R*)-**52**	(2*S*)-**52**
KH, THF, 15-20°	8	92
KH, 18-crown-6, -20°	98	2
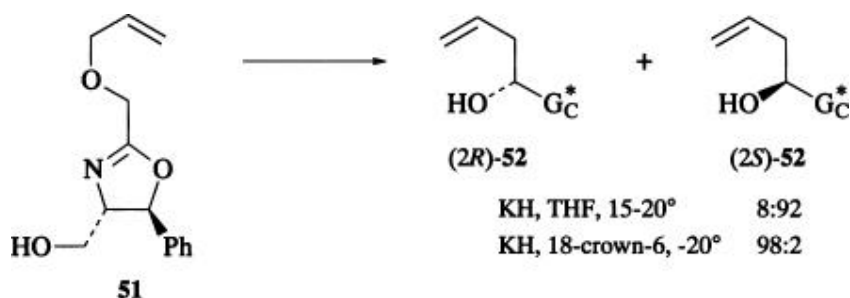
Other examples have been reported which involve a chiral amide enolate (61, 97) and a chiral ester enolate. (98) In view of the tremendous recent progress in chiral enolate chemistry, this type of asymmetric enolate [2,3]-Wittig strategy provides a powerful tool for asymmetric synthesis of a variety of α-hydroxy-β-alkylcarboxylic acid derivatives, an important class of intermediates for natural product synthesis.

$Y_C^* = $ pyrrolidine-CH$_2$OH		LDA, THF, -78°	(2*S*), 95% *erythro*, 52% de
$Y_C^* = $ pyrrolidine-CH$_2$OMEM		LDA, Cp$_2$ZrCl$_2$, THF, -78°	(2*R*), 98% *erythro*, 60% de
$Y_C^* = $ MOMO-pyrrolidine-CH$_2$OMOM		LDA, Cp$_2$ZrCl$_2$, THF, -70°	(2*S*), 97% *erythro*, 96% de
$Y_C^* = $ -O-bicyclic-Ph		LDA, HMPA-THF, -70°	(2*S*), 90% *erythro*, 97% de
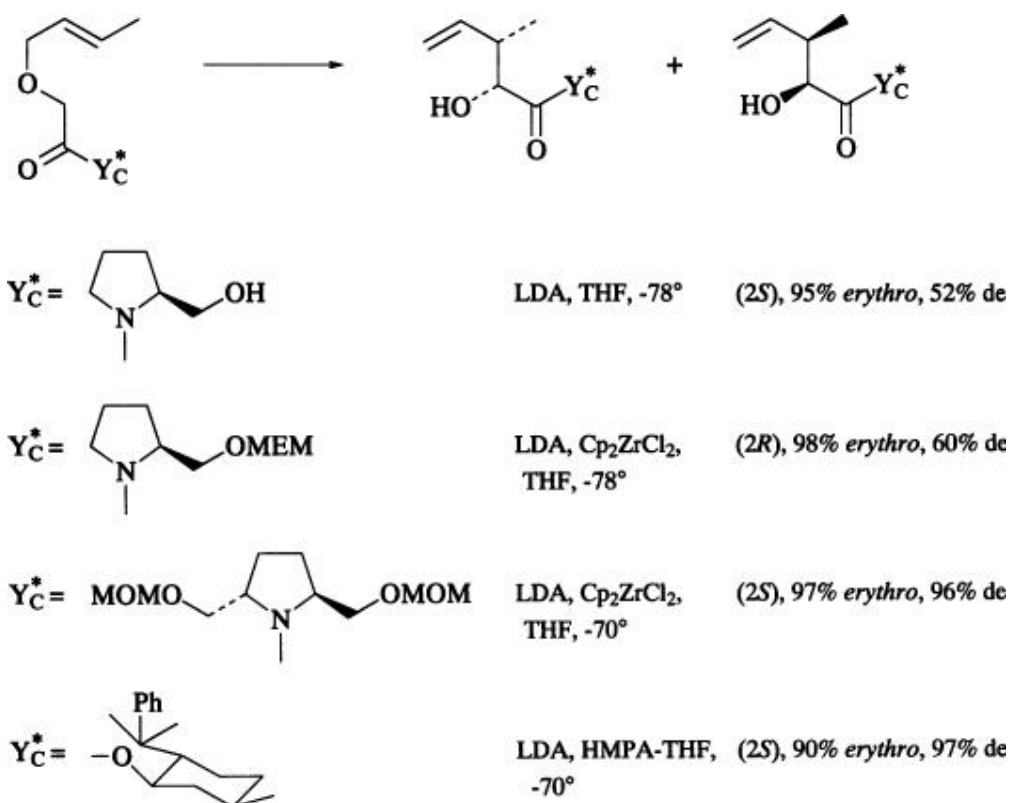
A novel example employs an enantiomerically pure (*o*-methoxybenzene) chromium complex as the G_C^* to afford exclusively the *erythro* product (97%) in 99% ee after oxidative demetalization (Eq. 30). (99-101) Also interesting is the ring

$$(30)$$

(67%) 99% ee
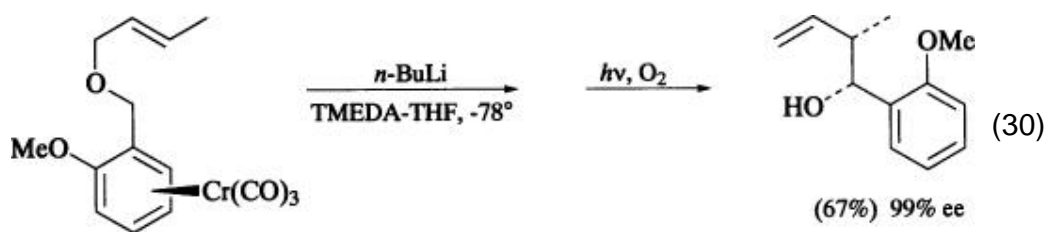
contractive rearrangement of **53**, in which a high asymmetric induction by a remote stereocenter is observed. (102, 103)

53 → (90%) 89:11
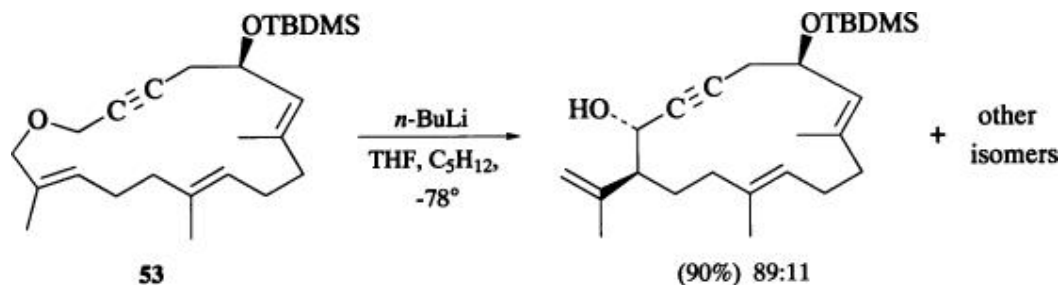
The rearrangement of type **B** is also amply precedented. The successful examples are shown in Eqs. 31 (104-108) and 32, (109) where high asymmetric induction by the chiral γ substituent is observed together with high *erythro* or *threo* selection, depending on the olefin geometry. Thus this type of asymmetric rearrangement provides an efficient way to achieve stereocontrol over three contiguous chiral centers.

(Z)-**54**		(79-87%)
(Z)-**54a**	G = C=CTMS[104, 105]	>99 : 0 : 0
(E)-**54a**[104]		12 : 81 : 7
(Z)-**54b**	G = CO$_2$Bu-t[106]	>99 : 0 : 0
(Z)-**54c**	G = Sn(Bu-n)$_3$[107]	>99 : 0 : 0 G = H

(31)

(88%) >99:1

(32)
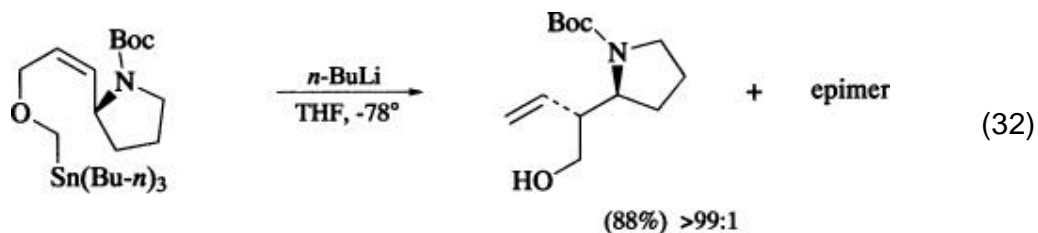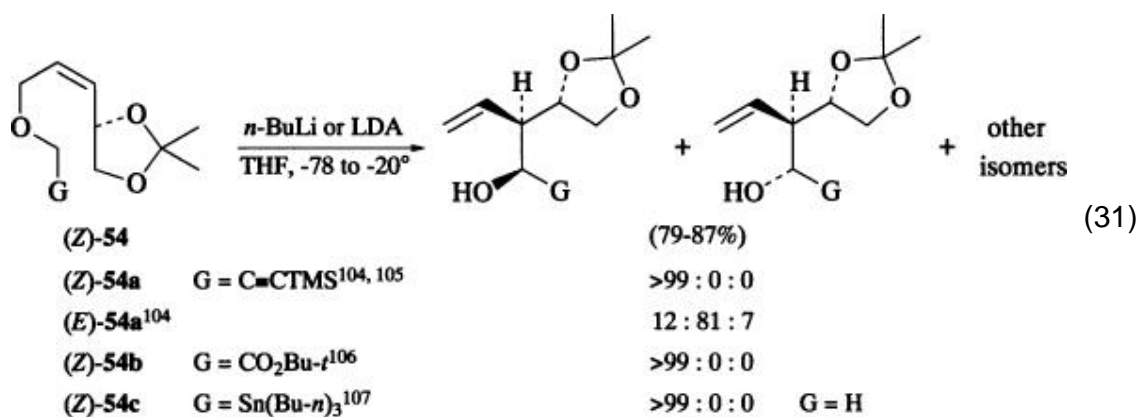
This methodology is also applicable to cyclic variants, as shown in Eqs. 25 and 26. Equations 33 (110) and 34 (58) illustrate the applicability to {4,5} and {5,5} rearrangements.

$$(33)$$

(98%) *trans:cis* = 93:7

$$(34)$$

(63%) 100:0
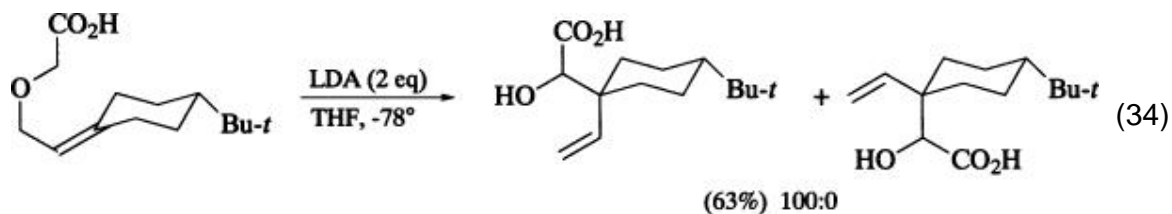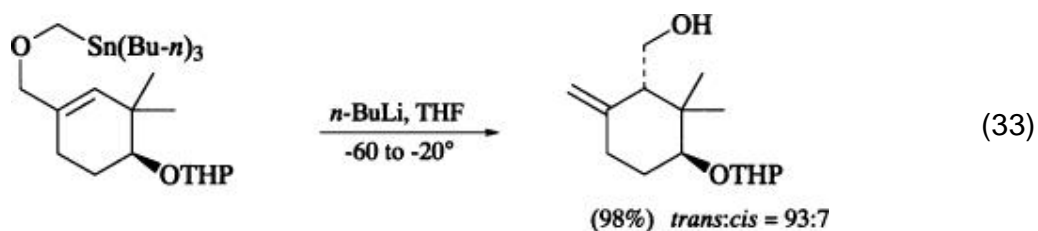
Rearrangements of type **C** are also known but with few examples. High levels of 1,3 asymmetric induction have been reported in the rearrangements of **55** and **56**, but their senses are opposite each other. (111) An extremely high *anti* asymmetric induction has also been observed in the {4,5} rearrangement of **57** to establish a quaternary stereocenter. (112, 113)

(E)-55, G = Sn(Bu-n)₃
(Z)-55
(E)-56, G = C≡CTMS

(70-89%)
3:97, G = H
95:5
88:6

57

(>75%)

refigeranic acid
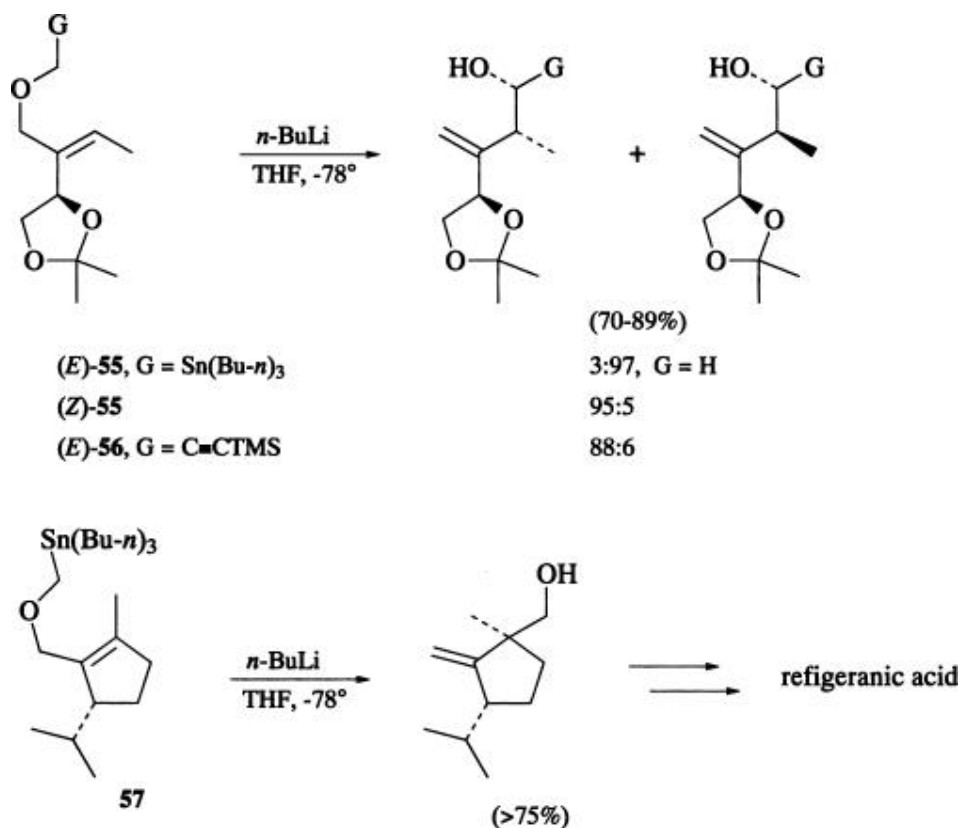
Of special interest is the rearrangement of **58**, which involves asymmetric induction of both types **B** and **C** to give the single stereoisomer **59**, a potentially useful intermediate for prostanoid synthesis. (114)

58

59 (89%)

prostanoid
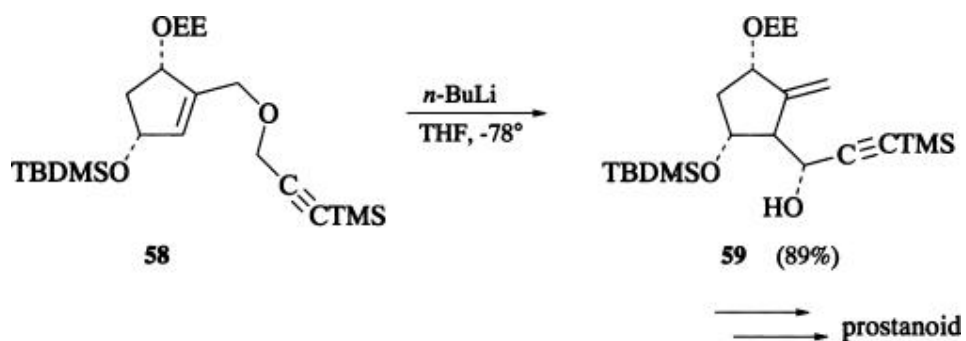
4.3.1.3. Chiral Base-Induced Type

In principle, the [2,3]-Wittig rearrangement with a chiral *nonracemic* base could produce an optically active product since the chiral terminus involved could be *nonracemic*. Thus this type of asymmetric process is enantioselective, and

hence is synthetically more valuable than the diastereoselective reactions described above. However, this is more difficult to practice. The first success was achieved in the {1,5} rearrangement of **60** with lithium amide (+)-**61**, which afforded (+)-alcohol **62** in 70% ee. (115, 116) The product was converted to aristolactone (+)-**63**. However, a similar rearrangement of
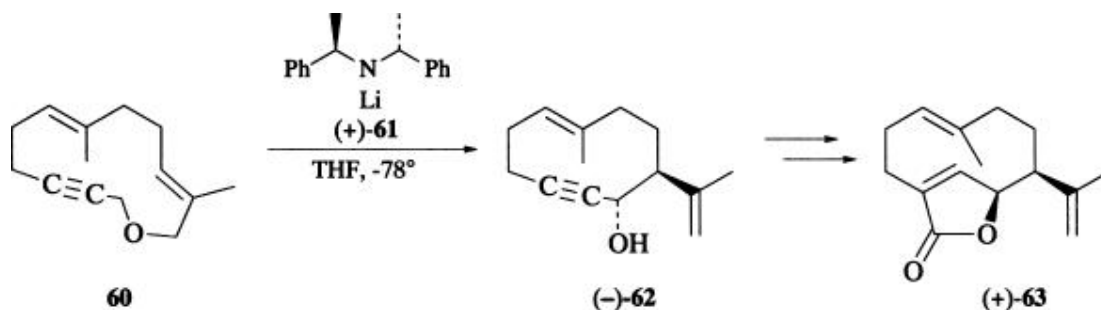
the closely related 9- and 17-membered substrates with (+)-**61** provided only 25 and 29% ee, respectively. (115-117) Accordingly, the level of enantioselection appears to depend critically upon the chiral environment provided by the cyclic framework. In fact, no appreciable levels of ee have been observed in the rearrangements of acyclic substrates with (+)-**61** (Eq. 35). (115, 116) However, the rearrangement of **64** with (+)-**61** has been shown to provide a higher optical yield. (118, 119)

$$G = CO_2H, C \equiv CH, CON(CH_2)_4 \qquad <5\% \text{ ee} \tag{35}$$
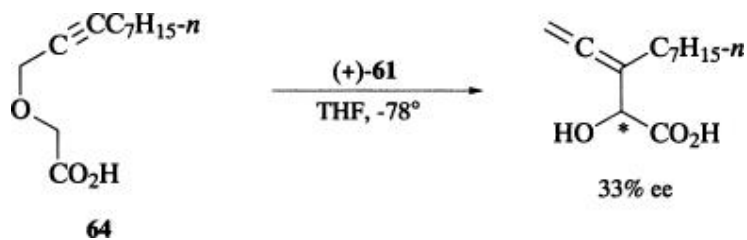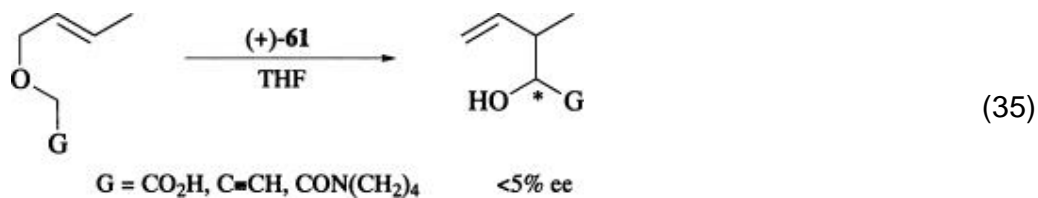
4.3.1.4. Configurationally Defined Carbanion Type

Since most asymmetric [2,3]-Wittig variants involve a chiral carbanion terminus, the fundamental problem encountered, which concerns the steric course, is inversion vs. retention at the lithium-bearing terminus (Eq. 36). That has been the subject of controversy.

(36)

inversion   retention
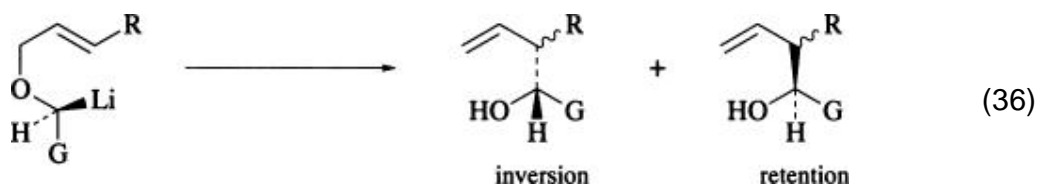
Conflicting conclusions have been drawn from the theoretical work based on ab initio molecular orbital calculations. (25, 27)

The first experimental evidence in support of the inversion course was reported in the rearrangement of the diastereomerically defined tetra hydropyran **65** which afforded the inverted [2,3]-Wittig product **66** along with the inverted [1,2]-Wittig product **67**. (120) More recently, rearrangement of the enantiomerically defined

Li 4,4'-di-*tert*-butylbiphenylide

THF, -78°

65   **66** (45%)   **67** (21%)
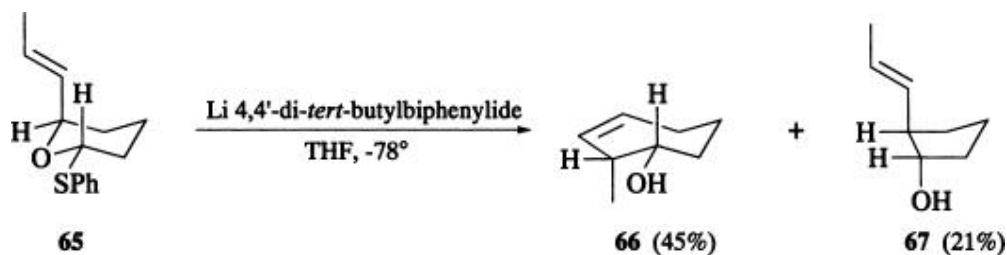
stannane (*R*)-**68** has been shown to proceed with complete inversion of configuration together with high *threo* selectivity in the synthesis of insect pheromone (+)-**69**. (121) Thus in general the [2,3]-Wittig rearrangement is likely to proceed with inversion of configuration at the lithium-bearing terminus.

n-BuLi

THF, -78°

(*R*)-**68**
88% ee

3*S*,4*R*
>99% de, 87% ee

(+)-**69**
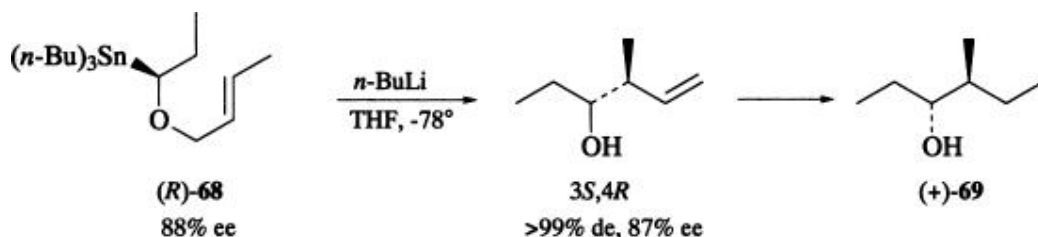
5. Synthetic Applications

The [2,3]-Wittig rearrangement has found many applications in stereocontrolled total syntheses of a vast array of natural products. In this section, a brief representative sampling of some uses of [2,3]-Wittig technology is described within selected contexts such as acyclic stereocontrol, steroid side chain synthesis, synthesis of medium- and large-ring natural products, and sigmatropic sequences.

5.1. Acyclic Stereocontrol

In the preceding sections some asymmetric [2,3]-Wittig variants were shown to create vicinal chiral centers with high asymmetric induction. Since the resulting stereodefined products possess a unique multifunctionality well suited for further stereocontrolled transformations, asymmetric [2,3]-Wittig technology provides a versatile method for acyclic stereocontrol over three or more chiral centers.

A typical example is the synthesis of (+)-blastmycinone (**73**). (122) This synthesis features the sequential combination of the rearrangement of (S)-**70** with zinc borohydride reduction (123) of hydroxy ketone **72** derived from **71**. This silylpropargyl ether protocol has also been utilized in the asymmetric synthesis of talanomycin A (**74**), (124) serricornin (**75**), (125, 126) and the fragment **76** of amphotericin B. (127)

74   75   76
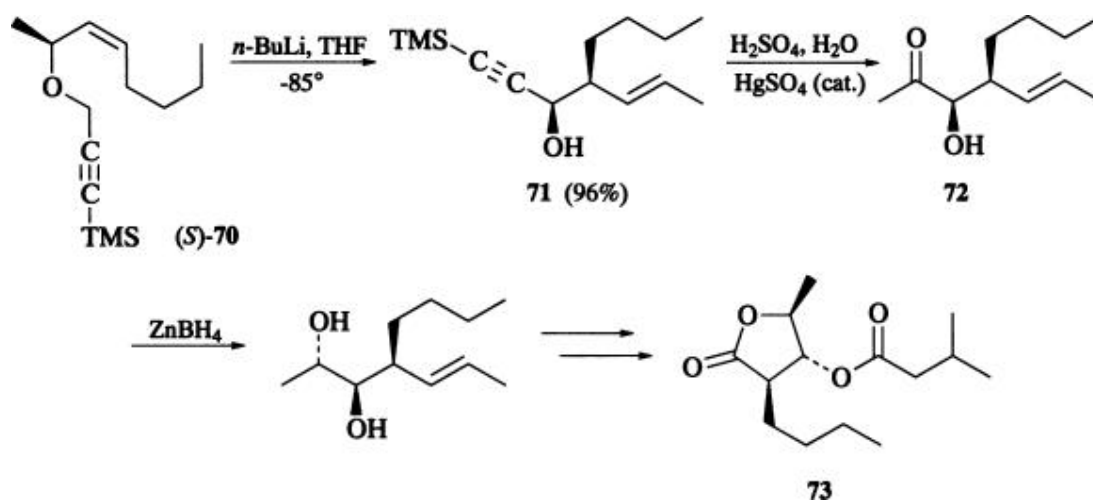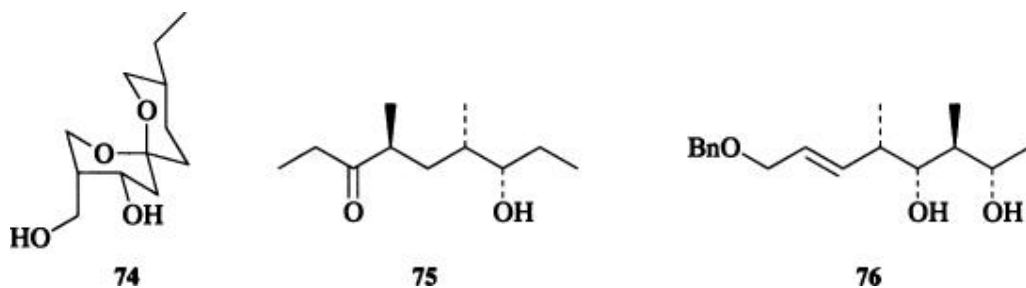
The asymmetric rearrangement of methallyl ether system **77a** has been used in the synthesis of the Prelog–Djerassi lactonic aldehyde **78** (128) and its acid from **77b**, (129) where the third chiral center is introduced by stereoselective hydroboration.

77a, R = *i*-Pr
77b, R = *i*-Bu

78
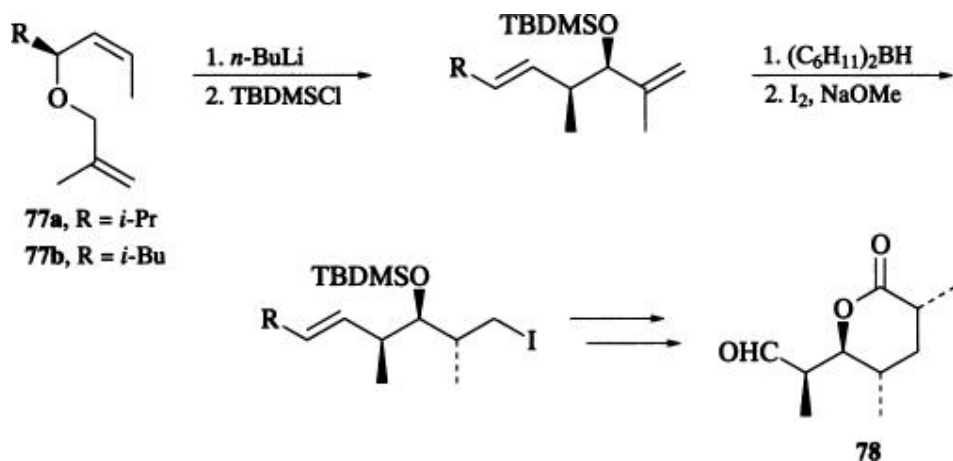
The [2,3]-Wittig product **41** from **40** described earlier has been elaborated to (+)-Ireland's acid **79** having four contiguous chiral centers, a key precursor of tirandamycin A (**80**). (130)

79

80
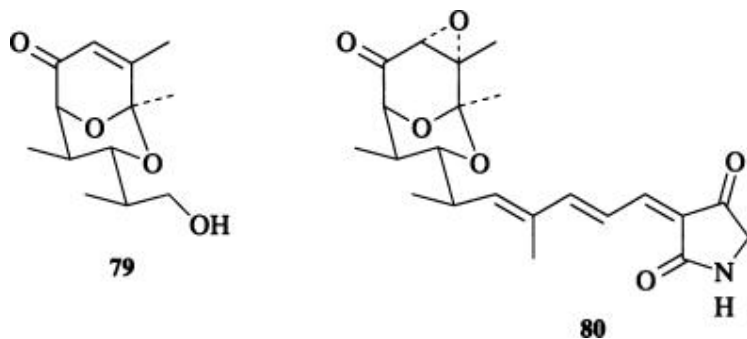
The asymmetric rearrangement of tertiary allylic ethers has also found

application in natural product synthesis. For example, the previously described rearrangement of (Z)-**48** provides a quick entry to (+)-2-epi-invictolide (**81**). (91-93) The asymmetric synthesis of subunit **82** of zincophorin has been achieved by rearrangement of a tertiary allylic ether of type (E)-**42** described earlier. (84) This type

81

82
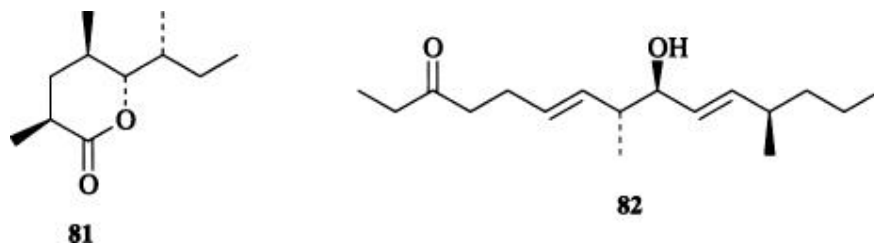
of tertiary [2,3]-Wittig protocol has also been utilized in the synthesis of key intermediate **83** to 18-deoxynargenicin A$_1$. (131) These examples demonstrate the
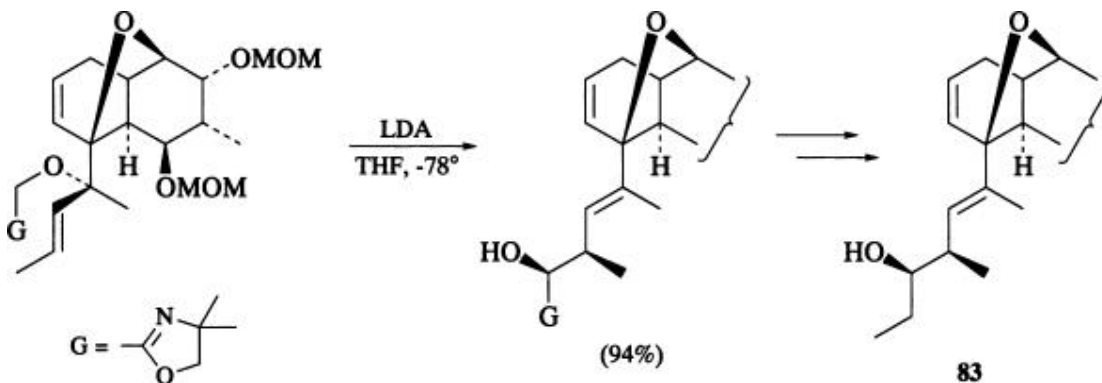
great potential of asymmetric [2,3]-Wittig technology as a general synthetic strategy for complex natural products with multiple chiral centers.

5.2. Steroid Side Chain Synthesis

Steroid side chain synthesis has attracted considerable synthetic effort over the decade, (132, 133) and within this context the concept of asymmetric transmission via [2,3]-Wittig rearrangement has found many applications. One general and simple application is to employ [2,3]-Wittig technology for effecting chirality transfer within side chain frameworks. The propargyl ether protocol has been used in the synthesis of petrosterol (**84**), a marine steroid. (134) Still's variant has been utilized

(50%) >95% S at C-25

84
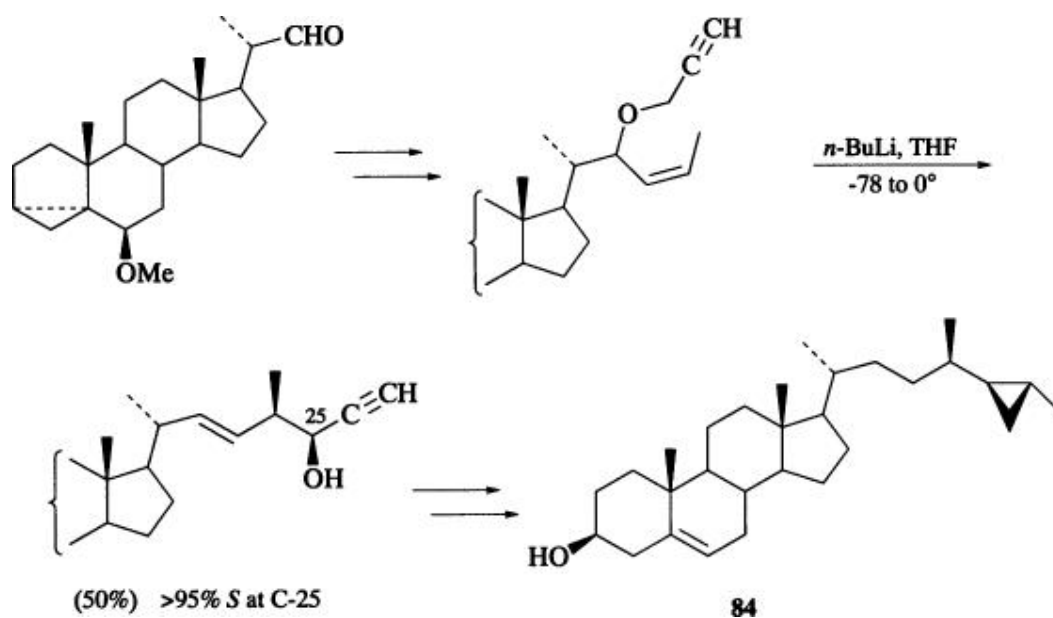
in the synthesis of (24R)-25,28-dihydroxy side chain (85) (135, 136) and (25R)-26-hydroxycholesterol (86), a potent inhibitor of cholesterol biosynthesis. (137) Notable

R = TBDMS

85 (82-84%) >99% R at C-24

86 (80%) >99% R at C-25
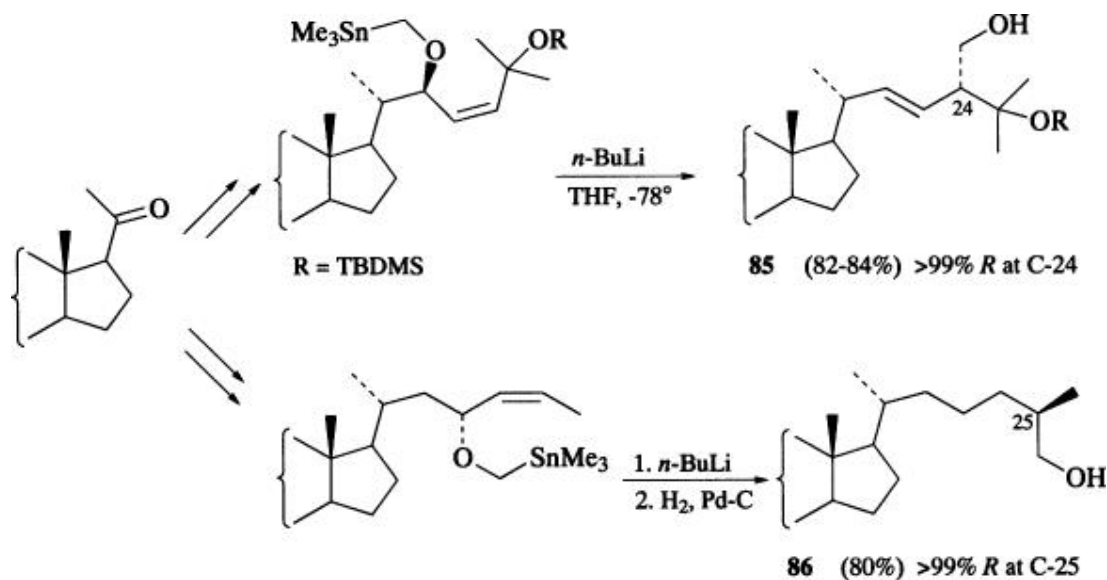
in these cases is the complete transfer of chirality coupled with the surprisingly high E selectivity.

Alternatively and more importantly, [2,3]-Wittig technology can be used for specifically transmitting an epimerically defined chirality at C-16 of the steroidal nucleus to the new chiral centers at C-20 and C-22 of the side chain as

generalized by Eq. 37. As already illustrated in Eqs. 10 and 24, this approach allows for the

$$(37)$$

erythro   threo
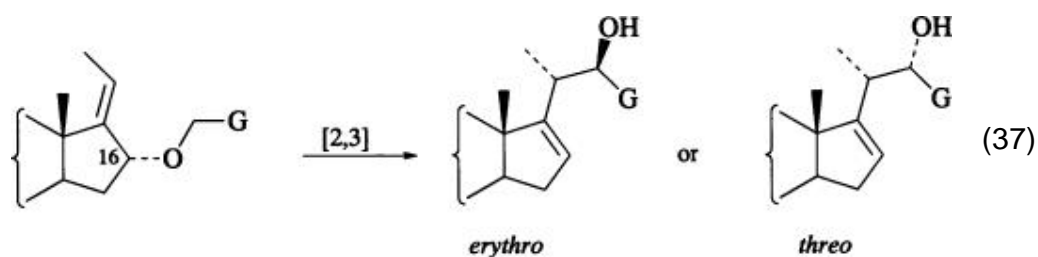
concurrent control of absolute and relative configuration at C-20 and C-22 through the proper combination of the *exo*-olefin geometry, the configuration (α and β) at C-16, and the G group. The most remarkable example is the stereocontrolled synthesis of either (22S)- or (22R)-hydroxy-23-acetylenic side chain from the single precursor **88a**, easily derived from the commercially available epoxypregnenolone **87**. (47) The dianion rearrangement of **88a** affords (20S, 22S)-**89** as a single stereoisomer, whereas introduction of the silyl group induces the reversal of diastereoselection to give (20S, 22R)-**90** as a single stereoisomer. Interestingly, the β -face rearrangement of (Z)-16 β -**88b** also affords **90** as a single stereoisomer. (138) These Wittig products can undoubtedly serve as key intermediates for the synthesis of many important sidechain modified steroids. For instance, **89** and **90** can be converted to the insect hormone ecdysone (139) and the plant growth regulator brassinolide, (140) respectively.
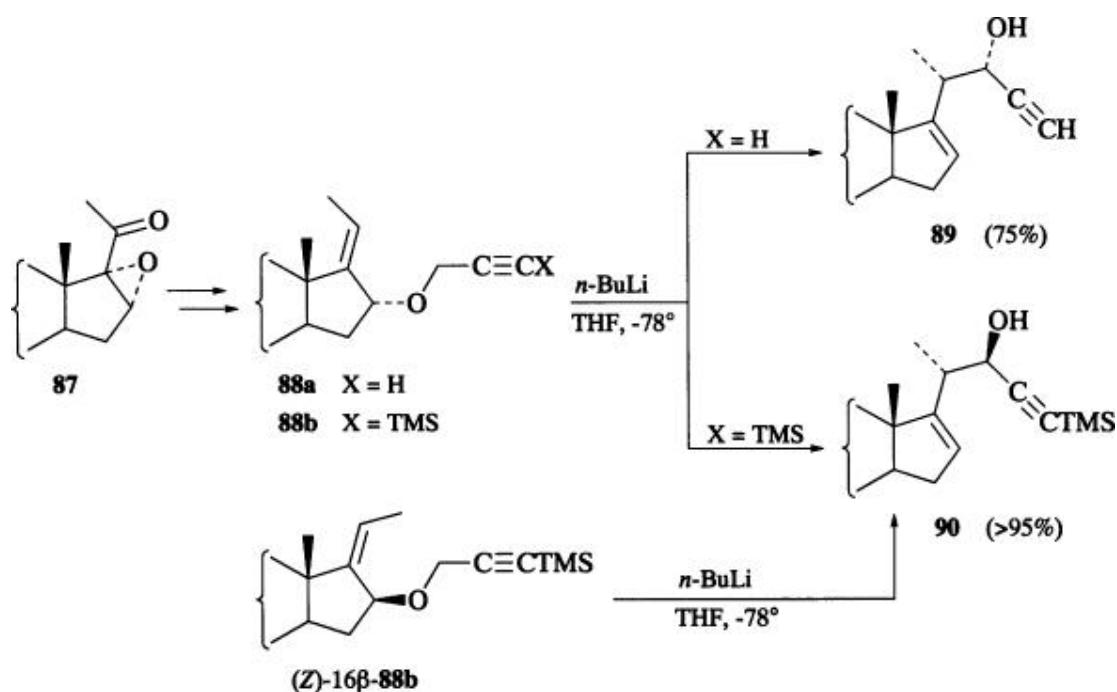
5.3. Medium and Large Ring Natural Product Synthesis

As mentioned in the preceding sections, various types of cyclic [2,3]-Wittig variants have found many applications in total synthesis of a variety of complex natural products. In this section, the synthetic utility of the {1,5} rearrangement ("[2,3]-Wittig ring contraction technology") is described within the context of total synthesis of medium and large ring natural products.

In the germacranolide area, (±)-costunolide (**93**) was synthesized via the rearrangement of 13-membered bis(allyl) ether **91**, which gave a mixture of **92** and its regioisomer(s) in a 75:25 ratio. (25, 41) A similar rearrangement of **94** provides a quick synthetic entry to (±)-hagenolide (**95**). (25, 141) The previously described rearrangements of the 13-membered (**32**) and 17-membered propargylic ethers (**11**) have been used as key steps in the synthesis of germacranolide (±)-aristolactone (**96**) (78, 79) and cembranoids, (±)-epimukulol (**97**), and (±)-desoxyasperdiol (**98**), (42, 43) respectively. Later, an enantioselective synthesis of (+)-**96** was accomplished via the chiral base-induced rearrangement of **60** as previously described. (116)

91   *t*-BuLi / THF, -78°   92 (98%)   93

94   95   96   97   98
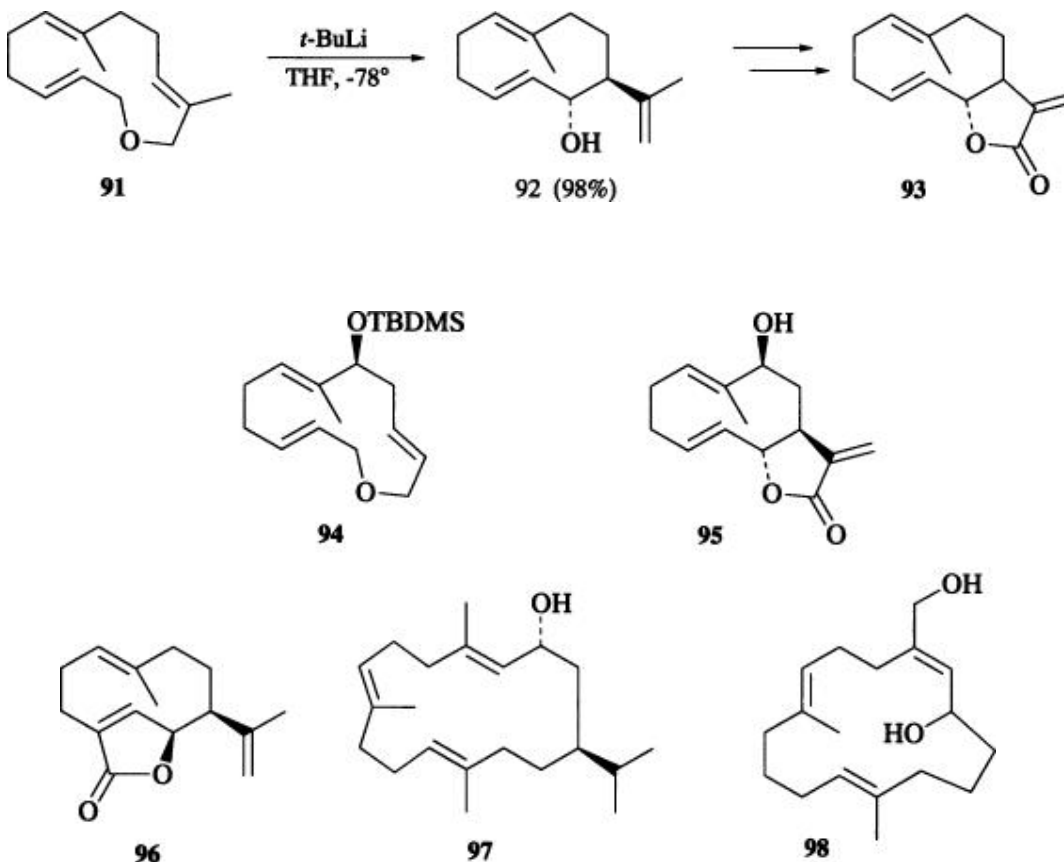
A similar [2,3]-Wittig ring contraction has also been used in the synthesis of a key precursor of kallolide A (**99**), an antiinflammatory diterpene, (142) and of (+)- α -2,7,11-cembratriene-4,5-diol (α -CBT, **100**) and its β -isomer, tumor inhibitory constituents of tobacco. (143, 144)
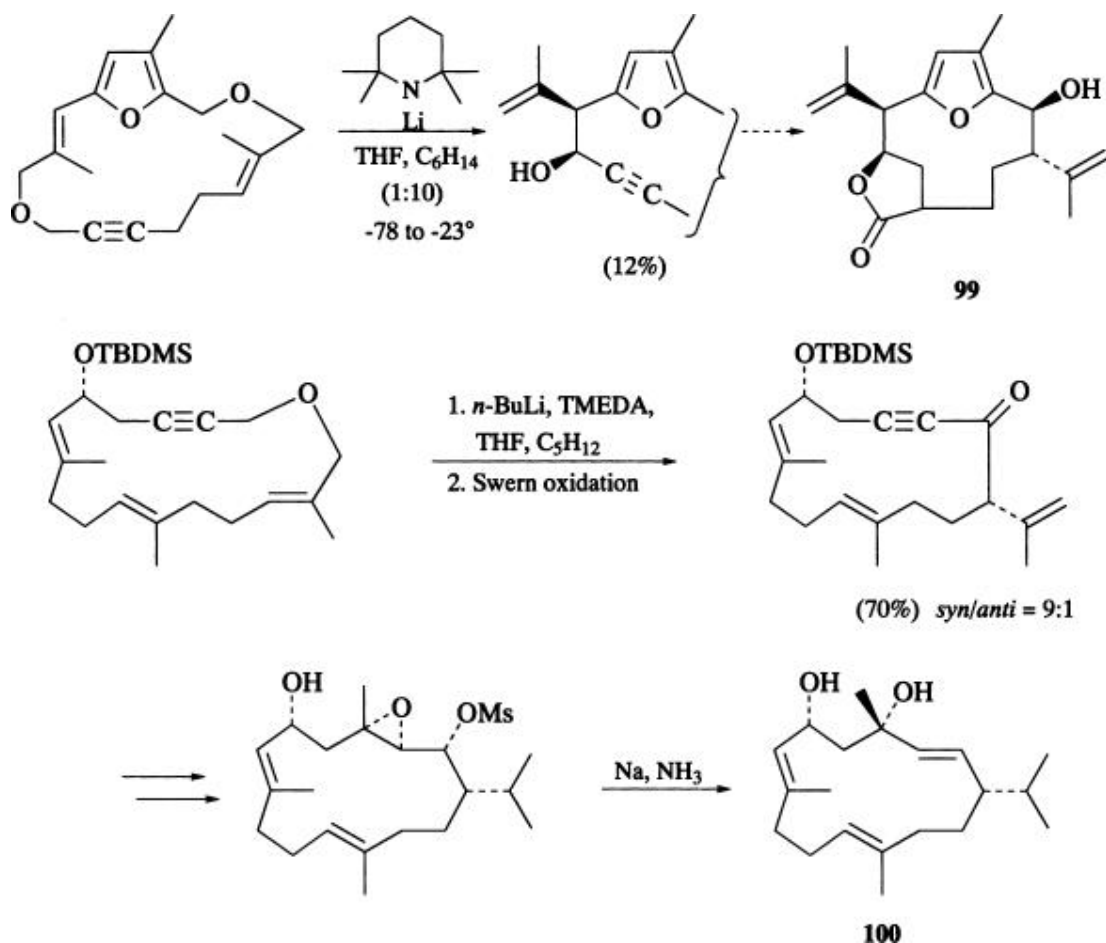
The utility of the [2,3]-Wittig rearrangement of 12-membered cyclic ether **101** has been demonstrated in the synthesis of the chromophore analogs **102** and **103** of antitumor antibiotic neocarzinostatin and esperamicin–calichemicin analog **104**. (145, 146) Thus [2,3]-Wittig ring contraction strategy provides a general and

101, R = H, Me

(62-66%) >98% cis

102, X = OAc, Y = H
103, XY = O

R = H

104
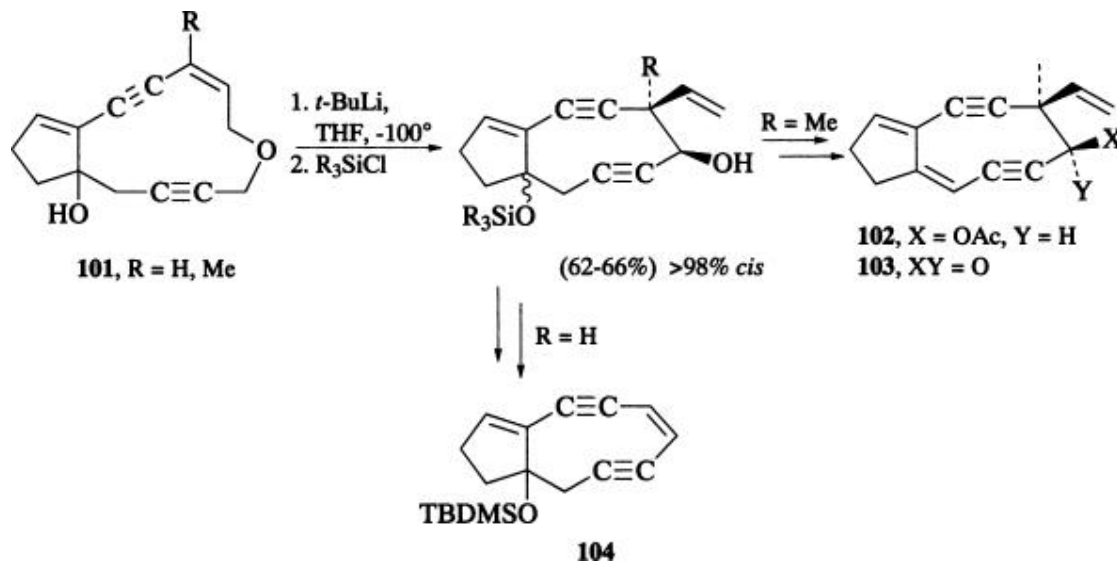
efficient approach to stereocontrolled construction of medium and large ring carbocycles.

5.4. Sigmatropic Sequences

In the preceding sections the [2,3]-Wittig rearrangement of unsymmetrical bis(allyl) ethers (or allyl propargyl ether variants followed by semihydrogenation) has been shown to afford 1,5-dien-3-ols in regio- and stereoselective fashions. Since the [2,3]-Wittig products and their derivatives are well qualified as substrates for different sigmatropic rearrangements, the particular [2,3]-Wittig variants may constitute various types of sigmatropic sequences. (147, 148) Equations 38–41 illustrate the four sequences developed thus far, which provide unique and facile synthetic methods for various classes of unsaturated carbonyl compounds possessing interesting molecular frameworks. (149, 150) Of particular value is that the net effect of these sequences allows two or three allylic moieties initially linked by an ether bond(s) to be recombined into a new C -C bond(s) in a regio- and stereocontrolled manner.

(38)

(39)

(40)

(41)
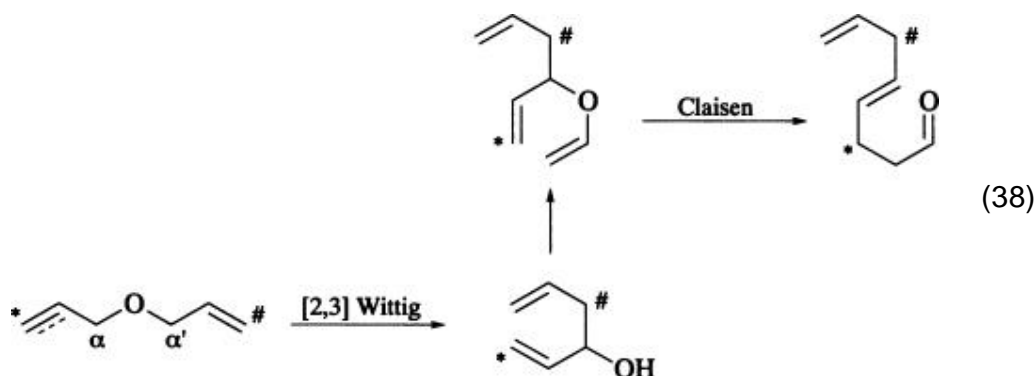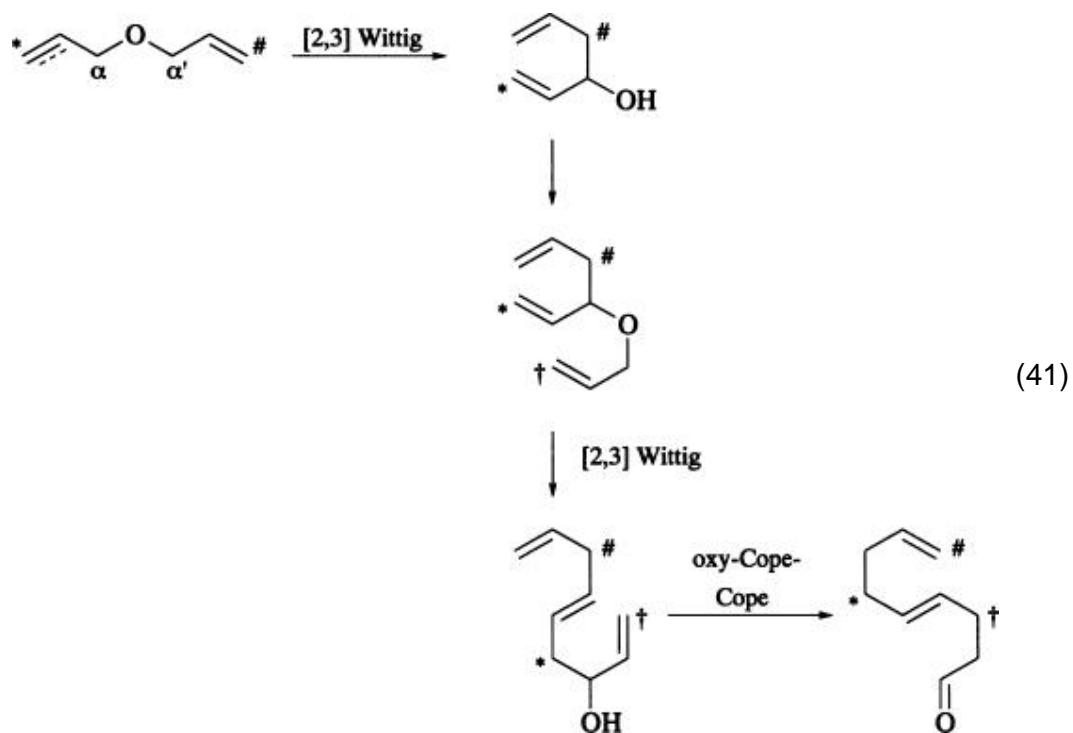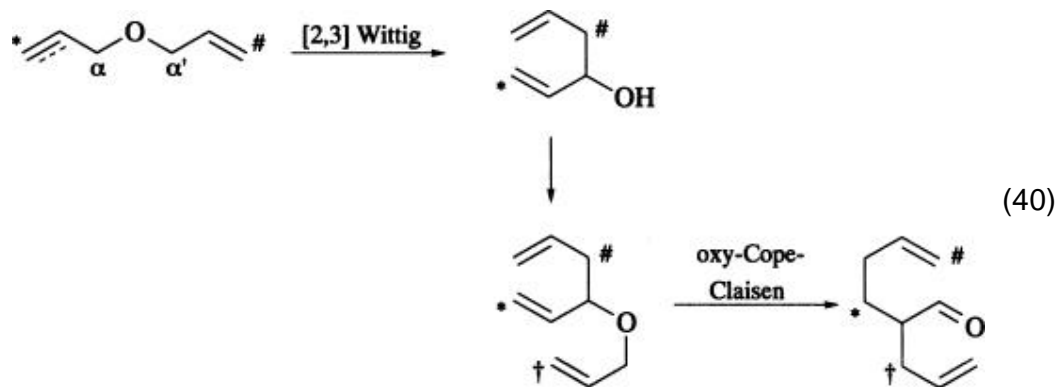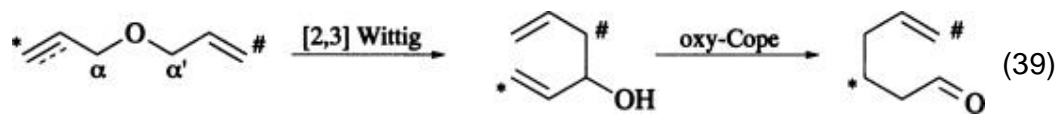
As illustrated by Eq. 38, [2,3]-Wittig products can be used as substrates for the Claisen rearrangement to afford a variety of the functionalized 1,4-dienes. (151)

For instance, the enol ether Claisen process (152) of **105a** affords (*E,E*)-dienal **106a** and the Johnson–Claisen modification (153) of **105b** gives (*E,E*)-dienoate **107b**, whereas the Ireland–Claisen modification (154) of the acetate of **105b** produces (*E,E*)-dienoic acid **108b**. Thus, the [2,3]-Wittig–Claisen sequence permits ready access to a wide variety of functionalized (*E,E*)-dienes which are often found in natural products as well as synthetic intermediates thereof. Its synthetic potential has been illustrated in the synthesis of butenolide **109**, a well-known precursor of antibiotic (±)-cerulenin (**110**). (151)

105a R^1 = Me, R^2 = H
105b R^1 = n-C$_5$H$_{11}$, R^2 = H

106 Y = H
107 Y = OEt
108 Y = OH

109

110
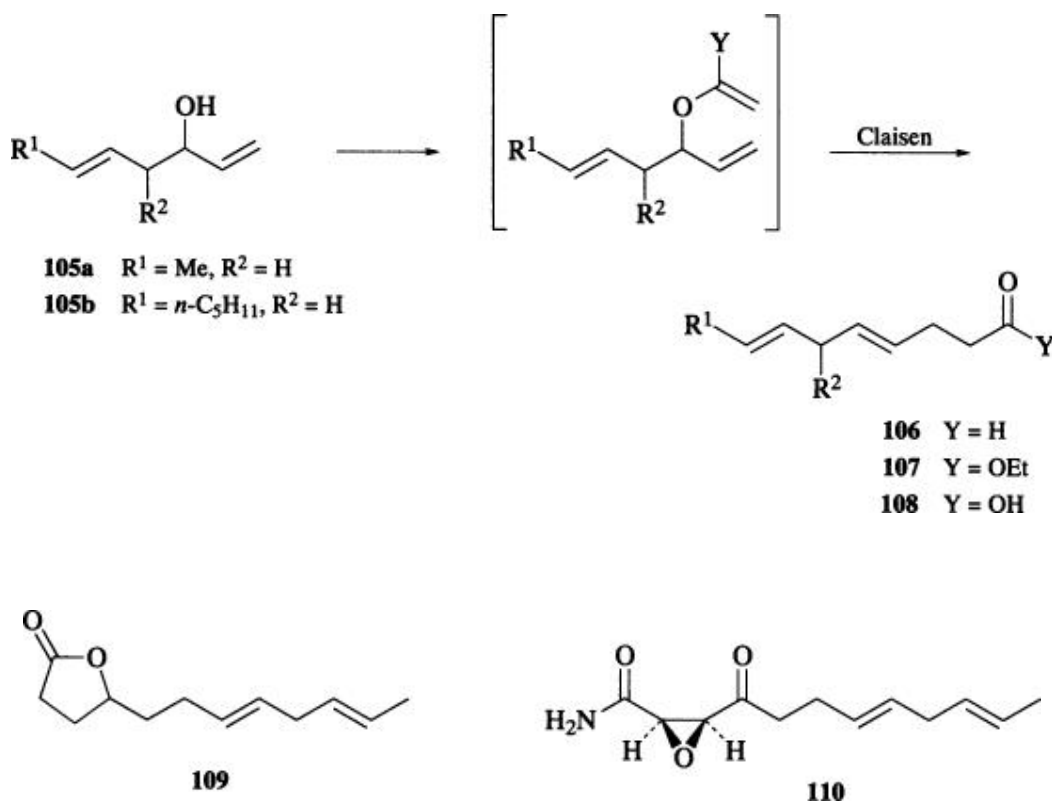
As depicted by Eq. 39, the sequential [2,3]-Wittig-oxy-Cópe rearrangement provides a versatile route to δ , ε -unsaturated carbonyl compounds. Of particular significance is that the easy availability of stereodefined 1,3-dien-3-ols via diastereoselective [2,3]-Wittig variants makes it possible to analyze the hitherto unsettled stereochemistry of the acyclic oxy-Cope process. (155) For instance, the *E/Z* selection in the oxy-Cope process of [2,3]-Wittig product of type **111** is not dependent on the substrate stereochemistry, but on the rearrangement procedure (Eq. 42). (149, 150) The anionic oxy-Cope procedure (156, 157) provides a modest *E* selectivity

(42)
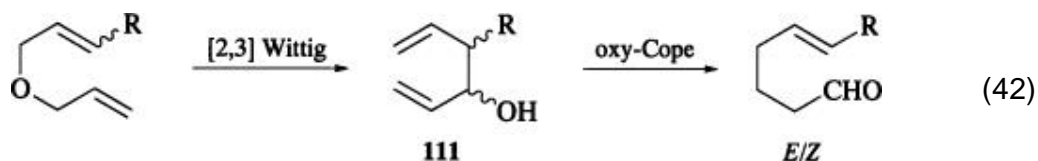
(67–72%), whereas thermolysis in decane (*ca.* 170°) affords an increased *E* selectivity (92–95%). The utility of the [2,3]-Wittig-thermolytic oxy-Cope sequence has been illustrated in the synthesis of insect pheromone (±)-brevicomine (**112**) and marine natural product oxocrinal (**113**) (158) and of functionalized vinyl silanes (Eq. 43). (159-161)

112   113

(43)
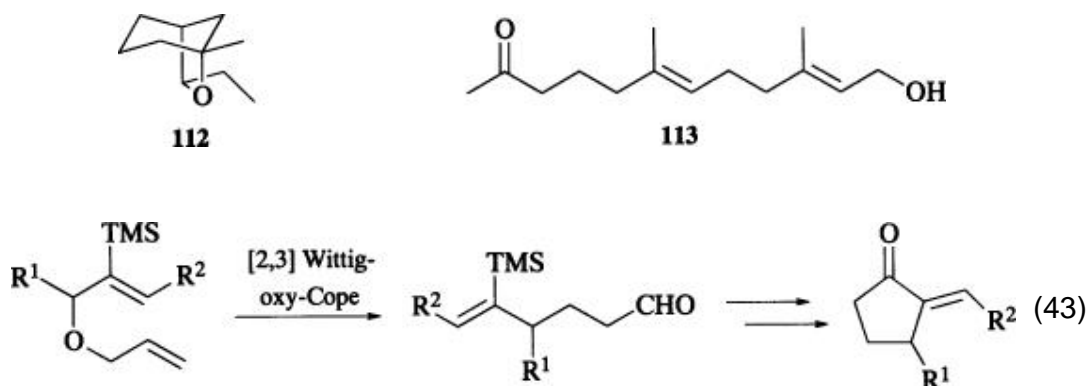
In contrast, however, the stereochemistry of the anionic oxy-Cope rearrangement of type **114** has been reported to depend critically on the substrate stereochemistry; e.g., (*Z, erythro*)- and (*Z, threo*)-**114** exhibit 98%*E* and 80%*Z*
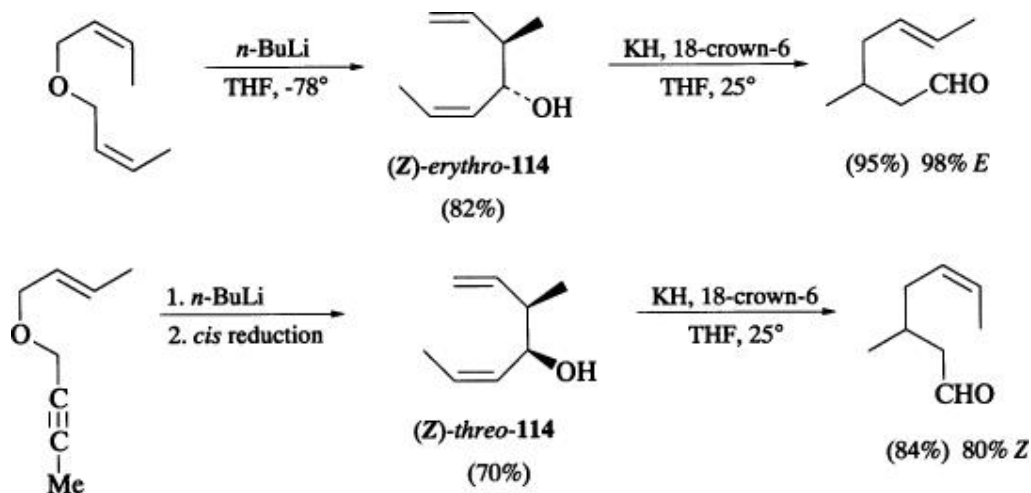
selectivity, respectively, while the *E* counterparts provide a moderate *E* selectivity. (162) More interestingly, the anionic oxy-Cope process of (*erythro*)-**116** derived from (*S*)-**115** proceeds with high *E* and *threo* selectivity together with nearly complete asymmetric transmission in the formal total synthesis of insect pheromone (+)-farnal (**117**). (163) Thus acyclic oxy-Cope technology, when properly designed in terms of the substrate stereochemistry, provides a new efficient method for acyclic stereocontrol.

The triple sigmatropic sequence depicted by Eq. 44 can be achieved by thermolysis of allylic ether **118**, prepared via etherification of the [2,3]-Wittig product, to afford dienal **119** as the major product. (149, 150) In certain cases cyclic alcohol **120** is also formed as a byproduct which arises from an intramolecular ene reaction of **119**.

(*S*)-**115** **116** >96% de (75%) 91% ee **117**

(44)

118 **119** (41-46%) **120**
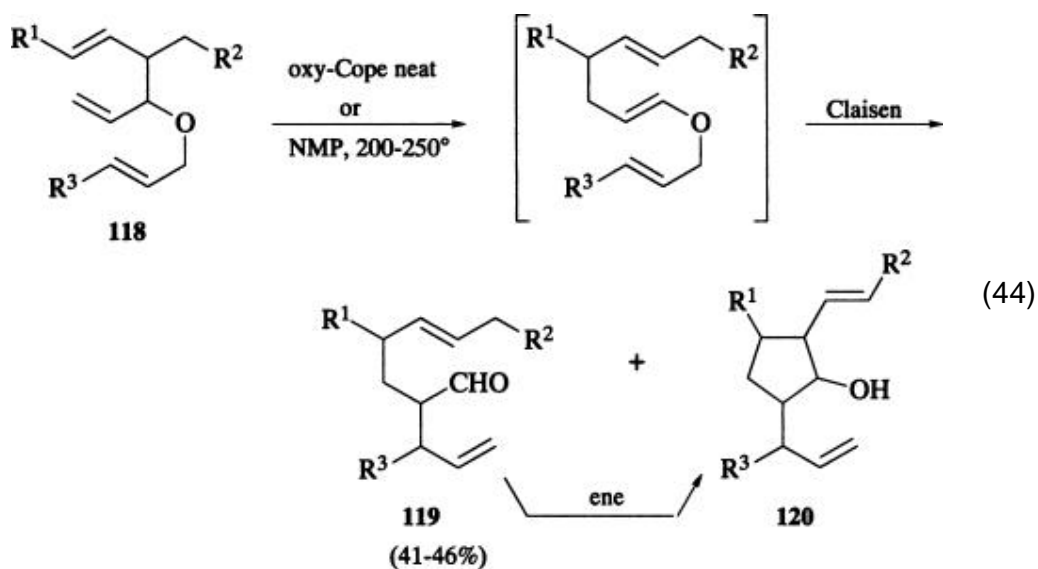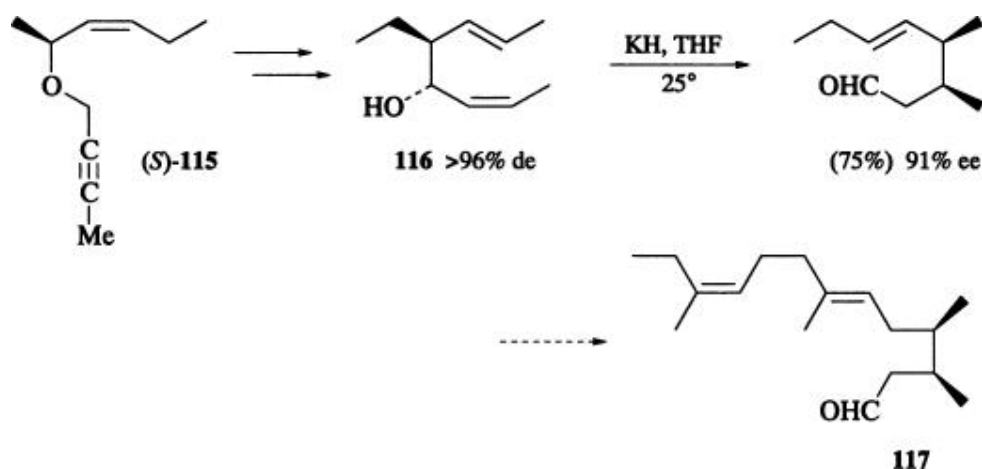
Furthermore, the quadruple sequence depicted by Eq. 45 can be effected by another [2,3]-Wittig process of ether **118** followed by thermolysis of the resulting trienol **121** to give trienal **122**.

118

118a, R = (CH₂)₂CH=CMe₂

[2,3] Wittig

121

OH

oxy-Cope
NMP, 202°

OH (Eq. 45)

Cope

122 (44%)

CHO

R

(45)
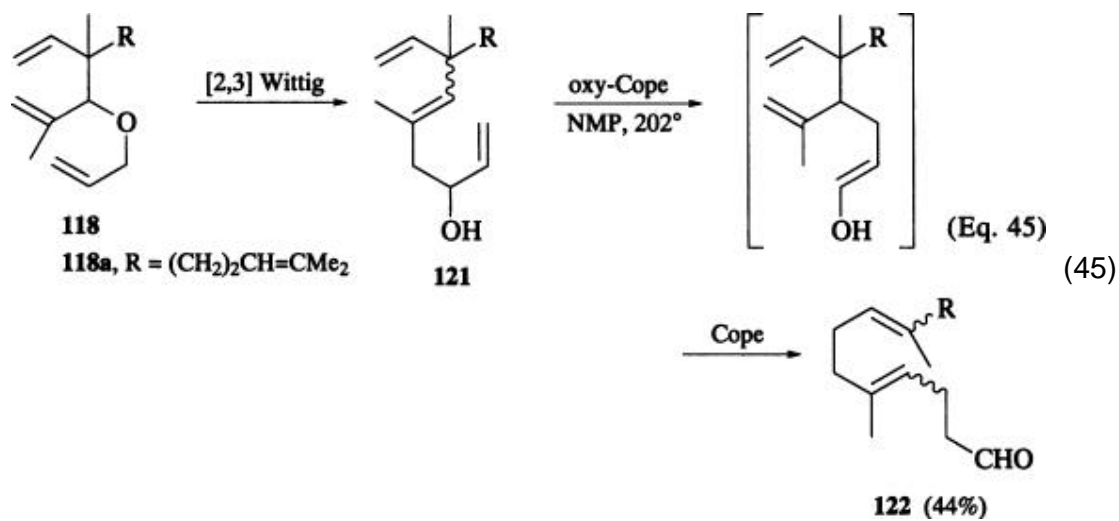
6. Experimental Procedures

6.1.1.1. threo-4-Methyl-5-hexen-1-yn-3-ol [Rearrangement of (E)-Crotyl Propargyl Ether] (29)

A solution of *n*-butyllithium in hexane (160 mL, 208 mmol) was added dropwise to a cold (–85°) solution of (*E*)-crotyl propargyl ether (8.8 g, 80 mmol) in tetrahydrofuran (160 mL) (in an ethanol/liquid nitrogen/dry ice bath). The resulting mixture was stirred at that temperature for 8 hours, allowed to warm to 0° (5 hours), and quenched with saturated aqueous ammonium chloride solution (50 mL). Usual workup followed by distillation afforded a predominantly *threo* mixture of 4-methyl-5-hexen-1-yn-3-ols (6.32 g, 72%) as an oil: bp 52–53°/10 mm Hg; IR (neat) 3500, 3300, 1645, 1000, 920 cm^{-1}; ^{1}H NMR δ 1.10 (d, *J* = 7.2 Hz, 3H), 2.10–2.63 (m, 1H), 2.32 (d, *J* = 2.3 Hz, 1H), 4.13 (dd, *J* = 5.4 and 2.3 Hz, 1H), 4.97–5.28 (m, 2H), 5.82 (ddd, *J* = 17.3, 10.1, and 7.5 Hz, 1H); GC (130°) t_R = 25 and 28 minutes (7:93). On addition of Eu(fod)$_3$ (8 mg) to a solution of the alcohol in carbon tetrachloride (7.6 mg in 0.3 mL), the doublet at δ 1.10 was changed into the two doublets at δ 1.88 and 2.13 (relative intensity = 1:13); the ^{1}H NMR ratio was identical with the GC ratio.

6.1.1.2. erythro-4-Methyl-5-hexen-1-yn-3-ol [Rearrangement of (Z)-Crotyl γ -(Trimethylsilyl)propargyl Ether] (29)

A solution of (*Z*)-crotyl γ -(trimethylsilyl) propargyl ether (9.12 g, 50 mmol) in tetrahydrofuran (50 mL) was treated with *n*-butyllithium (50 mL, 60 mmol) in the predescribed manner. To the resulting mixture was added a mixture of cesium fluoride (0.25 g, 1.67 mmol), water (2.7 mL), and methanol (4.65 mL), and the mixture was heated at 50° for 15 minutes. Usual workup followed by distillation gave a predominantly *erythro* mixture of 4-methyl-5-hexen-1-yn-3-ol (5.5 g, 75%): GC (130°) t_R = 25 and 28 minutes (98:2).

6.1.1.3. (–)-(3R,4S,5E)-2,4,7-Trimethyl-1,5-octadien-3-ol [Rearrangement of a Bis(allylic) Ether] (128)

Potassium *tert*-butoxide (6.17 g, 55 mmol) was dissolved in 100 mL of tetrahydrofuran. The solution was cooled to –78° and 8.51 g (50.6 mmol) of (*Z*)-1-(2-propyl)-2-butenyl-2-methylpropenyl ether was added. A solution of *n*-butyllithium (40 mL, 1.55 M, 62 mmol) was slowly added. The mixture was warmed to 0° over 4 hours. The reaction was quenched with water and the product was extracted with ether. The organic phase was dried over magnesium sulfate and concentrated. Kugelrohr distillation (90°/25 mm Hg) gave 7.41 g (87%) of the product. Analysis by HPLC (methanol:ethyl acetate:hexane = 1:5:100, Partisil M9 column) indicated a 97:3 mixture of *erythro* and *threo* products (the *erythro* isomer was eluted second). The ratio was confirmed by ^{1}H NMR (200 MHz): *erythro* δ 3.87 (d, *J* = 5.9 Hz); *threo* δ 3.66 (d, *J* = 8.3 Hz). A diastereomerically pure material was obtained by flash

chromatography (0.5 methanol, 5 ethyl acetate, 100 hexane): ^{1}H NMR
(200 MHz) δ 0.97 (d, J = 6.6 Hz, 6H), 0.99 (d, J = 6.8 Hz, 3H), 1.64 (br, OH),
1.70 (s, 3H), 2.20–2.40 (m, 2H), 3.87 (d, J = 5.9 Hz, 1H), 4.87 (m, 1H), 4.93 (m,
1H), 5.30 (dd, J = 15.6 and 6.8 Hz, 1H), 5.46 (dd, J = 15.6 and 6.2 Hz, 1H); [13]C
NMR (50.1 MHz) δ 14.6, 18.5, 22.6, 31.1, 39.7, 79.0, 111.7, 129.3, 138.1,

145.4; $[\alpha]_D^{24} + 2.56°$(c 3.36, THF). ^{1}H NMR analysis with the aid of Eu(hfc)$_3$

indicated a 95:5 mixture of enantiomers. Exact mass calcd for $C_{11}H_{20}O$: m/e
168.1514. Found: m/e 168.1517.

6.1.1.4. (1S,3aS,7aS)-7,7a-Dihydro-4-isobutyl-7a-methyl-1-[(2-trimethylsilyleth
oxy) methoxy]-3a(6H)-indanmethanol [Stille Rearrangement via Tin–Lithium
Exchange (51)
A solution of
(1S,5S,7aS)-5,6,7,7a-tetrahydro-7a-methyl-1-[(2-trimethylsilylethoxy)methoxy]
-5-indanol (9.75 g, 27.5 mmol) in dry tetrahydrofuran (50 mL) was added to a
suspension of potassium hydride (2.0 g, 1.8 eq) in the same solvent (50 mL),
and the mixture was stirred at room temperature for 2 hours. At this point,
iodomethyl(tri-*n*-butyl)stannane (12.5 g, 1.06 eq) was added, and stirring was
continued for 1.5 hours. A small amount of water was carefully introduced and
then 50 mL of saturated ammonium chloride solution was added. The product
was extracted into petroleum ether (3 times), and the combined organic layers
were dried and concentrated. The residue was chromatographed on 40 g of
silica gel (elution with 3% ethyl acetate in petroleum ether) to furnish 17.22 g
(95.1%) of the (tri-*n*-butylstannyl)methyl ether as a yellowish oil.

A cold (–78°) magnetically stirred solution of the above material (17.22 g,
26.2 mmol) in dry hexane (250 mL, distilled from calcium hydride) was
blanketed with argon and treated dropwise with *n*-butyllithium (17.8 mL of
1.55 N in hexane) during 5 minutes. After 2 hours, another 9 mL of the
n-butyllithium solution was introduced, and the reaction mixture was allowed to
warm to room temperature during 6 hours and stand overnight. After careful
addition of water, the product was extracted into dichloromethane (three times),
and the combined extracts were dried and evaporated. The crude product
(18.43 g) was purified by HPLC on silica gel (eluted with 10% ethyl acetate in
petroleum ether) to give 3.45 g (34%) of
(1S,3aS,7aS)-7,7a-dihydro-4-isobutyl-7a-methyl-1-[(2-trimethylsilylethoxy)met
hoxy]-3a(6H)-indanmethanol and 2.82 g (27.8%) of the [1,2] rearrangement

product: colorless oil, $[\alpha]_D^{22}$ 59.3°(c 4.0, benzene): IR (neat) 3500, 2942, 1244,

1050 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.69 (t, J = 3.8 Hz, 1H), 4.68 (d,
J = 6.9 Hz, 1H), 4.65 (d, J = 6.9 Hz, 1H), 3.90 (t, J = 7.0 Hz, 1H), 3.68–3.52 (m,
3H) 3.44 (d, J = 11.3 Hz, 1H), 2.10–2.07 (m, 2H), 1.96 (m, 1H), 1.82–1.79 (m,
3H), 1.68–1.43 (m, 6H), 0.99 (s, 3H), 0.95–0.87 (m, 8H), 0.01 (s, 9H); MS, m/z

($M^+-C_4H_8$) calcd 310.1964, obsd 310.2000. Its *p*-nitrobenzoate was a pale yellow oil.

6.1.1.5. 1-Undecen-4-ol [Reductive Lithiation-Mediated [2,3]-Wittig Rearrangement] (30)

Lithium naphthalenide in tetrahydrofuran was prepared by allowing equimolar amounts of lithium metal and naphthalene to stir overnight in a volume of tetrahydrofuran sufficient to afford a final concentration of 0.5 M. 1-(2-Propenyloxy)octyl phenyl sulfide (0.47 mmol) in 3 mL of tetrahydrofuran was cooled to 0° and 3 mL of the 0.5 M solution of lithium naphthalenide in tetrahydrofuran was introduced. After 20 minutes another 1-mL portion of lithium naphthalenide was added. After 1 hour the mixture was poured into water and extracted with ether. Flash chromatography on silica gel furnished 1-undecen-4-ol (67%).

6.1.1.6. (S,S)-anti-2-Isopropyl-9-cyclodecyn-1-ol ([2,3]-Wittig Ring Contraction of a 13-Membered Propargylic Allylic Ether through Use of a Chiral Base) (116)

The chiral amide base was prepared from 910 mg (7.5 mmol) of (*S,S*)-bis(1-phenylethyl)amine in 10 mL of tetrahydrofuran at 0° under a nitrogen atmosphere by dropwise addition of 2.7 mL (6.8 mmol) of 2.5 M *n*-butyllithium in hexane. After 30 minutes at 0°, the solution of the amide was slowly added via cannula to a stirred, cooled (–41°) solution of 438 mg (2.15 mmol) of the cyclic ether in 10 mL of tetrahydrofuran. The resulting mixture and the bath were allowed to warm slowly for 20 minutes to 30°, and the mixture was diluted with water. The separated aqueous layer was extracted with ether. The combined ether layers were washed with 5% hydrochloric acid, water, and brine, and dried over anhydrous magnesium sulfate. Filtration and removal of solvent gave an oil that was purified by column chromatography on silica gel (15% ethyl acetate-hexanes) to give 303 mg (70%) of (–)-(*S,S*)-*anti*-2-isopropenyl-9-cyclodecyn-1-ol: IR (film) 3450, 3050, 2900, 2895, 2250, 2200, 1640, 1440, 1025, 880 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.4–2.4 (m, CH$_2$s), 1.68 (s, vinyl CH$_3$s), 4.05 (m, carbinyl H), 4.80 (s, vinyl Hs, 2H), 5.08 (s, vinyl H); [α]$_D$ – 27.1° (*c*, 5.4, CHCl$_3$; ee = 57%). A material of 60–80% ee was obtained in 70–85% yield from rearrangements conducted under comparable conditions to those described above.

(1*R*,2*R*)-(5*E*)-2-Isopropenyl-5-methyl-5-cyclodecen-9-ynyl (*S*)-*O*-Methylmandelate. (Determination of the Absolute Configuration of (+)-(1*R*,2*R*)-*anti*-2-isopropenyl-9-cyclodecyn-1-ol) (116) To a solution of 330 mg (1.6 mmol) of (+)-(1*R*,2*R*)-*anti*-2-isopropenyl-9-cyclodecyn-1-ol [α]$_D$ + 33.4° (*c* 4.2, CHCl$_3$; ee = 70%)], 0.5 g (3 mmol) of (*S*)-*O*-methylmandelic acid, and 320 mg of dicyclohexylcarbodiimide in 7 mL of dichloromethane was added a catalytic amount of 4-dimethylamino-pyridine.

After being stirred overnight at room temperature under nitrogen, the mixture was concentrated under reduced pressure to afford a yellow solid. This solid was washed with ether and filtered, and the organic layer was concentrated to afford a white viscous oil that was chromatographed on silica gel (2% ethyl acetate-hexanes), yielding 322 mg (71%) of the (*S*)-*O*-methylmandelic ester as a colorless viscous oil (>90% pure by ^{1}H NMR analysis): ^{1}H NMR (300 MHz, CDCl$_3$)δ 2.46 (dt, *J* = 11 and 4 Hz, H-2).

(1*S*,2*S*)-(5*E*)-2-Isopropenyl-5-methyl-5-cyclodecen-9-ynyl (*S*)-*O*-Methylmandelate. (Determination of the Absolute Configuration of (–)-(1*S*,2*S*)-*anti*-2-isopropenyl-9-cyclodecyn-1-ol) (116) The procedure described above was followed with 326 mg (1.60 mmol) of (–)-(1*S*,2*S*)-*anti*-2-isopropenyl-9-cyclodecyn-1-ol [[α]$_D$ – 36.5° (*c* 4.94, CHCl$_3$; ee = 77%)], 0.5 g (3 mmol) of (*S*)-*O*-methylmandelic acid, 0.4 g (2.0 mmol) of dicyclohexylcarbodiimide, and a catalytic amount of 4-dimethylaminopyridine in 12 mL of dichloromethane. The mixture was stirred overnight, and the product was isolated by removal of solvent and chromatography on silica gel (2% ethyl acetate/hexanes) to give 360 mg (73%) of (*S*)-*O*-methylmandelate (>95% pure by ^{1}H NMR analysis) as a colorless viscous oil: ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.58 (dt, *J* = 11 and 4 Hz, H-2).

6.1.1.7. (2S,3R)-2-Hydroxy-3-methylpentanoic Acid [Rearrangement via the Transmetalation of a Lithium Enolate to a Zirconium Enolate] (97)
A solution of *n*-butyllithium (1.6 mol/L, 258 µL, 1.2 eq) was added slowly to a tetrahydrofuran solution (330 µL) of (2*S*,5*S*,2′*E*)-*N*-2′-butenyloxyacetyl-2,5-bis(methoxymethyl)pyrrolidine (114.0 mg) at –100° under a nitrogen atmosphere. After stirring at –100° for 2 hours, a solution of dicyclopentadienylzirconium dichloride (120 mg, 1.2 eq) in tetrahydrofuran (1.5 mL) was added slowly to the solution and the mixture was stirred at the same temperature for 3 hours and then at –70° for 3 hours. Saturated aqueous potassium fluoride (150 µL) was added and the mixture was allowed to warm to room temperature and then passed through a short column of silica gel. Concentration and chromatrography on silica gel gave *N*-′-hydroxy-3′-methyl-4′-pentenoyl-2,5-bis(methoxymethyl) pyrrolidine (47.4 mg, 42%). The product (32 mg) was hydrogenated (on palladium in ethanol) and hydrolyzed (1 mol/L, HCl, 100°) to afford a quantitative yield of

(2*S*, 3*R*)-2-hydroxy-3-methylpentanoic acid (11 mg); $[\alpha]_D^{25} + 11.2°$ (*c* = 0.36, H$_2$O).

6.1.1.8. 8-Phenylmenthyl 2-Hydroxy-3-methyl-4-pentenoate [Rearrangement via the Transmetalation of an Enol Silyl Ether with Titanium Tetrachloride] (65)
To a solution of diisopropylamine (0.21 mL, 1.5 mmol) in tetrahydrofuran (3 mL) was added a 1.55 N solution of *n*-butyllithium in hexane (0.9 mL, 1.3 mmol) at 0°, and the mixture was stirred for 30 minutes. To this solution was added

dropwise a solution of 8-phenylmenthyl (*E*)-3-oxa-5-heptenoate (94% *E*, 344 mg, 1.0 mmol) in tetrahydrofuran (3 mL) at –70°, and the solution was stirred for 5 minutes at that temperature, followed by rapid addition of chlorotrimethylsilane (0.19 mL, 1.5 mmol). The reaction mixture was warmed to room temperature, diluted with hexane, filtered through Celite, and evaporated. The residue was dissolved in hexane and filtered again. The filtrate was evaporated to afford the enol silyl ether of 8-phenylmenthyl (*E*)-3-oxa-5-heptenoate.

To a solution of the enol silyl ether (417 mg, 1.0 mmol) in dichloromethane (2 mL) was added titanium tetrachloride (0.11 mL, 1.0 mmol) at –50°. The mixture was stirred at that temperature for ca. 10 hours, then allowed to warm to 0°, poured into water, and extracted with dichloromethane. The organic layer was washed with an aqueous sodium bicarbonate solution, dried over magnesium sulfate, and evaporated. Subsequent silica gel chromatography gave 8-phenylmenthyl 2-hydroxy-3-methyl-4-pentenoate (276 mg, 80%): GC (XE-60, 30 m, 180°) t_R 24.3 (2*S*,3*S*), 24.6 (2*S*,3*R*), 29.9 (2*R*,3*R*), 30.9 (2*R*,3*S*), minutes; HPLC (Finepak SIL-5, hexane:ethyl acetate = 30:1) 18.3 (2*S*,3*S*), 13.8 (2*S*,3*R*), 13.6 (2*R*) minutes; TLC (hexane:ether = 3:1) R_f 0.28 (2*S*), 0.34 (2*R*); ^{1}H NMR (CDCl$_3$) for 2*S* δ 3.03 (m, 1H), 4.6–5.0 (m, 3H), 5.60 (ddd, *J* = 7.2, 9.0, and 18.0 Hz, 1H), 7.20 (m, 5H); for 2*R* δ 3.68 (m, 1H), 4.7–5.1 (m, 3H), 5.76 (ddd, *J* = 7.2, 9.6, and 16.5 Hz, 1H), 7.32 (m, 5H).

6.1.1.9. Methyl 2-Hydroxy-3-methyl-4-pentenoate [Silyl Triflate-Catalyzed Rearrangement] (164)

To a solution of methyl (2-butenyloxy)acetate (93% *E*, 0.144 g, 1.0 mmol) and triethylamine (0.15 mL, 1.1 mmol) in dichloromethane (5 mL) was added trimethylsilyl triflate (0.23 mL, 1.2 mmol) at 0°, and the mixture was stirred overnight at room temperature. The mixture was then diluted with water. The separated aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with 5% hydrochloric acid, water, and brine, and dried over anhydrous magnesium sulfate. Filtration and removal of solvent gave an oil which was chromatographed on silica gel (ethyl acetate-hexane) to give 0.12 g (83%) of methyl 2-hydroxy-3-methyl-4-pentenoate: GC (PEG 20 M): t_R 16 and 14 (*erythro*:*threo* = 92:8) minutes; ^{1}H NMR (CDCl$_3$) for *erythro* δ 1.00 (d, *J* = 7.2 Hz, 3H), 2.43–2.83 (m, 2H), 3.77 (s, 3H), 4.03–4.25 (m, 2H), 5.06 (d, *J* = 10.5 Hz, 1H), 5.09 (d, *J* = 16.8 Hz, 1H), 5.87 (ddd, *J* = 7.0, 10.5, and 16.8 Hz, 1H); for *threo* δ 1.14 (d, *J* = 7.2 Hz, 3H).

7. Tabular Survey

The [2,3]-Wittig rearrangements of benzyl ethers, alkyl ethers, allyl ethers, propargyl ethers, and α-(allyloxy)carbonyl compounds are grouped in Tables I–V. Table VI contains examples of [2,3]-Wittig contractions. Within each table entries are listed by increasing numbers of carbon atoms, using the *Chemical Abstracts* convention. Yields, in parentheses, are based on isolated products. A dash (—) indicates that no yield was reported. Numbers not in parentheses are product or diastereomeric ratios, and values in brackets [] are corresponding ratios corrected to 100% stereochemical purity of the products.

The literature has been reviewed to the end of 1991, and includes some papers that appeared up to mid-1992.

The following abbreviations are used in the tables:

18-c-6	18-crown-6
Bn	benzyl
Boc	*tert*-butoxycarbonyl
BOM	benzyloxymethyl
Cp	cyclopentadienyl
DB-18-c-6	dibenzo-18-crown-6
DC-18-c-6	dicyclohexyl-18-crown-6
ds	diastereoselectivity
EE	ethoxyethyl
HMPA	hexamethylphosphoric triamide
KHDS	potassium hexamethyldisilazane
LBPEA*R*	lithiobis[(*R*)-1-phenylethyl]amide
LBPEA*S*	lithiobis[(*S*)-1-phenylethyl]amide
LDA	lithium diisopropylamide
LDCA	lithium dicyclohexylamide
LHDS	lithium hexamethyldisilazane
LTBB	lithium 4,4¢-di-*tert*-butylbiphenylide
LTMP	lithium 2,2,6,6-tetramethylpiperidide
MEM	(2-methoxyethoxy)methyl
MOM	methoxymethyl
SEM	2-(trimethylsilyl)ethoxymethyl
TBAB	tetrabutylammonium bromide
TBDMS	*tert*-butyldimethylsilyl

TBDPS	*tert*-butyldiphenylsilyl
TBPB	tetrabutylphosphonium bromide
Tf	trifluoromethanesulfonyl (trifyl)
THF	tetrahydrofuran
THP	tetrahydropyranyl
TMEDA	*N*,*N*,*N*′,*N*′-tetramethylethylenediamine
TMS	trimethylsilyl
Ts	*p*-toluenesulfonyl

Table I. Rearrangements of Benzylic Ethers

View PDF

Table II. Rearrangements of Alkyl Ethers

View PDF

Table III. Rearrangement of Allylic Ethers

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Table IV. Rearrangements of Propargylic Ethers

View PDF

Table V. Enolate Rearrangements of α -(Allyloxy) Carbonyl Compounds

[View PDF](#)

Table VI. [2,3]-Wittig Ring Contractions

[View PDF](#)

Table I. REARRANGEMENTS OF BENZYL ETHERS
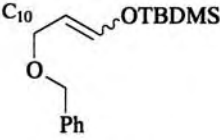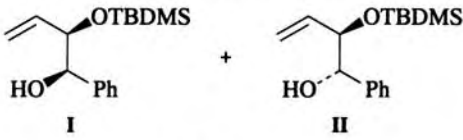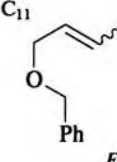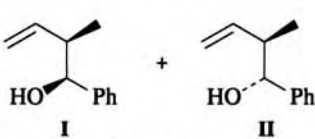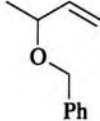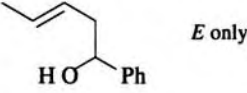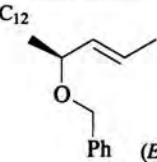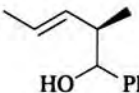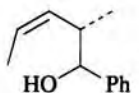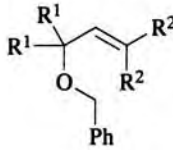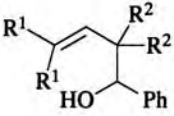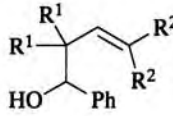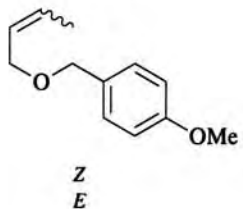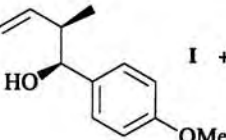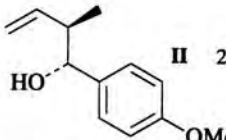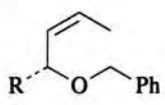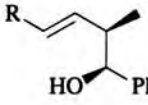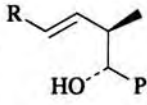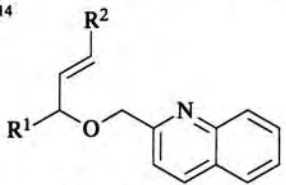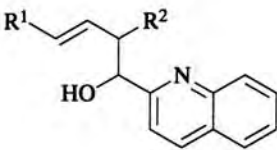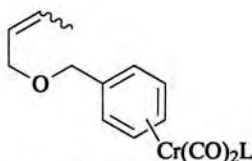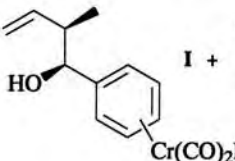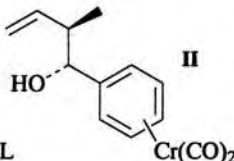
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
$E:Z = 29:71$	n-BuLi, THF-C_6H_{14}, -78 to -65°	(73), **I:II** = 18:82	77
$E:Z = 7:93$	"	(81), **I:II** = 23:77	77
E	n-BuLi, TMEDA-Et_2O-C_6H_{14}, -80 to -25°	**I:II** = 1:1	18
Z	"	**I** only	18
E	MeLi, THF-Et_2O, rt	**I:II** = 2:1	9
$E/Z = 93:7$	n-BuLi, THF-C_6H_{14} (1:1), -85°	**I:II** = 63:37 [61:39]	24
$E/Z = 5:95$	"	**I:II** = 93:7 [95:5]	24
$E/Z = 93:7$	n-BuLi, THF-C_6H_{14} (1:4), -85°	**I:II** = 68:32	24
$E/Z = 93:7$	TMEDA-Et_2O-THF (1:3:7)	**I:II** = 56:44	24
$E/Z = 93:7$	TMEDA-Et_2O-THF (1:1:1.2)	**I:II** = 49:51 [45:55]	24
$E/Z = 5:95$	"	**I:II**= 95:5 [98:2]	24
	n-BuLi, TMEDA-Et_2O-C_6H_{14}, -80 to -25°	E only	18

Table I. REARRANGEMENTS OF BENZYL ETHERS (*Continued*)
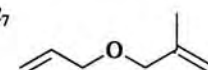
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{12}$			
(E) 72% ee	*n*-BuLi, THF, 0°	**I** + **II** **I:II** = 83:17, 72% ee	10

R^1	R^2		[2,3]:[1,2]	
			[2,3] + [1,2]	
H	Me	*n*-BuLi, THF, 25°	95:5	165
H	Me	*n*-BuLi, THF, -10°	98:2	165
H	Me	*n*-BuLi, TMEDA-Et$_2$O-C$_6$H$_{14}$, 25°	6:1	18
H	Me	*n*-BuLi, TMEDA-Et$_2$O-C$_6$H$_{14}$, -20°	7.5:1	18
H	Me	*n*-BuLi, TMEDA-Et$_2$O-C$_6$H$_{14}$, -80°	8:1	18
Me	H	*n*-BuLi, THF, 25°	77:23	165
Me	H	*n*-BuLi, THF, -20°	83:17	165

Ether (OMe, Z / E)	Conditions	Product(s) and Yield(s) (%)	Refs.
Z *E*	*n*-BuLi, THF-C$_6$H$_{14}$, -85°	**I** + **II** (79-98) **I:II** = 100:0 (70-98) **I:II** = 40:60	24

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
	n-BuLi, THF, -85°	**I** + **II**	
C$_{12}$ R = Me *(Z)* 95% ee		(—), **I:II** = 80:20, 92% ee	81
C$_{14}$ R = *i*-Pr *(Z)* 91% ee		(89), **I:II** = 93:7, 91% ee	82
R = *i*-Pr *(E)* 91% ee		(95), **I:II** = 20:62, 91% ee	135,136
C$_{15}$ R = *i*-Bu *(Z)* 68% ee		(—), **I:II** = 96:4, 64% ee	81

C$_{14}$

R^1	R^2	Conditions	Yield	Refs.
Me	H	NaNH$_2$, NH$_3$, -33°, 2 h	(74)	6
H	Me	NaNH$_2$, NH$_3$, -33°, 2 h	(78)	6
Me	H	*n*-BuLi, THF, -25°, 2 h	(90)	6
H	Me	*n*-BuLi, THF, -25°, 2 h	(quant)	6

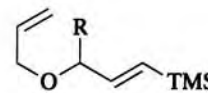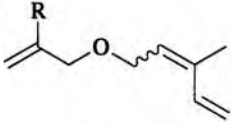| Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
	LDA, THF, -78°, 7 h	**I** + **II**	99, 100
C$_{14}$ L = CO, *E:Z* = 96:4		(69), **I:II** = 95:5	
L = CO, *E:Z* = 12:88		(40), **I:II** = 48:52	
C$_{31}$ L = PPh$_3$		(95), **I:II** = 88:12	

Table I. REARRANGEMENTS OF BENZYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

C_{14}, C_{16} ether (structure with R^1, R^2, $Cr(CO)_3$) → product (structure with R^2, R^2, HO, R^1, $Cr(CO)_3$)

R^1	R^2	Conditions	Yield	Refs.
C_{14} OMe	H	n-BuLi, THF, 0°, 20 min	(16)	101
OMe	H	n-BuLi, THF, -40°, 2 h	(30)	101
OMe	H	n-BuLi, THF, -50°, 4 h	(48)	101
C_{16} Me	Me	n-BuLi, THF, -60°, 4 h	(88)	101
Me	Me	n-BuLi, THF, -20°, 4 h	(90)	101

C_{15} ether (structure with R, $Cr(CO)_3$) → products I + II

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
R = Me, *E:Z* = 80:20	n-BuLi, THF, -60°, 6 h	(90), **I:II** = 80:20	101
R = OMe, >99.3% *E*	n-BuLi, THF-TMEDA, -78°	(67), **I:II** = 97:3	99, 100

OMe-substituted ether → product

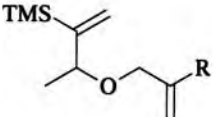| Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
(+)-*R*, >99.3% *E*	n-BuLi, THF-TMEDA, -78°	(+)-(1*R*,2*S*), >99.5% ee	99, 100

Table I. REARRANGEMENTS OF BENZYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

C_{17} ether (fluorene structure with R^1, R^2) → product

R^1	R^2	Conditions	Yield	Refs.
Me	H	MeLi, THF, -50°, 3 h	(95)	5
H	Me	MeLi, THF, -50°, 3 h	(94)	5
Me	H	NaNH$_2$, NH$_3$, -33°, 2 h	(70)	6
H	Me	NaNH$_2$, NH$_3$, -33°, 2 h	(85)	6
H	Me	KOH (20%), TBAB , C$_6$H$_6$, rt, 6 h	(93)	7
H	Me	KOH (20%), TBPB , C$_6$H$_6$, rt, 6 h	(87)	7
H	Me	KOH (20%), 18-c-6 , C$_6$H$_6$, rt, 6 h	(89)	7
H	Me	KOH (20%), DC-18-c-6 , C$_6$H$_6$, rt, 6 h	(90)	7
H	Me	KOH (20%), DB-18-c-6 , C$_6$H$_6$, rt, 6 h	(55)	7

C_{18} ether ((CO)$_3$Cr, OMe structure) → products **I** + **II**

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{18}	n-BuLi	(60), **I:II** = 88:12	99, 100

154

155

Table II. REARRANGEMENTS OF ALKYL ETHERS

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C₇	n-BuLi, THF, -78°	(93)	11
C₈ 92% ee	n-BuLi, THF, -78°, 40 min; 0°, 40 min	(72) 92% ee	136
C₈ 92% ee	n-BuLi, THF, -78°, 40 min; 0°, 40 min	92% ee (72) 53:47 92% ee	136
C₈	n-BuLi, THF, -78°, 1 h		107

R
C₈   i-Pr   (78)   93:7
C₉   t-Bu   (67)   45:55
C₁₁   Ph   (71)   89:11
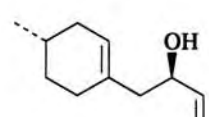C₁₂   Bn   (81)   96:4

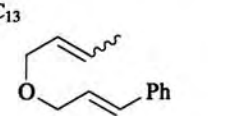Table II. REARRANGEMENTS OF ALKYL ETHERS (Continued)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C₈	n-BuLi, THF, -78°, 1 h		107

R
MOM   (66)   98:2
MEM   (89)   98:2
Bn   (78)   93:7
i-Pr   (81)   93:7

| C₈ | n-BuLi, THF, HMPA, -70°, 1.5-6 h | (88) ds >99.8:0.2 | 109 |
| | n-BuLi, THF, -78° | | 11 |

R¹   R²   R³
C₉   n-Bu   Me   H   (quant)   96-97% Z
C₁₁   n-C₇H₁₅   H   H   (>95)   60% Z
C₁₂   n-C₇H₁₅   H   Me E   (96)   100% E
     n-C₇H₁₅   H   Me Z   (91)   65% Z
C₁₄   Me   H   (83)   95-96% Z

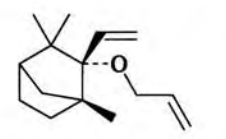Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)
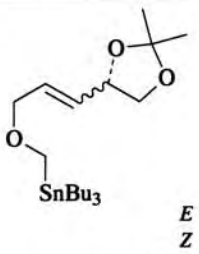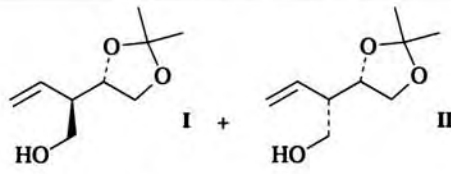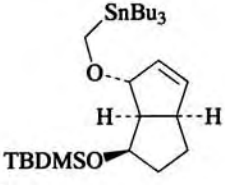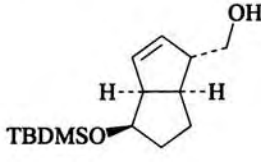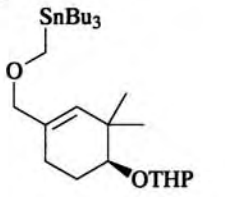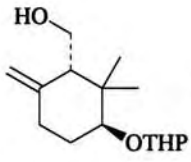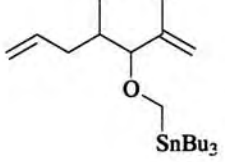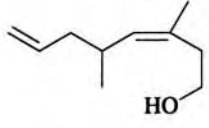
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
E / *Z*	*n*-BuLi, THF, -78°	**I** + **II** **I** (79) + **II** (6) **I:II** = >99:1	107-109
H—···—H TBDMSO	*n*-BuLi, C₆H₁₄, -78°, 2 h	(quant)	87
C₁₀ OTHP	*n*-BuLi, THF, <-60 to -20°, 1 h	(—) ds 92.7:7.3	110
SnBu₃	*n*-BuLi, -78°	(>75) + *E*-diene (tr)	166

Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)
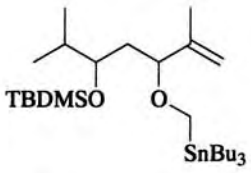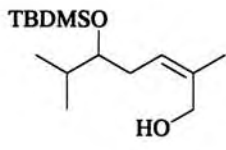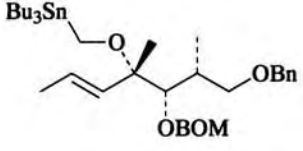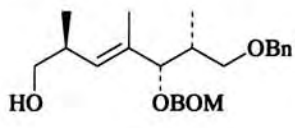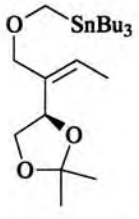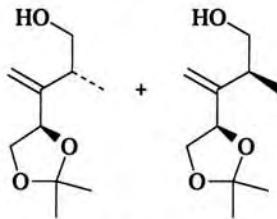
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
TBDMSO O SnBu₃	*n*-BuLi	(>65)	30, 31
Bu₃Sn OBn OBOM	*n*-BuLi, THF, -78°	OBn OBOM + (65) 71:29	91-93
O SnBu₃ *Z* / *E*	*n*-BuLi, THF, -78°, 2 h	+ (89) 95:5 (70) 3:97	111

Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)
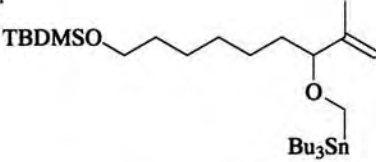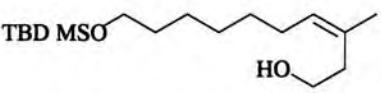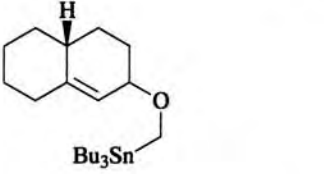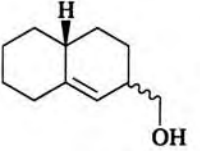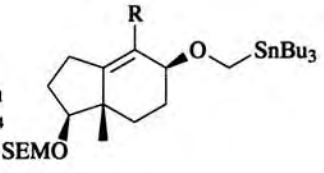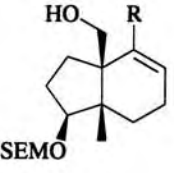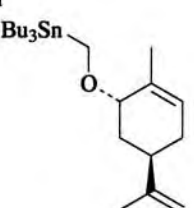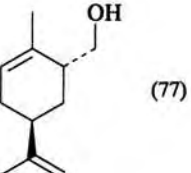
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₁ 	*n*-BuLi, -78°	(—)	167
	n-BuLi, THF, -78°	(—)	11
C₁₁ C₁₄ 	*n*-BuLi, C₆H₁₄, -78 to 0°	R = H (45) R = *i*-Pr (34)	50, 51
C₁₁ 	*n*-BuLi, THF, -78° to rt, 20 min	(77)	46

Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)
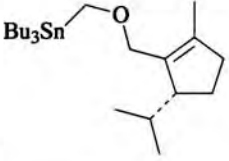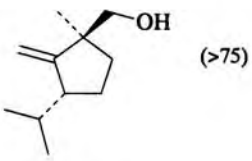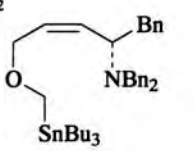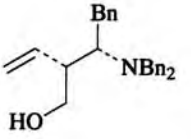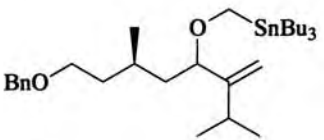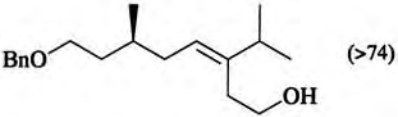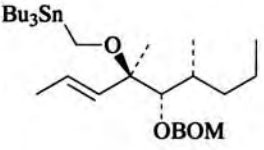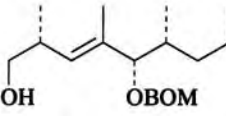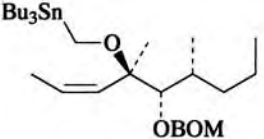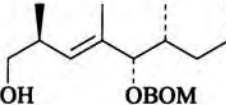
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
	n-BuLi, THF, -78°, 2 h	(>75)	112, 113
C₁₂ 	*n*-BuLi, THF, -78°, 1 h	(45) ds >95:5	109
	n-BuLi, -65 to -70°, 45 min	(>74)	168
	n-BuLi, THF, -78°	(57) >100:1	91-93
	n-BuLi, THF, -78°	(64) >100:1	91-93

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Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
(Bu₃Sn–O structure with OBOM)	*n*-BuLi, THF, -78°	(57) 60:40	91-93
(Bu₃Sn–O structure with OBOM, Z)	*n*-BuLi, THF, -78°	(81) 93:7	91-93
C₁₃ (Ph...O–Ts structure)	RLi, HMPA, THF, -78°	R = Bu (42) R = (59) R = (41)	169
	3 *n*-BuLi, Et₂O, HMPA/THF (3%), -78°, 1 h; to -40°, 1 h	" R = Bu (63)	169

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Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
(O, C₉H₁₉-*n*, PhS structure with R)	Li•C₁₀H₈, THF, 0°, 1 h		30, 31
C₁₄ R = H		(67)	
C₁₅ R = Me, *E*		(71) 12:1	
R = Me, *Z*		(77) 1:2.5	
C₁₄ (SnBu₃ ether structure)	*n*-BuLi, -78°	(>75) 96.5% *Z*	170
(Ph–O, O, SnBu₃ sugar structure)	*n*-BuLi, THF, -78° to rt, 0.5-12 h	(—) 25:75	52, 53
C₁₅ (MeO–phenyl, O, SnBu₃ structure)	2 BuLi, THF, -5 to 5°, 2 h	(61) *trans* only	11

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Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)
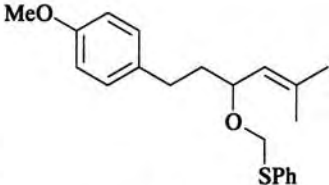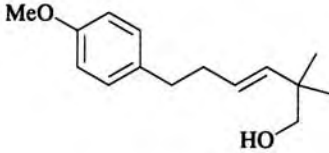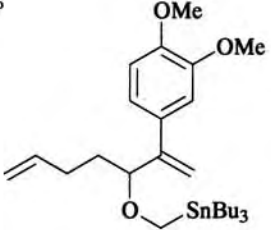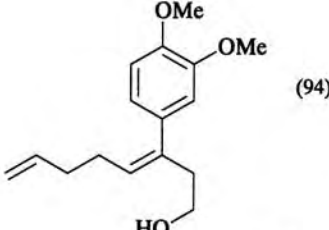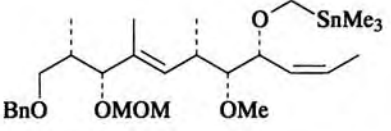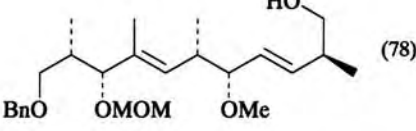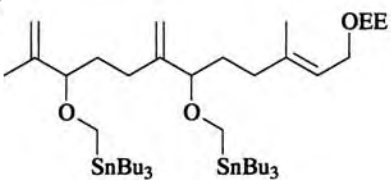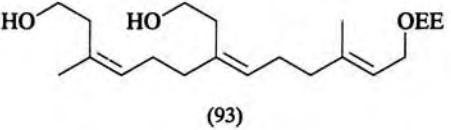
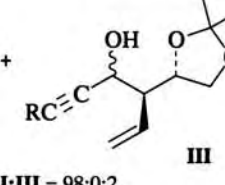| Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
MeO— (structure with OCH₂SPh)	Li·C₁₀H₈, THF, -5 to 5°, 2 h	MeO— (structure, HO)	11
C₁₆ (OMe, OMe aromatic; OCH₂SnBu₃)	*n*-BuLi, THF, -78°, 30 min; to 0°, 10 min	(OMe, OMe aromatic; HO) (94)	171
(structure with OCH₂SnMe₃; BnO, OMOM, OMe)	MeLi, THF, -78°	(structure HO; BnO, OMOM, OMe) (78)	91-93
C₁₇ (structure OEE; O-CH₂-SnBu₃, O-CH₂-SnBu₃)	*n*-BuLi, THF, -78 to -20°	(HO, HO, OEE structure) (93)	68

Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)
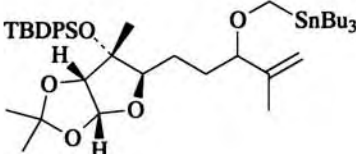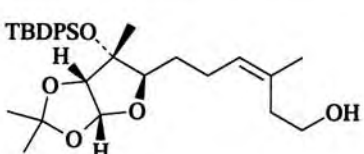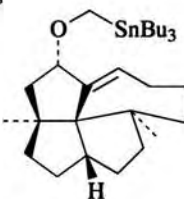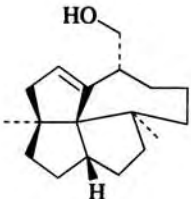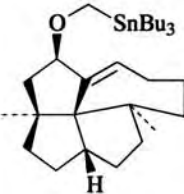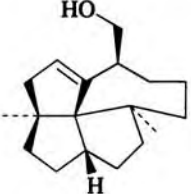
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
TBDPSO (bicyclic structure with OCH₂SnBu₃)	*n*-BuLi, THF	TBDPSO (structure, OH) (>53)	30, 31
C₁₈ (polycyclic structure with OCH₂SnBu₃)	*n*-BuLi, C₆H₁₄, 0°	(polycyclic structure, HO) (>57)	89
(polycyclic structure with OCH₂SnBu₃)	*n*-BuLi, C₆H₁₄, 0°	(polycyclic structure, HO) (>60)	89

Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{23}$ $\begin{array}{cc} R^1 & R^2 \\ \hline Me & H \\ H & Me \end{array}$	*n*-BuLi, THF, -78°, 15 min	 (70) (83)	45
	t-BuLi, THF, reflux	(89)	46
C$_{27}$	*n*-BuLi, THF, -78 to 0°	 (80) >120:1	137

Table II. REARRANGEMENTS OF ALKYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{28}$ R = TBDMS	*n*-BuLi, THF, -78°, 40 min; 0°, 40 min		135
 R = TBDMS	*n*-BuLi, THF, -78°, 40 min; 0°, 40 min		135
	n-BuLi, THF, -78 to rt	 C$_{28}$ R = H (79) C$_{29}$ R = Me (83)	90

Table III. REARRANGEMENTS OF ALLYL ETHERS
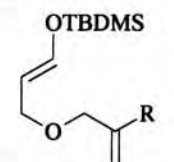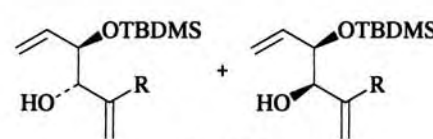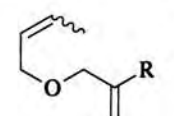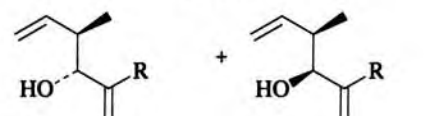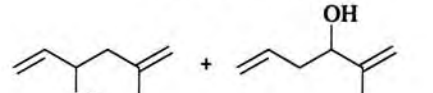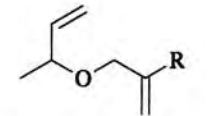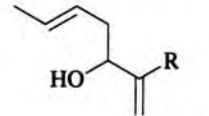
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C_6 R = H C_7 R = Me (70% Z)	n-BuLi, THF-C_6H_{14} (1:1), -78°	(53) 95:5 (74) 91:9	77

C_7 R = H, 93% E
      R = H, 95% Z
 C_8 R = Me, 93% E
      R = Me, 83% Z
	n-BuLi, THF-C_6H_{14}, -85°, 6-8 h	(81) 79:21 [84:16]
		 (88) 12:88 [8:92]
		 (70) 67:33 [72:28]
		 (71) 16:84 [5:95]
			12

C_7	n-BuLi, THF-C_6H_{14}, -85°, 6-8 h	(77) 4:3	12
C_7 R = H C_8 R = Me	n-BuLi, THF-C_6H_{14}, -85°, 6-8 h	(79) E (60) E	12

Table III. REARRANGEMENTS OF ALLYL ETHERS (*Continued*)
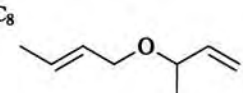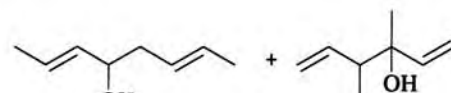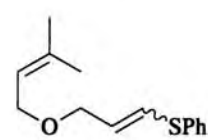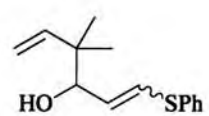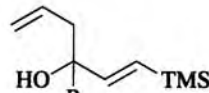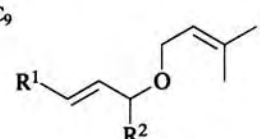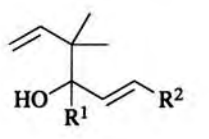
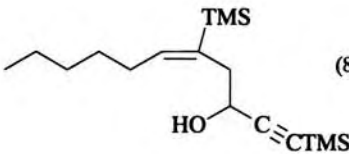| Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C_8	n-BuLi, THF-C_6H_{14}, -85°, 6-8 h	(82) 1:2	12
	n-BuLi, THF, -40 to -50°, 2 h	(—)	32
C_9 R = H C_{10} R = Me	n-BuLi, THF-C_6H_{14}, -78°	(93) (50)	33
C_9 R^1 = Me, R^2 = H R^1 = H, R^2 = Me	n-BuLi, THF-C_6H_{14}, -85°, 6-8 h	(65) (66)	12

Table III. REARRANGEMENTS OF ALLYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

C₉	R = H	*n*-BuLi, THF, -90°, 2 h	**I** (27) + **II** (33)	172
	R = H	KNH₂, NH₃, -33°	**I** (68)	
C₁₀	R = Me	*n*-BuLi, THF, -90°	**I** (36)	
	R = Me	KNH₂, NH₃, -33°	**I** (50)	

	R^1	R^2			
C₁₀	*i*-Pr	H *Z*	} 91% ee	(84) **I:II:III** = 92:8:0	} 91% ee
	i-Pr	H *E*		(75) **I:II:III** = 40:60:0	
C₁₁	*i*-Pr	Me *Z*	} 91% ee	(93) **I:II:III** = 93:7:0	} 91% ee
	i-Pr	Me *E*		(89) **I:II:III** = 40:50:10	
C₁₂	*i*-Bu	Me *Z*		(95)	

Table III. REARRANGEMENTS OF ALLYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₀			

	Conditions	Products	Refs.
	n-BuLi, THF, 25°	**I** + **II** (—) 1:1	165
	n-BuLi, THF, -15°	**I** (—)	165
	n-BuLi, THF, -25°	**I** (67) + **II** (14)	18

		LDCA, THF, -30°, 6 h		70
C₁₀	R = H		(62) 64% *Z*	
C₁₁	R = Me		(89) 59% *Z*	

		LDCA, THF, -30°, 6 h		70
C₁₀	R = H 92% *Z*		(80) 82:18	
C₁₁	R = Me 92% *Z*		(73) 91:9	

Table III. REARRANGEMENTS OF ALLYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{10}$			
95% E 98% Z	*n*-BuLi, THF-C$_6$H$_{14}$, -78°	(58) 51:49 (72) 7:93	33
C$_{11}$	*n*-BuLi, THF, -78°	(>58)	94
C$_{13}$ Z E	*n*-BuLi, THF-C$_6$H$_{14}$, -78°	(70-98) 72:28 (70-98) 24:76	28, 29
C$_{15}$	*t*-BuLi, *t*-BuOK, THF-C$_5$H$_{12}$, -85°	I + II (92) I:II = 70:30	173

Table III. REARRANGEMENTS OF ALLYL ETHERS (*Continued*)
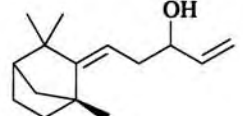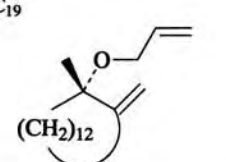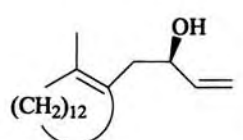
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
	t-BuLi, *t*-BuOK, HMPA-THF-C$_5$H$_{12}$, -85°	(74)	173
C$_{19}$ (CH$_2$)$_{12}$	*n*-BuLi, HMPA-C$_6$H$_{14}$, -85°	(CH$_2$)$_{12}$ (51) 63% chirality transfer	73

Table IV. REARRANGEMENTS OF PROPARGYL ETHERS
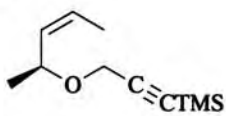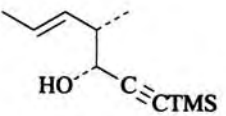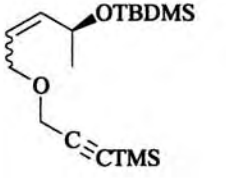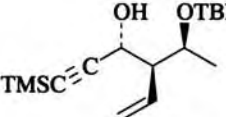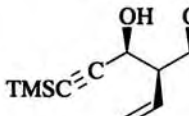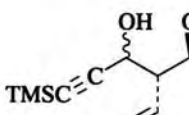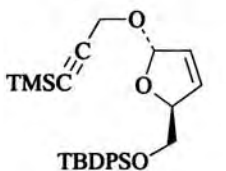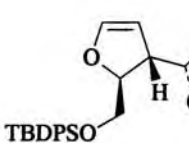
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
(propargyl allyl ether structure, products I + II)			28, 29
C_7 R = H 93% E	n-BuLi, THF-C_6H_{14} (1:1), -85°, 8 h	(72) I:II = 93:7 [99:1]	
R = H 98% Z	"	(76) I:II = 12:88 [10:90]	
R = H 93% E	THF-Et_2O (1:1)	(81) I:II = 89:11	
R = H 98% Z	"	(58) I:II = 36:64	
C_8 R = Me 93% E	"	(48) I:II = 85:15	
R = Me 93% E	n-BuLi, THF-C_6H_{14} (1:1), -85°, 8 h"	(78) I:II = 92:8 [99:1]	
R = Me 98% Z	"	(74) I:II = 2:98 [0:100]	
C_{10} R = TMS 93% E	"	(72) I:II = 25:75 [27:73]	
R = TMS 98% Z	"	(74) I:II = 2:98 [0:100]	
(branched propargyl allyl ether structure)	n-BuLi, THF, -85°, 6 h		67
C_7 R = H 90% ee		(—) 98% E, 84% ee	
R = H 94% ee		(—) 95% E, 86% ee	
C_8 R = Me 90% ee		(—) 97% E, 80% ee	
C_{10} R = TMS 94% ee		(—) 93% E, 76% ee	

Table IV. REARRANGEMENTS OF PROPARGYL ETHERS (*Continued*)

Ether		Conditions	Product(s) and Yield(s) (%)	Refs.
(ether structure, products I + II + III)				
R^1	R^2			
C_8 Me	H 99% E	n-BuLi, THF, -78°, 6 h	(62) I:II:III = 91:9:0	28, 29
Me	H 99% E	THF, C_6H_{14} (1:1)	(62) I:II:III = 88:12:0	28, 29
C_9 Me	Me >99% Z, 98% ee	n-BuLi, THF, -78°	(64) I:II:III = >99:1:0, 98% ee	28, 29
C_{10} i-Pr	H 100% Z	n-BuLi, THF, -78°	(89) I:II:III = 91:9:0	81
i-Pr	H 100% E	n-BuLi, THF, -78°	(63) I:II:III = 10:82:8	81
C_{11} Me	TMS 97% Z	n-BuLi, THF, -78°, 6 h	(64) I:II:III = 1:99:0	28, 29
BnOCH$_2$	TMS —	n-BuLi, THF, -78°	(90)	127
C_{12} Me	n-Bu —	n-BuLi, THF, -78°	(96)	125,126
C_{13} i-Pr	TMS 100% Z	n-BuLi, THF, -78°	(62) I:II:III = >98:2:0	81
C_{14} i-Pr	TBDMSOCH$_2$ Z, 92% ee	n-BuLi, THF, -78°	(85) 92% ee	124
C_9 *(OTBDMS ether structure, products I + II)*		n-BuLi, THF, -78°, 5 h		77
65% E			(79) I:II = 98:2	
95% E			(66) I:II = 95:5	
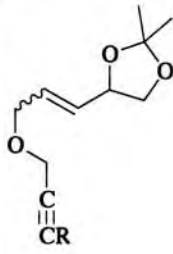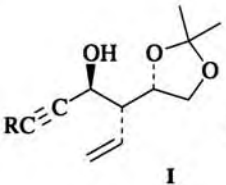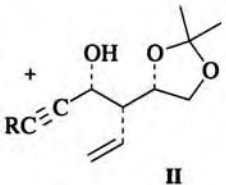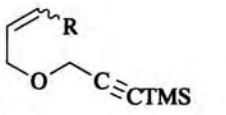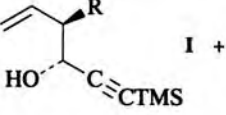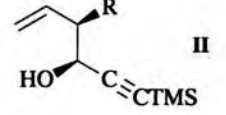
Table IV. REARRANGEMENTS OF PROPARGYL ETHERS (*Continued*)

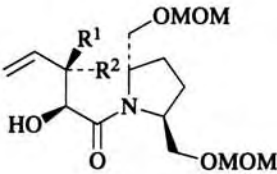| Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₁			

C₁₁

[Structure: (Z)-alkene propargyl ether with OCTMS and O-CH₂-C≡CTMS]

| | *n*-BuLi, THF, -85°, 6 h | [Product: HO, C≡CTMS] (>64) | 80 |

[Structure: OTBDMS propargyl ether, O-CH₂-C≡CTMS]

| | *n*-BuLi, THF, -78° | [Product I: OH, OTBDMS, TMSC≡C, vinyl] **I** + | 104, 105 |

[Product II: OH, OTBDMS, TMSC≡C, vinyl] **II** +

[Product III: OH, OTBDMS, TMSC≡C, vinyl] **III**

97% *Z*
97% *E*

(77) **I:II:III** = 94:1:5
(93) **I:II:III** = 10:21:69

[Structure: TMSC≡C-O-dihydrofuran, TBDPSO]

| | *n*-BuLi, THF, -78° | [Product: dihydrofuran, C≡CTMS, H, OH, TBDPSO] (73) | 54 |

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

[Structure: dioxolane alkene propargyl ether, O-CH₂-C≡CR]

[Product I: OH, dioxolane, RC≡C, vinyl] **I** + [Product II: OH, dioxolane, RC≡C, vinyl] **II** — 104, 105

+ [Product III: OH, dioxolane, RC≡C, vinyl] **III**

C₁₂	R = Me	100% *Z*	*n*-BuLi, THF, -78°	(62) **I:II:III** = 98:0:2
	R = Me	100% *E*	"	(73) **I:II:III** = 7:77:16
C₁₄	R = TMS	100% *Z*	"	(77) **I:II:III** = >99:0:0
	R = TMS	100% *E*	"	(86) **I:II:III** = 12:81:7
	R = TMS	*Z*	-78 to 20°	(87) **I:II** = 100:0
	R = TMS	*E*	"	(84) **I:II** = 17:83

[Structure: (Z)-alkene with R, O-CH₂-C≡CTMS]

| | *n*-BuLi, THF, -78°, 8 h | [Product I: vinyl, R, HO, C≡CTMS] **I** + [Product II: vinyl, R, HO, C≡CTMS] **II** | |

| C₁₂ | R = TMS 98% *E* | | (65) **I:II** = 3:97 | 75 |
| C₁₅ | R = Ph *E* | | (85) **I:II** = <5:>95 | 174 |

Table IV. REARRANGEMENTS OF PROPARGYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

	R^1	R^2			
C_9	TMS	H		(60)	33
C_{10}	TMS	Me		(64)	33
C_{12}	Ph	H		(67)	174

n-BuLi, THF, -78°, 8 h

n-BuLi, THF, -78° 75, 76

C_{12}	R = H	98% *E*	(93) **I:II** = 97:3
C_{13}	R = Me	95% *E*	(85) **I:II** = 4:96, 97% *E*
C_{14}	R = Et	100% *E*	(80) **I:II** = 3:97, 100% *E*
C_{16}	R = *n*-Bu	100% *E*	(61) **I:II** = 11:89, 100% *E*

C_{13}

n-BuLi, THF, -78° (>85) 124

Table IV. REARRANGEMENTS OF PROPARGYL ETHERS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

n-BuLi, THF, -85 to -15° 42, 43

	R^1	R^2	Additive		
C_{13}	H	H	TMEDA	(45) **I:II** = 87:13	
	MOM	H	—	(28) **I:II** = 67:33	
C_{14}	MOM	CH$_2$OH	—	(0)	
	MOM	CH$_2$OH	TMEDA	(63) **I:II** = 67:33	
	MOM	CH$_2$OH	HMPA	(15) **I:II** = 67:33	
	TBS	CH$_2$OH	—	(0)	
	TBS	CH$_2$OH	TMEDA	(57) **I:II** = 55:45	

C_{16}

n-BuLi, THF, -78°, 5.5 h; to -20°, 20 h (—) 111

Table IV. REARRANGEMENTS OF PROPARGYL ETHERS (*Continued*)
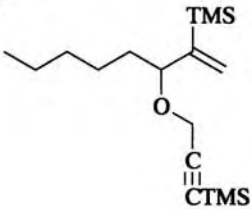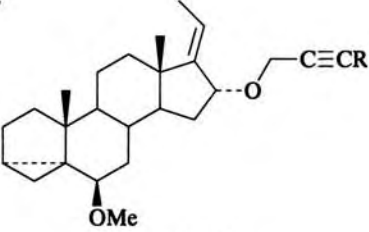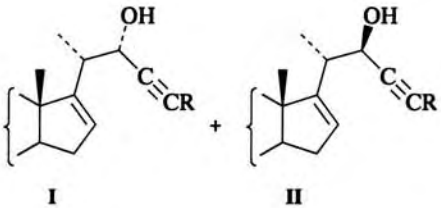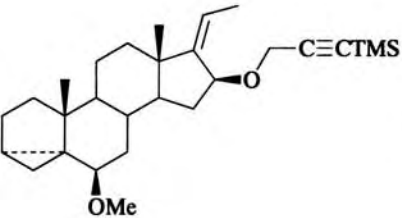
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{17}$	*n*-BuLi, THF, -78°, 6 h	(84) >80% *E*	71
C$_{28}$ R = H R = TMS	*n*-BuLi, THF, -78°	**I** + **II** **I** (75) **II** (quant)	47
	n-BuLi, THF, -78°	**II** (85)	138

Table IV. REARRANGEMENTS OF PROPARGYL ETHERS (*Continued*)
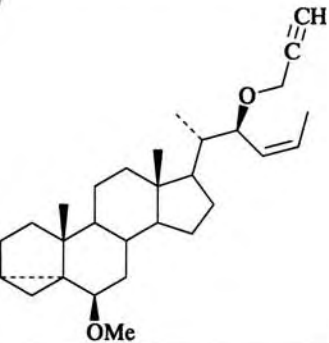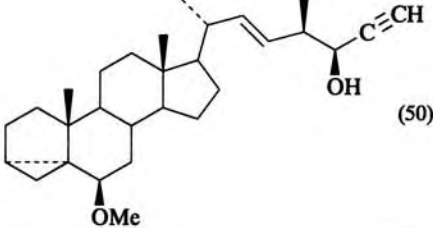
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{29}$	*n*-BuLi, THF, -78 to 0°	(50)	134

Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_6$	LDA, THF, -78°	(80) 74% *E*	58
93% *E* 95% *Z*	LDA, THF, -78°	I + II (60) I:II = 88:12 [92:8] (73) I:II = 25:75 [21:79]	58
C$_7$ R = H C$_8$ R = Me	TMSOTf, Et$_3$N CH$_2$Cl$_2$, rt	(93) 69% *Z* (98) 69% *Z*	164
C$_7$ R = Me 93% *E* R = Me 93% *Z* C$_9$ R = *i*-Pr 93% *E*	TMSOTf, Et$_3$N CH$_2$Cl$_2$, rt	(83) 92% *erythro* (86) 53% *erythro* (86) 95% *erythro*	164

Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS (*Continued*)

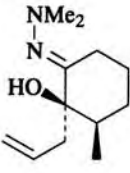| Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_7$ 93% *E*	TMSOTf (20 mol %), CH$_2$Cl$_2$, -72°	(72) 97% *erythro*	164
C$_7$ R = H C$_8$ R = Me	TMSOTf (20 mol %), CH$_2$Cl$_2$, -72°	(76) 81% *Z* (78) 78% *Z*	164
C$_7$			65

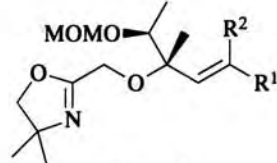| R^1	R^2		
Me	H	TiCl$_4$, CH$_2$Cl$_2$, -50°, 5 h	(78) 54% *E*
Me	H	SnCl$_4$, CH$_2$Cl$_2$, -50°, 5 h	(76) 59% *Z*
H	Me, 93% *E*	TiCl$_4$, CH$_2$Cl$_2$, -50°, 5 h	(75) 91% *erythro*
H	Me, 93% *E*	SnCl$_4$, CH$_2$Cl$_2$, -50°, 5 h	(73) 92% *erythro*
H	Me, 93% *Z*	TiCl$_4$, CH$_2$Cl$_2$, -50°, 5 h	(75) 52% *erythro*
H	Me, 93% *Z*	SnCl$_4$, CH$_2$Cl$_2$, -50°, 5 h	(63) 63% *erythro*

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C₈	LDA, THF, -78°	(78)	58
	KOBu-*t*, *t*-BuOH, THF, 0°, 40 min	(64)	55
C₉	KOBu-*t*, *t*-BuOH, 0°, 26 h	(22)	55
	LDA, THF, -78°		35-37

	R¹	R²	R³	
C₉	H	H	*i*-Bu	(76)
C₁₀	Me	H	*i*-Bu	(65)
C₁₁	Me	Me	CH₂CH(OMe)Me	(60)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
	LDA, THF, -100°, 1 h; to -20°, 18 h	**I** + **II**	69

	R		Additive	
C₉	H	Z	—	(20) **I:II** = 2:1
	H	Z	Cp₂ZrCl₂	(15) **I:II** = 7:1
	H	E	—	(14) **I:II** = 4.5:1
	H	E	Cp₂ZrCl₂	(47) **I:II** = 45:1
C₁₀	Me	E	—	(72) **I:II** = 4:1
	Me	E, S	Cp₂ZrCl₂	(91) **I:II** = 100*:1 *>96% ee, *S, Z*
C₁₂	*i*-Pr	E, R	Cp₂ZrCl₂	(26) **I:II** = 50*:1 *>96% ee, *R, Z*
C₁₃	*n*-Bu	E, R	Cp₂ZrCl₂	(81) **I:II** = 61*:1 *>96% ee, *R, Z*
C₁₇	*n*-C₈H₁₇	E, R	Cp₂ZrCl₂	(70) **I:II** = 90*:1 *>96% ee, *R, Z*

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₀		**I** + **II**	74
93% *E*	*n*-BuLi, THF, -78°	(98) **I:II** = 66:34	
93% *E*	LDA, THF, -78°	(80) **I:II** = 84:16	
94% *Z*	LDA, THF, -78°	(80) **I:II** = 28:78	
	LDA, THF, Cp₂ZrCl₂, -20°	(67)	83

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Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
BnO— (structure) 79% ee	LDA, THF, Cp$_2$TiCl$_2$, -20°	BnO— (structure) HO / CO$_2$Pr-i (—) 79% ee	83
BnO—()$_n$ (structure)	LDA, THF, -20°	BnO—()$_n$ (structure) HO / CO$_2$Pr-i **I** + ; BnO—()$_n$ HO / CO$_2$Pr-i **II** + ; BnO—()$_n$ HO / CO$_2$Pr-i **III**	83

		Additive		
C$_{10}$	n = 1	—	(37) **I:II:III** = 1:10:10	
		Cp$_2$TiCl$_2$	(72) **I:II:III** = 1:58:1	
		Cp$_2$ZrCl$_2$	(53) **I:II:III** = 1:1.5:0	
		Cp$_2$HfCl$_2$	(37) **I:II:III** = 2:29:1	
C$_{11}$	n = 2	—	(56) **I:II:III** = 1.5:3.8:1	
		Cp$_2$TiCl$_2$	(31) **I:II:III** = 1:4:1.2	
		Cp$_2$ZrCl$_2$	(62) **I:II:III** = 55:1:1	
		Cp$_2$HfCl$_2$	(58) **I:II:III** = 21:1:1	
C$_{12}$	n = 3	—	(59) **I:II:III** = 3.2:4.3:1	
		Cp$_2$TiCl$_2$	(37) **I:II:III** = 1:2:1.7	
		Cp$_2$ZrCl$_2$	(57) **I:II:III** = 54:2:1	

Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS (*Continued*)

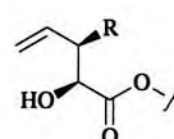| Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{10}$ (pyrrolidine allyloxy structure)		(vinyl methyl pyrrolidine amide structures) HO / O **I** + ; HO / O **II**	61
	LDA, THF, -85°	(98) **I:II** = 96:4	
	LHDS	(96) **I:II** = 96:4	
	LDA, HMPA-THF (23%)	(98) **I:II** = 96:4	
	KHDS, THF, -85°	(88) **I:II** = 96:4	
	LHDS, 0°	(96) **I:II** = 96:4	
(proline-derived structure) ...OR		(structures) HO / O ...OR **I** + ; HO / O ...OR **II**	61
C$_{11}$ R = H, 93% *E*	LDA, THF, -85°	(—) **I:II** = 95*:5 *52% ee *R*	
	LDA, THF, MgBr$_2$, -85°	(—) **I:II** = 96*:4 *36% ee *R*	
	KH, LDA	(—) **I:II** = 93*:7 *20% ee *R*	
	LHDS	(—) **I:II** = 95*:5 *20% ee *R*	
C$_{15}$ R = MEM, 93% *E*	LDA, THF, -85°	(—) **I:II** = 97*:3 *20% ee *S*	
	LDA, THF, Cp$_2$ZrCl$_2$, -85°	(—) **I:II** = 98*:2 *60% ee *S*	
	LDA	(—) **I:II** = 95*:5 *12% ee *S*	

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

LDA, THF, -100°, 3 h;
-70°, 3 h

I +

II

	R^1	R^2		Additive		
C_{11}	H	H		—	(61) 96% ee	
C_{12}	Me	H		Cp_2ZrCl_2	(43) **I:II** = 28*:1 *96% ee	
C_{13}	Et	H		—	(75) **I:II** = 2*:1 *92% ee	
	Et	H		Cp_2ZrCl_2	(65) **I:II** = 30*:1 *96% ee	
	Et	H		$MgBr_2$	(13) **I:II** = 4*:1 *82% ee	
	H	Et		$MgBr_2$	(33) **I:II** = 1*:3.5 *90% ee	
	H	Et		Cp_2ZrCl_2	(7) **I:II** = 1*:1 *92% ee	

C_{11}

LDA, HMPA-THF (20%), -78°

(60)

35-37

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

C_{12}

LDA, THF, -78°

(63)

58

LiH, MeOH, THF, 67°

(20)

60

LDA, HMPA-THF (1:4), -78° to rt

(45) ds 69%

59

175

R = TMS   LDA, THF, -78°   (46) 98% *Z*
R = Br   LDA, THF, -100 to -20°   (31) *Z:E* >25:1

188

189
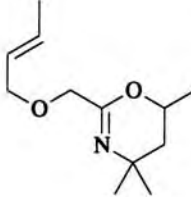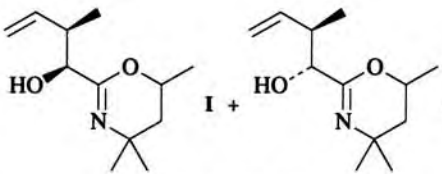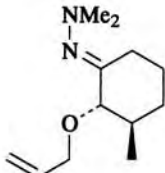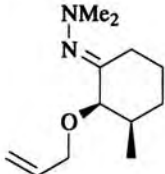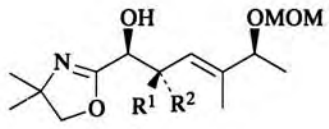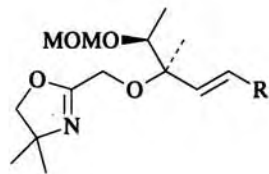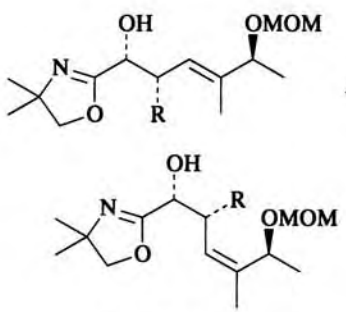
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

95% *E*	*n*-BuLi, THF, -78°	(98) **I:II** = 98:2	
95% *E*	LDA, THF, -78°	(86) **I:II** = 96:4	
98% *Z*	LDA, THF, -78°	(82) **I:II** = 65:35	

	KH, KOBu-*t*, THF, rt, 10 h	(91)	176

	KH, KOBu-*t*, THF, reflux, 12 h	" (92)	176

190

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

	R^1	R^2			
C$_{12}$	H	H	*n*-BuLi, THF, -78°	(82) ds >100:1	72, 84
C$_{13}$	Me	H	"	(87) ds 68:1	
	Me	H	HMPA, THF	(85) ds 8.8:1	
	H	Me	*n*-BuLi, THF, -78°	(91) ds >100:1	

C$_{12}$	R = H	*n*-BuLi, THF, -78°	(95) ds 1.8:1	72, 84
		MeMgBr, THF, 0°	(20) ds >100:1	
C$_{13}$	R = Me	*n*-BuLi, THF, -78°	(87) ds 2.2:1	
		n-BuLi, HMPA, THF, -78°	(85) ds 1.2:1	

191

Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}	*n*-BuLi, THF, -78°	**I** + **II** $I:II = 72:28$	72
C_{13} R = Et C_{14} R = *i*-Pr C_{17} R = C_6H_{11}	LDA, Cp$_2$ZrCl$_2$, THF, -78 to -20°	(72) (66) (30)	177
C_{13}	*n*-BuLi, THF, -85°	(98) ds 62:22:3:13	178

Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{14}	*n*-BuLi, THF, -78°	(63)	58
	LDA, THF, TMEDA -78°, 30 min; to -40°, 3 h	(40) >98% selective	106

	R		
	R	Conditions	I and II
C_{14}	H	KH, THF, 20°	(—) 84% ee, *S*
	H	KH, 18-c-6, THF, -20°	(—) 96% ee, *R*
C_{15}	Me, 93% *E*	KH, THF, 20°	(—) **I**:**II** = 41:59; **I**, 0% ee; **II**, 74% ee, *S*
	Me, 93% *Z*	KH, THF, 20°	(—) **I**:**II** = 43:57; **I**, 64% ee, *S*; **II**, 78% ee, *S*
	Me, 93% *E*	KH, 18-c-6, THF, -20°	(—) **I**:**II** = 46:54; **I**,86% ee, *R*; **II**, 84% ee, *R*
	Me, 93% *Z*	KH, 18-c-6, THF, -20°	(—) **I**:**II** = 54:46; **I**,86% ee, *R*; **II**, 86% ee, *R*
C_{16}	Me$_2$	KH, THF, 20°	(—) 56% ee, *S*

96

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₅	LDA, THF, -78°	(95) ds 35:1	72, 84
	LDA, THF, -78°	I + II (90) **I:II** = 1.7:1	72, 84

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
		I + II	95

	R		
C₁₅	H	*n*-BuLi, THF, -78°	(—) 38% ee, *R*
	H	LDA, THF, -78°	(—) 14% ee, *R*
C₁₆	Me	*n*-BuLi, THF, -78°	(—) I:II = 90:10; I, 78% ee, *R*; II, 8% ee, *S*
	Me	LDA, THF, -78°	(—) I:II = 84:16; I, 64% ee, *R*; II, 28% ee, *S*
C₁₇	Me₂	*n*-BuLi, THF, -78°	(—) 75% ee, *R*

Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS (*Continued*)
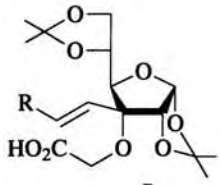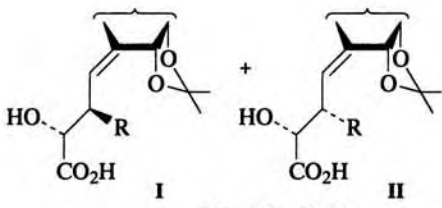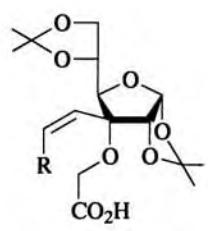
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17} $\quad$ Me C_{18} $\quad$ Et C_{19} $\quad$ *i*-Pr	LDA, THF, -78 to 0°, 10 min	 (60) **I:II** = 75:25 (63) **I:II** = 95:5 (78) **I:II** = 95:5	56
C_{17} $\quad$ Me C_{18} $\quad$ Et C_{19} $\quad$ *i*-Pr	LDA, THF, -78 to 0°, 10 min	**I** (56) **I** (89) **I + II** (66), **I:II** = 95:5	56

Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS (*Continued*)
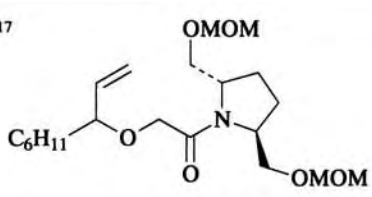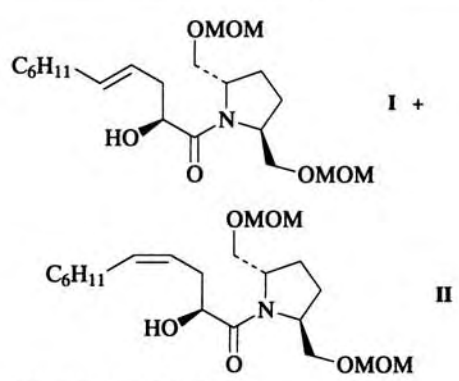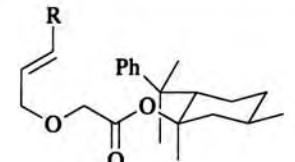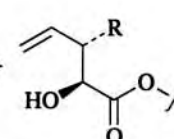
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{17}	LDA, THF, -100°, 3 h; -70°, 3 h LDA, THF, Cp$_2$ZrCl$_2$, -100°, 3 h; -70°, 3 h LDA, THF, Cp$_2$ZrCl$_2$, -100°, 3 h; -20°, 3 h	**I** + **II** (83) **I:II** = 4:1; **I**, 33% ee (25) **I:II** = 1:3; **II**, 87% ee (70) **I:II** = 1:3; **II**, 41% ee	97

Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

		I + II	98

	R			
C_{21}	H	LDA, THF, HMPA, -78°	(—) 11% ee, *S*
C_{22}	Me	LDA, THF, HMPA, -78°	(—) **I:II** = 90:10; **I**, 97% ee, *S*
	Me	LHDS, THF, HMPA, -78°	(—) **I:II** = 93:7; **I**, 96% ee, *S*
	Me	LTMP, THF, HMPA, -78°	(—) **I:II** = 92:8; **I**, 97% ee, *S*
C_{23}	Me$_2$	LDA, THF, HMPA, -78°	(—) 96% ee, *S*
C_{25}	*n*-Bu	LDA, THF, HMPA, -78°	(—) **I:II** = 92:8; **I**, 95% ee, *S*
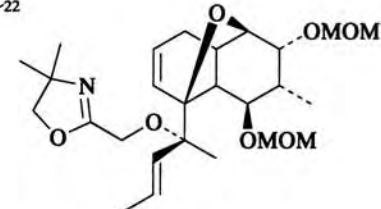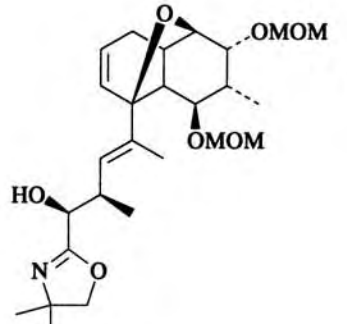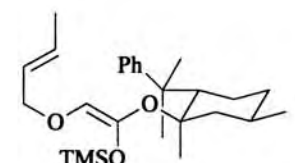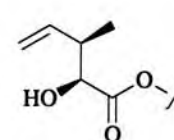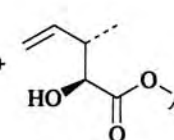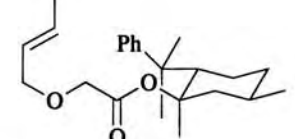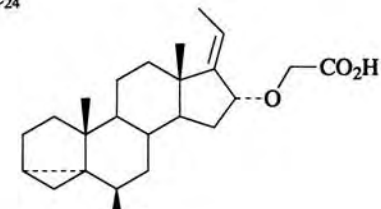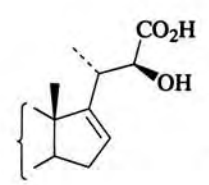
C_{22}

LDA, THF, -78°   (94)   131

Table V. ENOLATE REARRANGEMENTS OF α–(ALLYLOXY)CARBONYL COMPOUNDS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.

I + II   65

93% *E*	TiCl$_4$, CH$_2$Cl$_2$, -50°, 5 h	(80) **I:II** = 85:15; **I**, 8% ee, *S*
93% *E*	SnCl$_4$, CH$_2$Cl$_2$, -50°, 5 h	(79) **I:II** = 93:7; **I**, 12% ee, *S*

LDA, THF, Cp$_2$ZrCl$_2$, -78°   **I** + **II** (75); **I:II** = 94:6; **I**, 91% ee, *S*   179

C_{24}

LDA, THF, -78°   (82)   85, 86
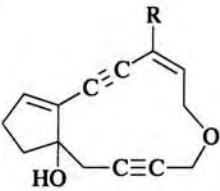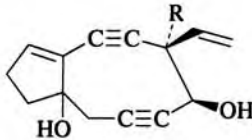
Table VI. [2,3]-WITTIG RING CONTRACTIONS

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
C8	LTBB, THF, -78 to 0°, 2 h or -78°, 2 h	(45) + (21)	120
C10	LTMP, THF, -78°, 5 h LTMP, THF, 0°, 14 h n-BuLi, THF, HMPA, 0°, 12 h LBPEAS, THF, 0°, 24 h LBPEAS, THF, 25°, 36 h LBPEAS, THF, HMPA, 0°, 24 h	+ (10) (78) decomposition (40) 25% ee R,R (52) 25% ee R,R (45) 25% ee R,R	42-44
C12	t-BuLi, THF, -78°, 6-10 h	I (94)	41
	t-BuLi, THF, -78°, 6-10 h	I + II + III (95) I:II:III = 9:50:41	41

Table VI. [2,3]-WITTIG RING CONTRACTIONS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
	t-BuLi, THF, -78°, 6-10 h	(96)	41
C14	LTMP, THF, -20°	(—)	78, 79
	n-BuLi, C5H12-THF, (9:1), -78°, 2.5 h	(92)	78, 79
	LBPEAS, THF, -70 to -15°, 45 min LBPEAS, C5H12, THF, -25 to 0°, 90 min LBPEAS, Et2O, -25 to -15°, 30 min LBPEAS, THF, -20°, 60 min LBPEAR, THF, -35 to -25°, 60 min LBPEAR, THF, -20°, 40 min	(82) 69% ee (68) 43% ee (70) 9% ee (82) 2% ee (78) 70% ee (75) 60% ee	115-117

Table VI. [2,3]-WITTIG RING CONTRACTIONS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
R = H	*n*-BuLi, HMPA, -78°	(<29)	146
R = Me	*t*-BuLi, THF, -100°	(62-66)	145
C$_{15}$	*t*-BuLi, Et$_2$O, -70°	I + II + III +	25, 141
		III I + II + III (90)	
		I:II:III = 39:9:52	
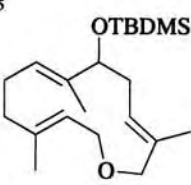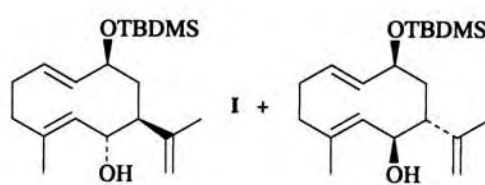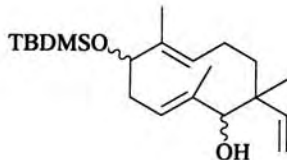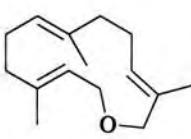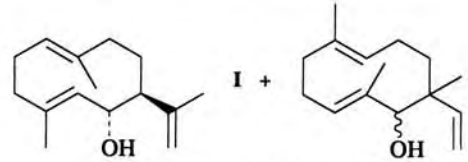
Table VI. [2,3]-WITTIG RING CONTRACTIONS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
		I + II	
	t-BuLi, Et$_2$O, -78°, 10 h to 0°, 30 min	I + II (90); I:II = 75:25	41
	t-BuLi, C$_6$H$_{14}$, -70°	I + II (0)	25, 141
	t-BuLi, Et$_2$O, -70°	I + II (98); I:II = 75:25	25, 141
	t-BuLi, THF, -70°	I + II (95); I:II = 55:45	25, 141
	t-BuLi, THF-DME (3:1), -70°	I + II (—); I:II = 10:90	25, 141
	t-BuLi, THF-TMEDA (3:1), -70°	II (—)	25, 141
	t-BuLi, THF-HMPA (3:1), -70°	II (—)	25, 141
C$_{19}$	LTMP, C$_6$H$_{14}$-THF, (10:1), -78 to -23°	(12)	142
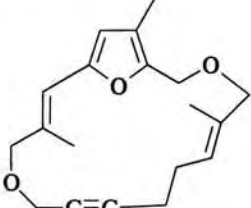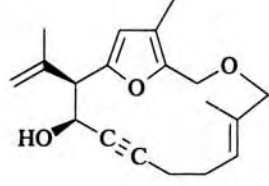
Table VI. [2,3]-WITTIG RING CONTRACTIONS (*Continued*)
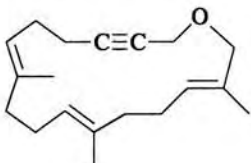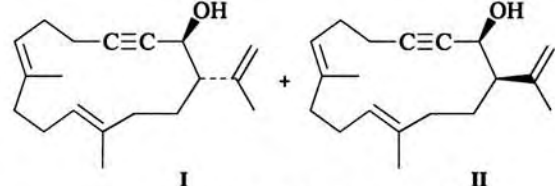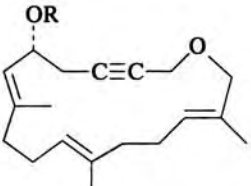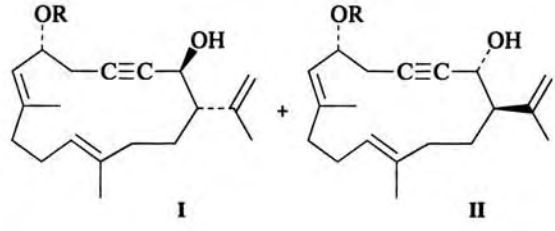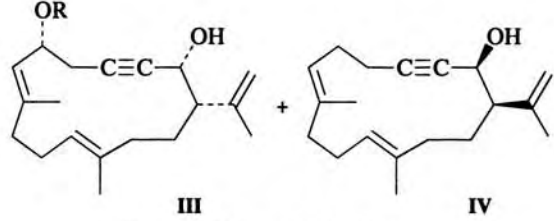
Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
		I + **II**	
	LBPEAS, THF, -55 to -10°	**I** + **II**, (56); **I:II** = 70:30, <5% ee	115-117
	LBPEAS, C$_5$H$_{12}$, -55 to -10°	**I** + **II**, (68); **I:II** = 60:40, 33% ee	115-117
	n-BuLi, THF, -78°	**I** + **II**, (80); **I:II** = 70:30	42, 43
	n-BuLi, THF-C$_6$H$_{14}$ (1:10), -78°	**I** + **II**, (73); **I:II** = 29:71	42, 43
	n-BuLi, THF-C$_6$H$_{14}$ (1:10), -20°	**I** + **II**, (78); **I:II** = 18:82	42, 43
	n-BuLi, THF-HMPA (25:1), -78°	**I** + **II**, (76); **I:II** = 75:25	42, 43
	n-BuLi, THF-HMPA (25:2), -78°	**I** + **II**, (49); **I:II** = 84:16	42, 43
	n-BuLi, THF-HMPA (4:1), -78°	**I** + **II**, (45); **I:II** = 88:12	42, 43

Table VI. [2,3]-WITTIG RING CONTRACTIONS (*Continued*)

Ether	Conditions	Product(s) and Yield(s) (%)	Refs.
	n-BuLi, TMEDA, C$_5$H$_{12}$, THF, -78°	**I** + **II** +	102,103 143,144
		III + **IV**	

R		
H	(71)	**I:II:III:IV** = 20:29:39:12
THP	(90)	**I:II:III:IV** = 81:7:6:6
TBS	(94)	**I:II:III:IV** = 74:8:14:4

8. Acknowledgments

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Tin(II) Enolates in the Aldol, Michael, and Related Reactions

Teruaki Mukaiyama, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo, Japan
Shu Kobayashi, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo, Japan

1. Introduction

The element tin has played an increasingly important role in organic chemistry as well as organometallic chemistry, serving as a source of new reagents for selective transformations. (1-3) The main activity in these fields has been focused for a long time on tin(IV) compounds, and tin(II) compounds have been used primarily as reductants of aromatic nitro compounds to aromatic amines. (4)

During the last decade, generation and reactions of various metal enolates have been extensively studied, and successful applications to the controlled formation of carbon–carbon bonds have been realized under mild conditions. (5-16) The chemistry of tin(IV) enolates has also been studied and several interesting features of these enolates have been reported, (17, 18) whereas tin(II) analogs were relatively unknown in synthetic organic chemistry, probably because of the lack of general methods for generating them.

In 1979, tin(II) fluoride was employed as a reductant of several α -halocarbonyl compounds and allylic halides to generate tin(IV) species, which subsequently reacted with aldehydes to form new carbon–carbon bonds (Eqs. 1–5). (19-23) When metallic tin was used instead of tin(II) fluoride, similar reactions proceeded smoothly. Because the reducing ability of metallic tin is superior to that of tin(II) fluoride, allyl bromide and α -bromoesters, which could not be reduced by tin(II) fluoride, were easily reduced by metallic tin to generate tin(II) enolates, which in turn reacted with aldehydes to yield homoallyl alcohols or β -hydroxyesters (Eqs. 6 and 7). (24, 25) The latter reaction was the first example of the reaction of tin(II) enolates. More conveniently, tin(II) enolates could be generated

(1)

2-deoxy-D-ribose

(2)

(3)

(4)

SnX$_2$
X = F, Cl

(5)

1. CBr$_4$
2.
3. Ac$_2$O

D-erythronolactone

(6)

(7)

syn/anti >90/10
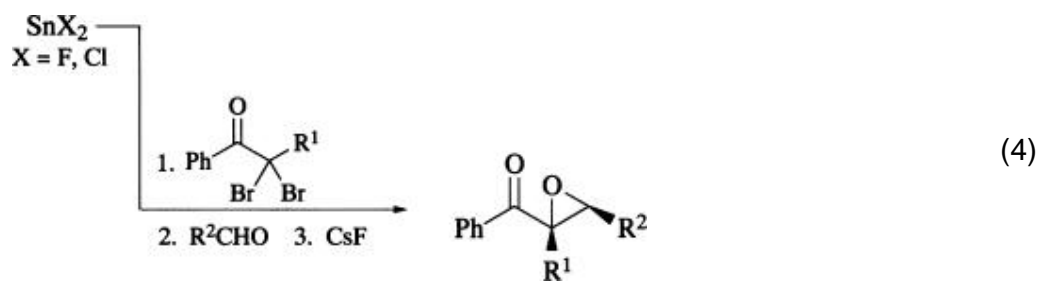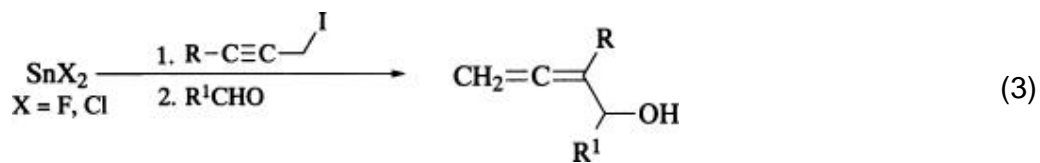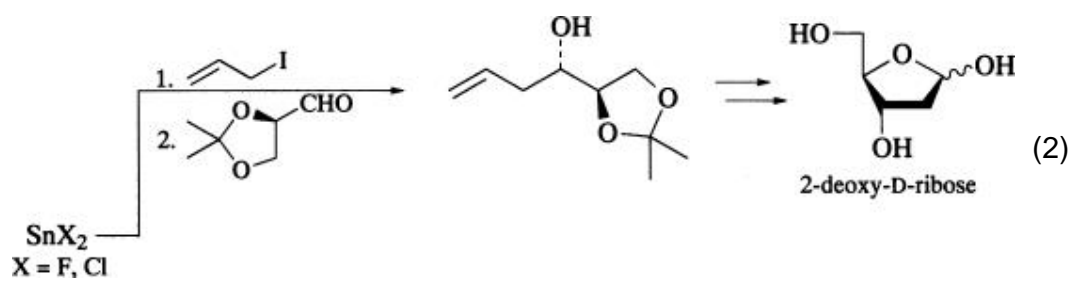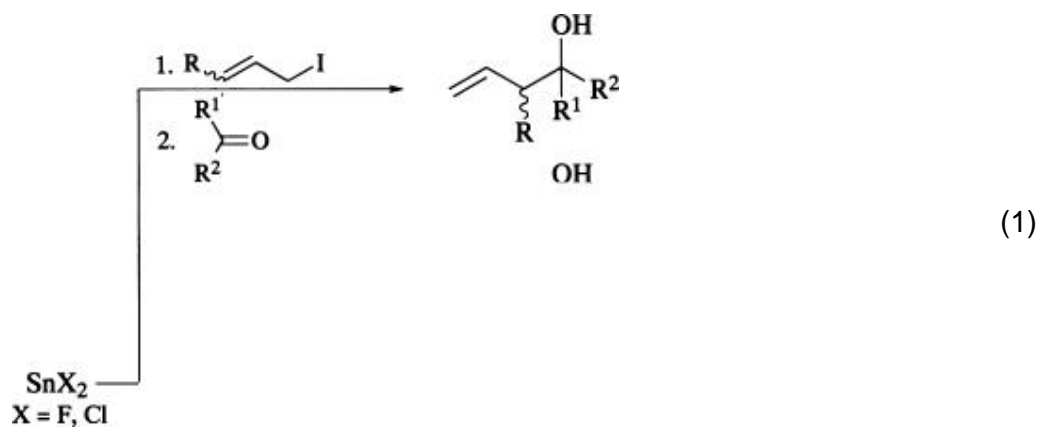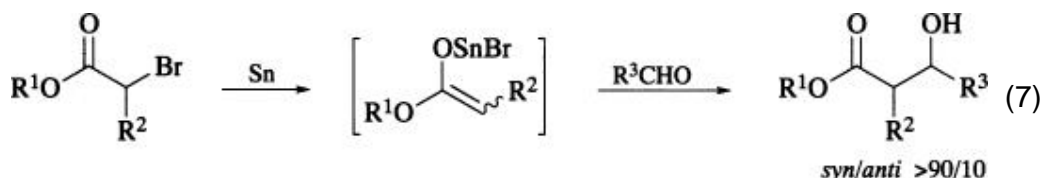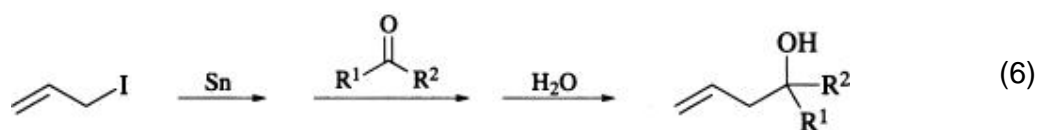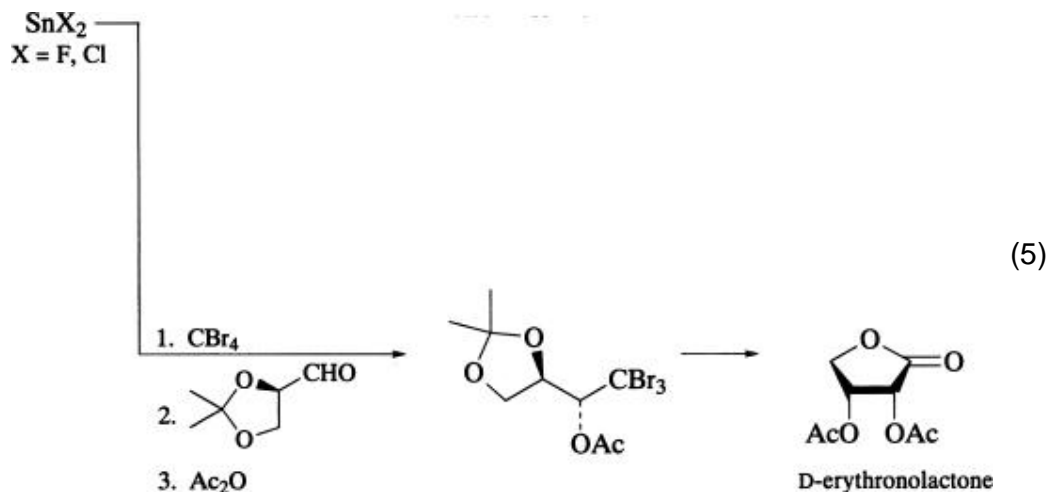
directly from ketones by using tin(II) triflate and a tertiary amine under neutral conditions. (26)

While strongly basic conditions are required to prepare lithium enolates, tin(II) enolates can be generated under extremely mild conditions. Tin(II) enolates can behave as interesting chemical species in synthetic reactions that cannot be realized with other metal enolates. One of the characteristic features of tin(II) enolate mediated reactions is a highly enantioselective version employing chiral diamines.

Recent developments in the field of stereoselective aldol reactions have resulted in exploitation of the asymmetric version of this reaction, and several successful methods have been reported using chiral carbonyl compounds and/or chiral enolates. (6, 27, 28) However, the efficiency of these reactions is greatly diminished by the tedious procedures for attachment and removal of the chiral auxiliaries. Thus development of a highly enantioselective aldol

reaction between two achiral carbonyl compounds utilizing chiral chelating agents became desirable, though the use of chiral addends in the aldol reaction had not met with much success. (29-31) Chiral diamines derived from (*S*)-proline, which are postulated to form rigid *cis*-fused 5-membered bicyclic structures by chelation to a metal center, were found to be effective ligands for several highly enantioselective reactions. (32-35) Coordination of a chiral diamine to the metal center of the tin(II) enolate effected highly enantioselective cross aldol and Michael reactions between two prochiral reactants.

This review covers the literatures on tin(II) enolates to the middle of 1991.

2. Scope and Limitations

At the beginning of this section, general preparative methods for tin(II) enolates are briefly surveyed, followed by a detailed description of the reactions of tin(II) enolates. The reactions are roughly classified into two parts, simple diastereoselective reactions and asymmetric reactions. In the first part, the simple diastereoselective reaction between two achiral substrates is described; for example, the aldol reaction of enolates having prochiral faces with aldehydes gives four diastereomeric and enantiomeric aldols (Eq. 8). In an unselective reaction,

$$R^1CHO \quad + \quad \underset{R^2}{\overset{OM}{\diagdown}}R^3 \quad \longrightarrow$$

(8)
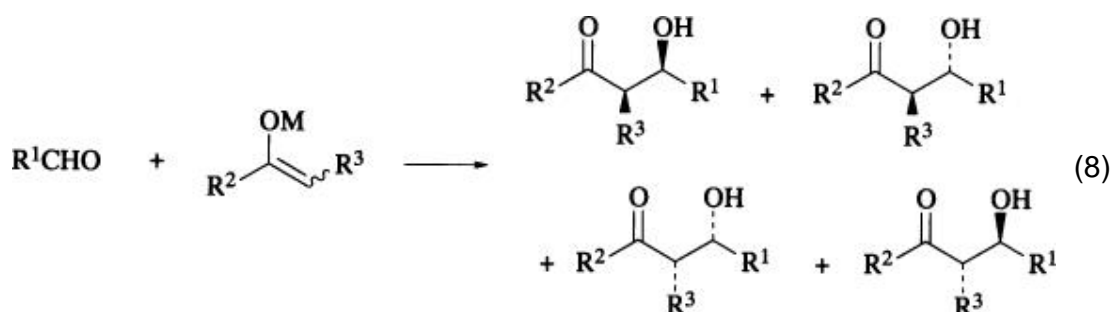
two racemic diastereomers result. The simple diastereoselective reaction gives a surplus of one of these diastereomers. The second part, asymmetric reactions, is further grouped into enantioselective reactions and diastereoselective reactions. One characteristic feature of tin(II) enolates is the asymmetric version in which two achiral substrates combine to give a chiral, optically active product with the aid of a chiral ligand which is not covalently bonded to the substrates (enantioselective reaction). Conventional asymmetric reactions of achiral tin(II) enolates with chiral compounds, chiral tin(II) enolates with achiral compounds, and chiral tin(II) enolates with chiral compounds are discussed in the section on diastereoselective reactions.

2.1. General Preparative Methods for Tin(II) Enolates
Tin(II) enolates are generated in situ according to the following procedures and then immediately reacted with electrophiles. Isolation of tin(II) enolates is generally difficult compared to that of silyl and tin(IV) enolates.

2.1.1.1.1. The Tin(II) Triflate Method
Most commonly and conveniently, tin(II) enolates can be generated by reaction of ketones and tin(II) triflate in the presence of a tertiary amine (Eq. 9). (26, 36) The choice of the tertiary amine is crucial; for example,

$$(9)$$
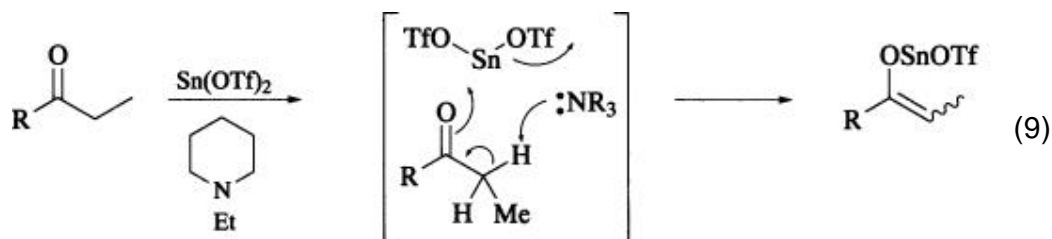
pyridine or 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) fail to promote the reaction because of the formation of a coordinated complex with divalent tin, while other amines give problems with self-aldol reactions. *N*-Ethylpiperidine gives excellent results in the cross-aldol reaction of propiophenone with 3-phenylpropanal (Eq. 10).

R_3N	I (%)	II (%)
pyridine	(0)	(0)
DBU	(0)	(0)
Et_3N	(50)	(15)
N-methylmorpholine	(22)	(65)
N-ethylpiperidine	(80)	(trace)

$$(10)$$
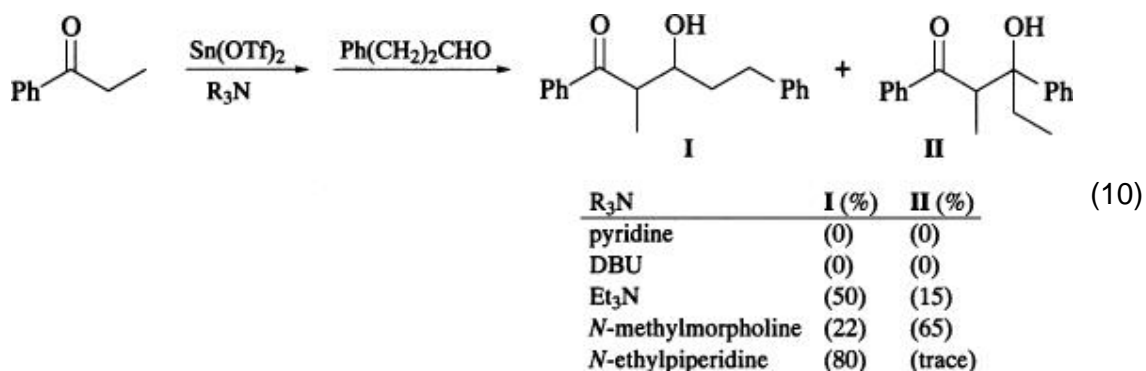
Tin(II) enolates of 3-acylthiazolidine-2-thiones, (37) 3-acyloxazolidine-2-thiones, (38) or 3-acyloxazolidinones (39, 40) are readily generated by the procedure described above, while tin(II) enolates of esters or thioesters cannot be smoothly generated by the same procedure because of the relatively low acidity of their α -protons.

Tin(II) dienolates are also successfully generated by this procedure (Eq. 11). (41)

$$(11)$$
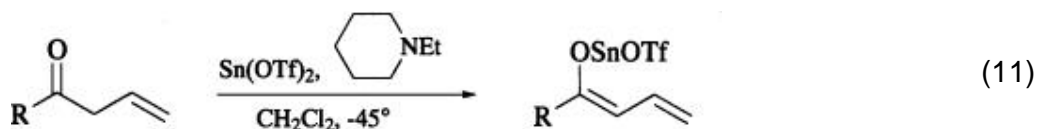
2.1.1.1.2. Reduction of α -bromocarbonyls

Tin(II) enolates can also be generated in situ by the reduction of α -bromoesters or α -bromoketones by metallic tin (Eq. 12). (42) Instead of metallic tin, the tin(II) chloride–lithium aluminum hydride (LAH) system is effective with some α -bromoesters. (25)

$$R^1 \overset{O}{\underset{R^2}{\bigwedge}} Br \xrightarrow[\text{DMF, rt}]{\text{Sn}} R^1 \overset{OSnBr}{\underset{}{\bigwedge}} R^2 \tag{12}$$
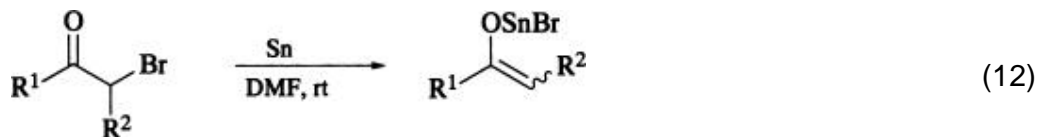
2.1.1.1.3. Addition to Ketenes

Tin(II) enolates of thioesters are conveniently generated by the addition of tin(II) thiolates (generated in situ from 1,1 -dimethylstannocene and a thiol) to ketenes (Eq. 13). (43)

$$\overset{R^1}{\underset{H}{\bigwedge}}{=}C{=}O \xrightarrow[\text{THF, rt}]{\text{Sn}(SR^2)_2} R^2S \overset{OSnSR^2}{\underset{}{\bigwedge}} R^1 \tag{13}$$
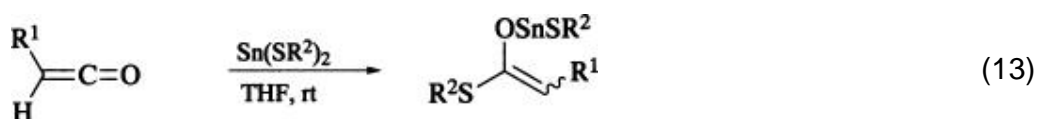
2.1.1.1.4. Metal Exchange Reaction of Lithium Enolates

Tin(II) enolates of thioesters are also generated by metal exchange of lithium enolates with tin(II) chloride or tin(II) triflate (Eq. 14). (44-46)

$$t\text{-BuS} \overset{O}{\underset{}{\bigwedge}} R \xrightarrow[\text{2. SnCl}_2]{\text{1. LDA, Et}_2O} t\text{-BuS} \overset{OSnCl}{\underset{}{\bigwedge}} R \tag{14}$$
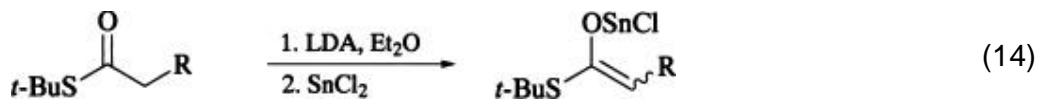
2.1.1.1.5. 1,4-Addition of Tin(II) Triflate Sulfide to α , β -Unsaturated Ketones

Tin(II) enolates of β -thioketones are generated by the conjugate addition of tin(II) triflate sulfide, prepared in situ from tin(II) triflate and a lithium thiolate, to α , β -unsaturated ketones (Eq. 15). (47)

$$\overset{O}{\underset{}{\bigwedge}} \xrightarrow[\text{THF, -45°}]{\text{EtSSnOTf}} \overset{OSnOTf}{\underset{}{\bigwedge}} SEt \tag{15}$$
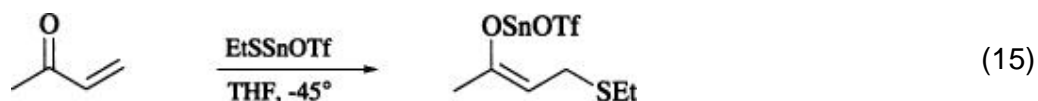
2.1.1.1.6. Reduction of α -Dicarbonyl Compounds [Tin(II) Enediolates]

Tin(II) enediolates are generated by reduction of α -dicarbonyl compounds with activated metallic tin prepared from tin(II) chloride and metallic potas sium (Eq. 16). (48)

$$(16)$$
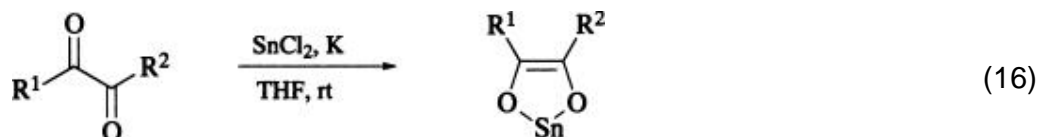
2.2. Simple Diastereoselective Reactions

2.2.1. Aldol Reaction

2.2.1.1.1. Aldehydes and Ketones as Acceptors

α -Haloesters react with metallic tin to generate tin(II) enolates, which readily add to carbonyl compounds to give β -hydroxyesters in high yields (Reformatsky-type reaction) (Eq. 17). Activated

$$(17)$$

tin, prepared by reduction of tin(II) chloride with lithium aluminum hydride (LAH) (2:1 molar ratio), is also effective in some of these reactions (Eq. 18). (25)

$$(18)$$

Sn	DMF, rt, 24 h	(6%)
SnCl$_2$ - LAH, 2:1	THF, rt, 2 h	(84%)
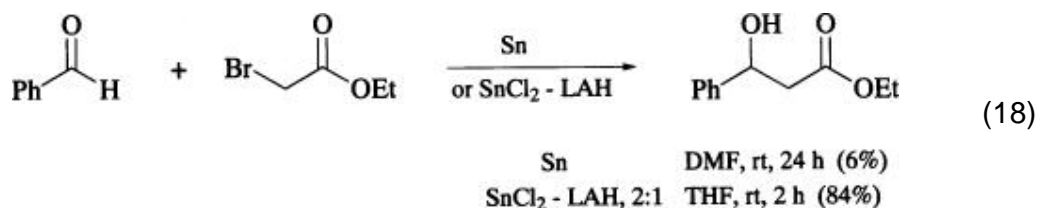
The reduction of α-bromoketones by metallic tin also generates tin(II) enolates which react with aldehydes and ketones regiospecifically with high *syn* selectivity (Eq. 19). (42) Generation of tin(IV) species via reduction of α -bromoketones or α -bromoesters with initially generated tin(II) species does not take place under the reaction conditions.

$$(19)$$

(28-99%)
syn:anti = 90:10 - 94:6
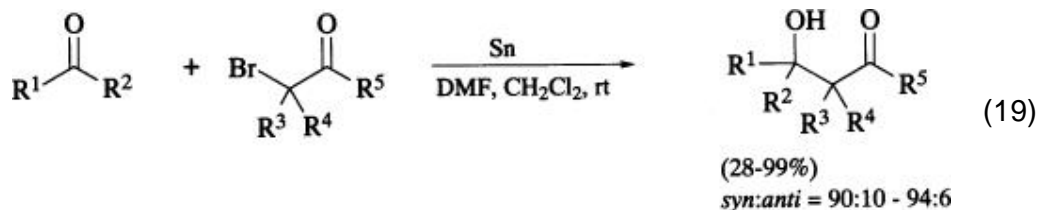
In the above described reaction, α -bromoketones are prepared by the bromination of ketones (49-51) and then are reduced by metallic tin to generate tin(II) enolates. Instead, more conveniently and efficiently, tin(II) enolates can be generated by reaction of ketones with tin(II) triflate in the presence of *N*-ethylpiperidine, and they undergo aldol reactions with aldehydes to give the corresponding β -hydroxyketones in good yields under extremely mild conditions with good to excellent *syn* selectivity (Eq. 20). (26)

$$(20)$$

syn/anti >90/10
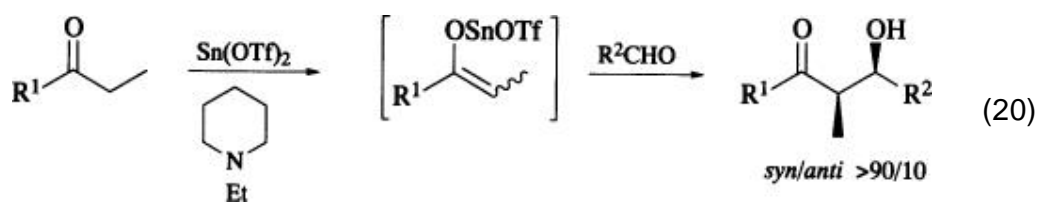
Tin(II) enolates generated by the procedure described above are highly reactive with a ketone acceptor, and ketone–ketone cross-coupling products can be obtained in good yields (Eq. 21). (52) Enhanced *anti*-selectivity is observed when

$$(21)$$

(41-96%)
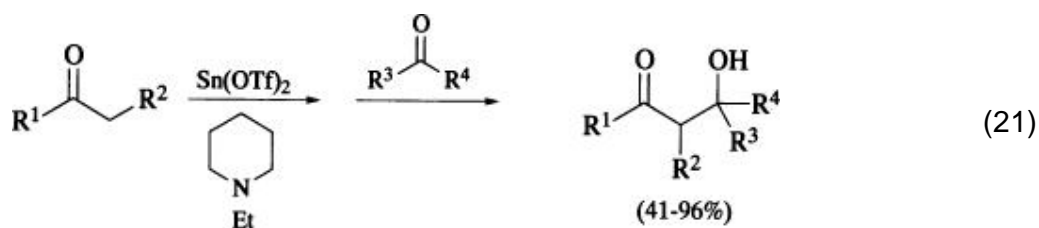
aromatic ketones are the acceptor carbonyl compounds. This high reactivity towards ketones is characteristic of tin(II) enolates. Versatile and frequently employed boron enolates display poor reactivity toward ketones, (53-56) and the even more nucleophilic lithium enolates react with only less hindered ketones in moderate yields. 57,57a

A branched-chain sugar, ethyl 2-*C*-methyl-DL-lyxofuranoside, is synthesized stereoselectively by application of this ketone–ketone cross-coupling reaction starting from a 1,3-dihydroxy-2-propanone derivative and methyl pyruvate (Eq. 22). (58)

$$(22)$$
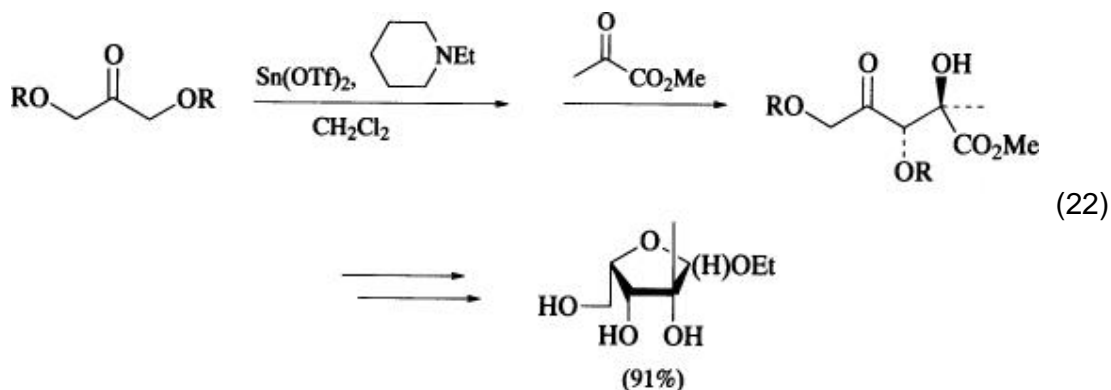
A convenient method for the stereoselective synthesis of *cis*- β -substituted- α , β -epoxyketones involves the tin(II) triflate mediated cross aldol reaction of α -bromoketones with aldehydes. The corresponding adducts, *syn*- α -bromo- β -hydroxyketones, are preferentially produced. In turn, these are converted to *cis*- α , β -epoxyketones with minimum isomerization to *trans* isomers via intramolecular S_N2-type ring closure to oxiranes by the action of potassium fluoride-dicyclohexyl-18-crown-6 (Eq. 23). (59)

$$(23)$$
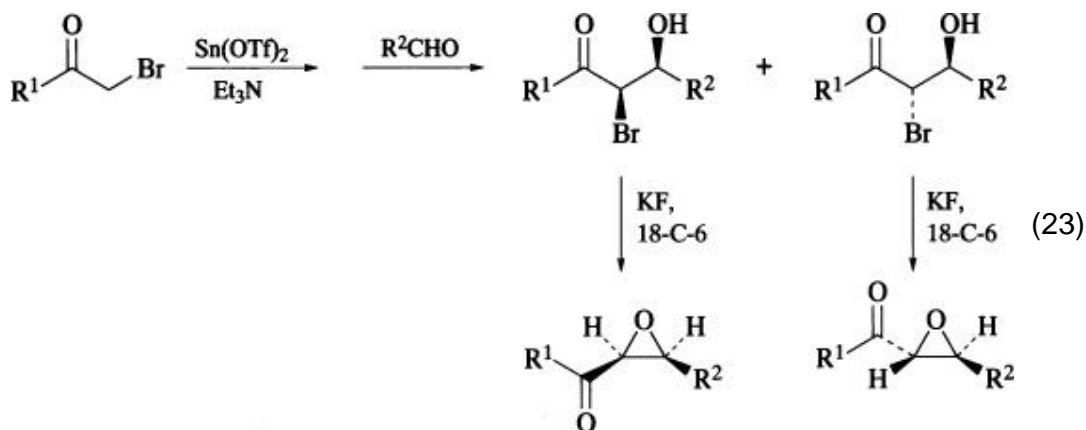
Dialkyl-(2,3-epoxy-4-oxoalkyl)phosphonates are synthesized by this procedure starting from (1-formylalkyl)phosphonates and the tin(II) enolates of α -bromoketones (Eq. 24). (60)

$$(24)$$
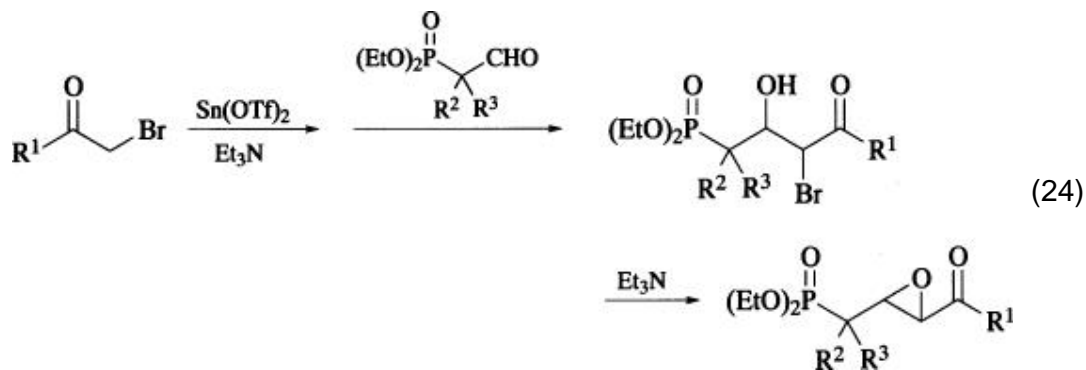
α , β -Epoxyesters or aldehydes are frequently prepared by the Darzens reaction (61-63) or by epoxidation of the corresponding α , β -unsaturated ketones or esters. (64) However, the stereoselective synthesis of *cis*- β -substituted α , β -epoxyesters or aldehydes by these methods is not easily achieved because of the low stereoselectivity of the Darzens reaction or the difficulty in obtaining the starting Z olefins. In an extension of the tin(II) enolate mediated stereoselective aldol reaction, various *cis*- α , β -epoxy esters and *cis*- α, β -epoxy aldehydes are prepared with high stereoselectivities by using an α -bromo- α '-siloxyketone as the starting carbonyl compound. (65) The cross-aldol product is obtained by treatment of tin(II) triflate with the α -bromoketone in the presence of *N*-ethylpiperidine, followed by addition of the aldehyde. On treatment of the crude adduct with sodium carbonate, the *cis* oxirane ring is formed stereospecifically. Oxidative cleavage of the α -hydroxyketone affords an α , β -epoxycarboxylic acid, which is in turn converted to the methyl ester with diazomethane. The *cis*- α , β -epoxyketone is also easily converted to a *cis*- α , β -epoxyaldehyde by reducing the carbonyl group with sodium borohydride prior to oxidative cleavage (Eq. 25). (66)

$$(25)$$

cis:trans 95:5
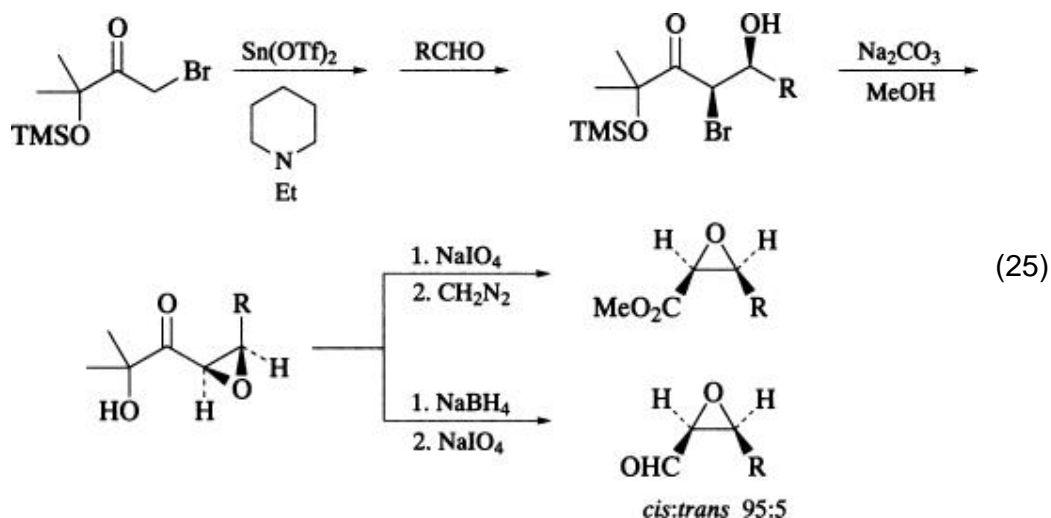
β -Hydroxy aldehydes or β -hydroxy carboxylic acid derivatives are useful synthetic building blocks. In particular, β -hydroxy aldehydes have been used for the construction of a variety of polyoxygenated natural products. (67, 68) Direct generation of tin(II) enolates from esters by using the tin(II) triflate method is not generally successful. Though the reaction with benzaldehyde affords the aldol product in good yield, only products of polymerization of the aldehyde result from aldehydes containing an α hydrogen atom. Self-polymerization of the starting material takes place with aldehyde enolates.

3-Acylthiazolidine-2-thiones, prepared from acyl chlorides and thiazolidine-2-thione or from carboxylic acids and thiazolidine-2-thione with dicyclohexylcarbodiimide (DCC) or pyridinium salts, (69) are aldehyde or ester equivalents because they can be cleanly converted to the corresponding aldehydes by the reduction with diisobutylaluminum hydride (DIBAL) or transformed into a variety of carboxylic acid derivatives under mild conditions. (70, 71) They undergo a similar tin(II) triflate-mediated aldol-type reaction to give β -hydroxy carbonyl compounds in excellent yields with excellent *syn* selectivity (Eq. 26). These cross coupling products are versatile synthetic intermediates and can be transformed into esters, amides, aldehydes, and diols in good yields (Eqs. 27–29). (36, 72)

A dramatic reversal is observed in the stereochemical course of the tin(II) triflate mediated aldol-type reaction of 3-(2-benzyloxyacetyl)thiazolidine-2-thione. The *syn* isomers are preferentially obtained by the reaction with aldehydes in the absence of tetramethylethylenediamine (TMEDA), while *anti* isomers are observed in the same reaction carried out in the presence of TMEDA (Eq. 30). (73)

$$(26)$$

(27)

$$\text{K}_2\text{CO}_3 \text{ (3 eq)}$$
$$\text{MeOH or EtOH, rt}$$

Ph, OH, O, OMe (Et)   (~95%)

Ph, OH, O, N (thiazolidinethione, S)

(28)

$$\text{BnNH}_2 \text{ (3 eq)}$$
$$\text{CH}_2\text{Cl}_2\text{, rt}$$

Ph, OH, O, NHBn   (90%)

(29)

1. TMSCl, Et$_3$N,
   CH$_2$Cl$_2$, 0°
2. DIBAL, PhMe, -78°

TMSO, Ph, O, H   (65%)

1. NaBH$_4$
2. H$^+$

Ph, OH, OH   (quant)

(30)
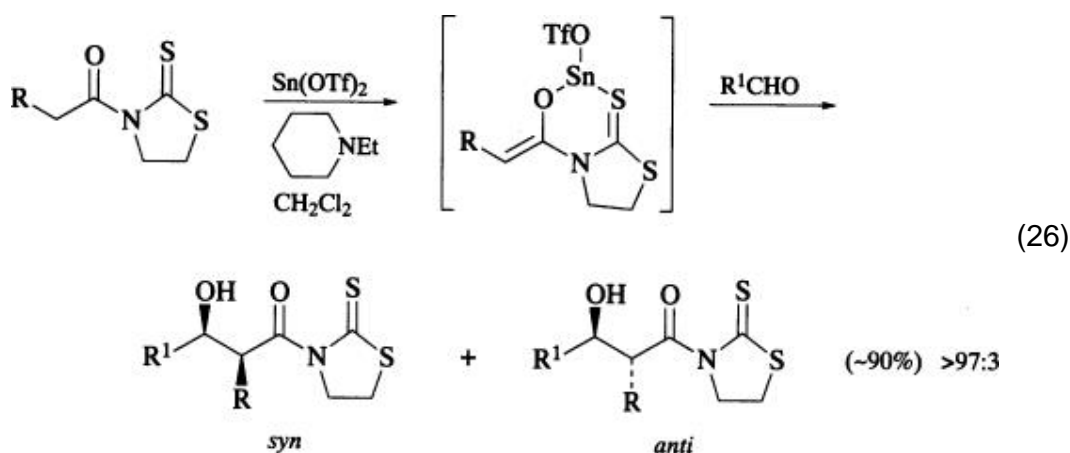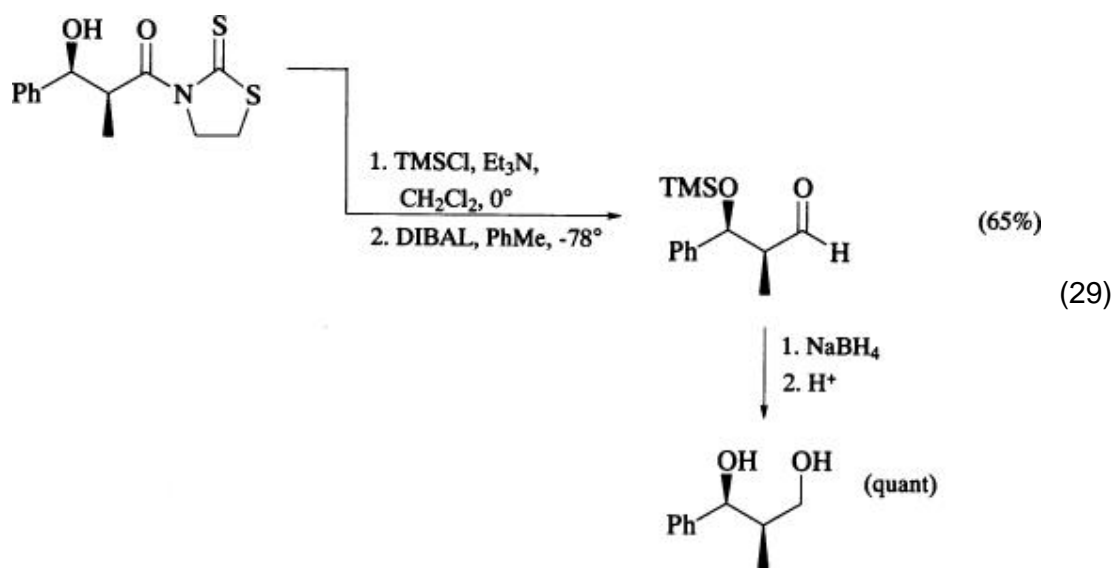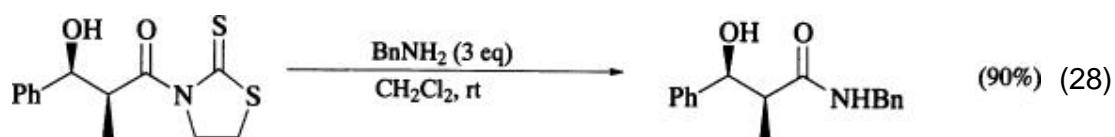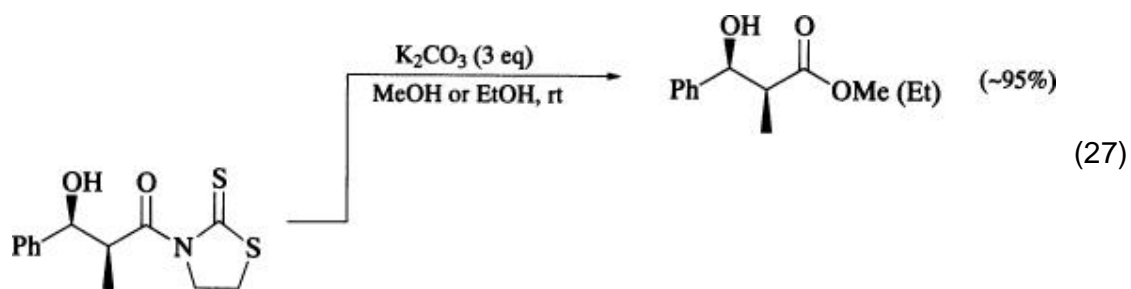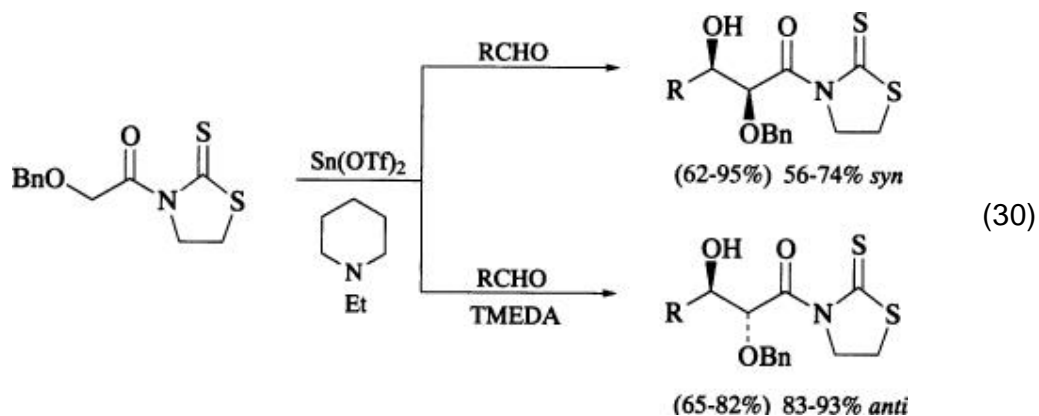
Furthermore, enolate formation from 3-acylthiazolidine-2-thiones bearing heteroatoms (X) on the β -carbon of the acyl group takes place without β elimination of the heterosubstituent, and polyfunctionalized aldol adducts are obtained by subsequent treatment with aldehydes (Eq. 31). Adducts where X = nitrogen

(31)
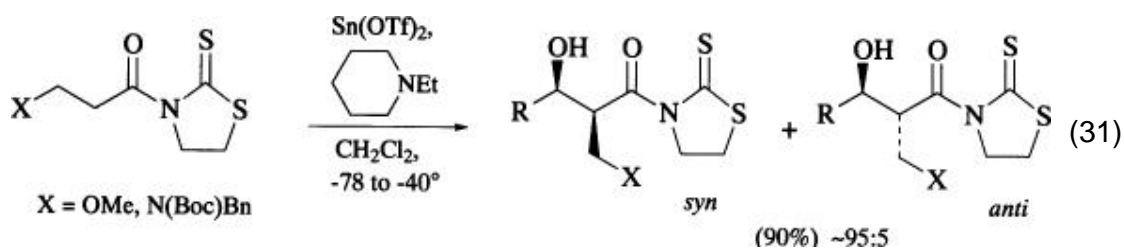
are cyclized to β -lactams on treatment of the corresponding acids with 2-chloro-1-methylpyridinium iodide (Eq. 32). (74)

(32)
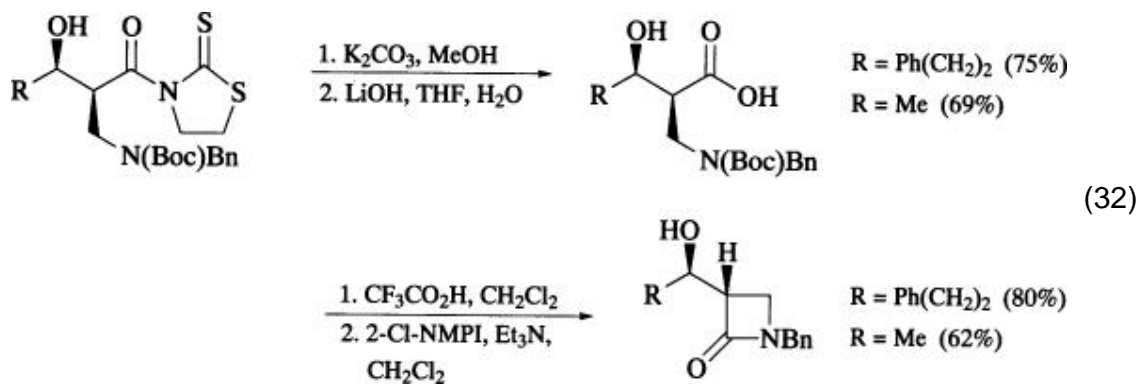
Tin(II) enolates of thioesters can be generated by the reaction of ketenes with tin(II) thiolates and they react smoothly with aldehydes to give *syn*- β -hydroxy thioesters in high yields with high diastereoselectivity (Eq. 33). (43)

$$(33)$$

(67-98%) *syn:anti* 90:10
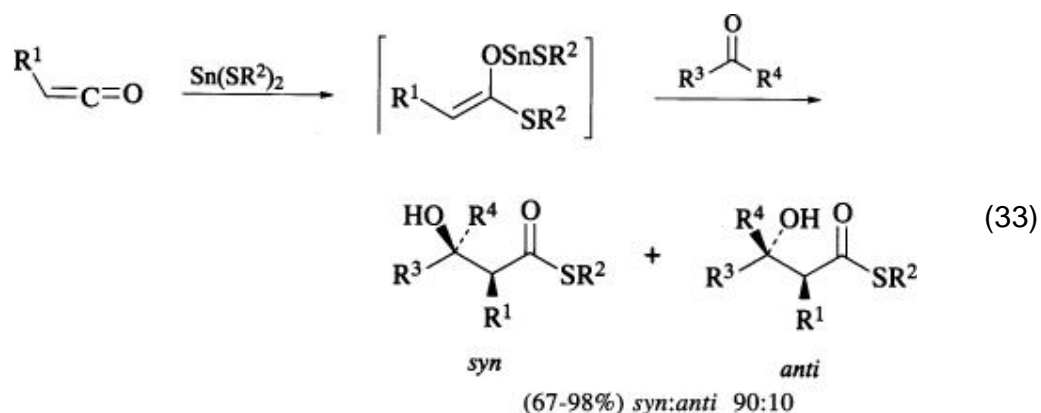
α , β -Dihydroxyketones are obtained by the reaction of α -dicarbonyl compounds with aldehydes in the presence of activated tin, prepared from tin(II) chloride and potassium. In this reaction, tin enediolates are formed as key intermediates, and improvement of diastereoselectivity is observed by the addition of hexafluorobenzene (Eq. 34). (48)

$$(34)$$

(68-95%)
syn:anti ≈ 1:1
syn:anti ≈ 3:1
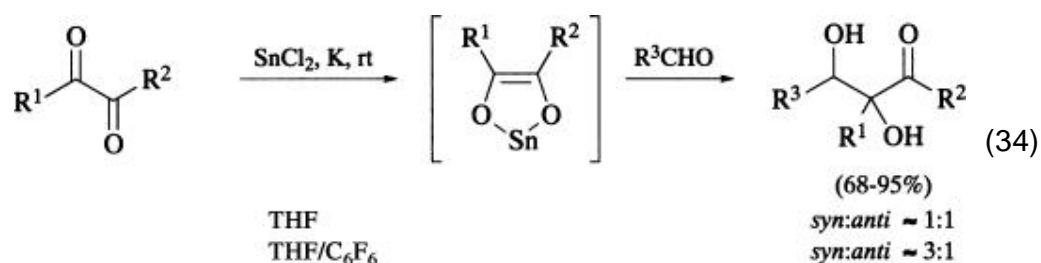
Although methylglyoxal is a synthetically useful compound, it is difficult to handle because of its volatility and ease of polymerization. This unstable compound is successfully converted to the tin(II) enediolate on treatment with activated tin. The tin(II) enediolate reacts with aldehydes to give α , β -dihydroxyketones in good yields (Eq. 35). (75)

$$\text{RCHO} \quad + \quad \text{[structure]} \quad \xrightarrow[\text{overnight}]{\text{THF, 0°}} \quad \text{[product]} \qquad (35)$$
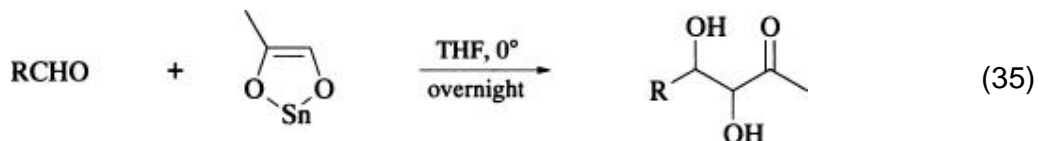
Activated tin is effective for the preparation of aldehyde enolates from α -bromoaldehydes. The cross aldol reaction between two aldehydes is generally quite difficult because of competitive side reactions such as preferential self-condensation, or further reaction of the enolate with the initially produced β -hydroxy aldehydes. Tin(II) enolates prepared from 2-bromo-2-methylpropanal and the activated tin ($SnCl_2$-K) react smoothly with aldehydes to give β -hydroxy aldehydes, cross aldol adducts between two different aldehydes, in fairly good yields (Eq. 36). (76)

$$\text{Br} \diagdown \text{CHO} \quad \xrightarrow[\text{overnight}]{\substack{\text{SnCl}_2, \text{K,} \\ \text{THF, 0°}}} \quad \left[\text{[enolate]} \right] \quad \xrightarrow{\text{RCHO}} \quad \text{[product]} \qquad (36)$$

$$(64\text{-}74\%)$$
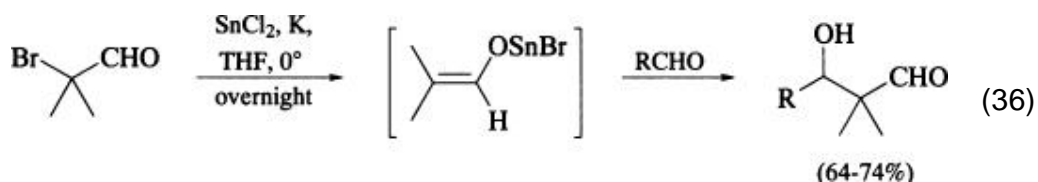
In most aldol reactions based on intermediate metal enolates, the starting carbonyl compound is quantitatively converted to the metal enolate prior to reaction with the second carbonyl compound. Therefore a stoichiometric amount of metal reagent is generally required. By use of only a catalytic amount of the tin(II) thiolate, the aldol reaction of tin(II) enolates with aldehydes takes place successfully to afford the cross aldol products in good yields with high stereoselectivity (Eq. 37). (77, 78)

$$\text{[structure]} \quad + \quad \text{R}^1\text{CHO} \quad + \quad \text{EtSTMS} \quad \xrightarrow[\text{2. H}_3\text{O}^+]{\substack{\text{1. EtSSnOTf (10 mol\%),} \\ \text{THF, -45°}}}$$

$$\text{[product]} \quad + \quad \text{[product]} \qquad (\sim 70\%) \ \sim 90{:}10 \qquad (37)$$

syn   anti
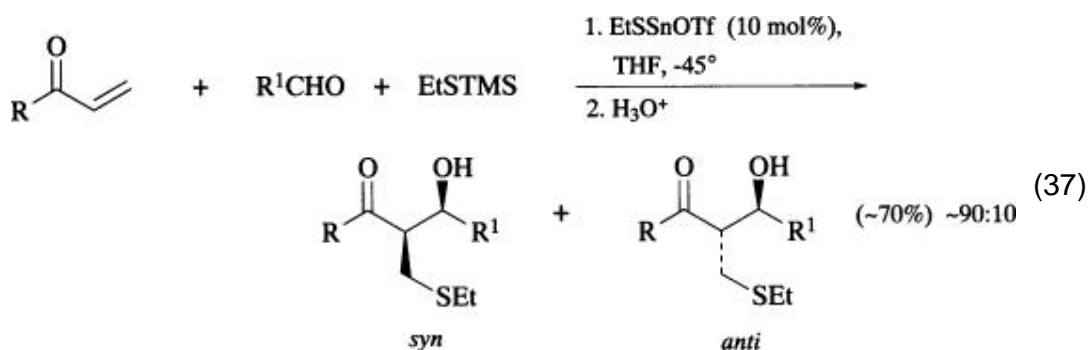
Regeneration of the tin(II) enolate in the catalytic cycle is assumed as shown in Eq. 38. In the first step, conjugate addition of the tin(II) species **1** to vinyl

(38)
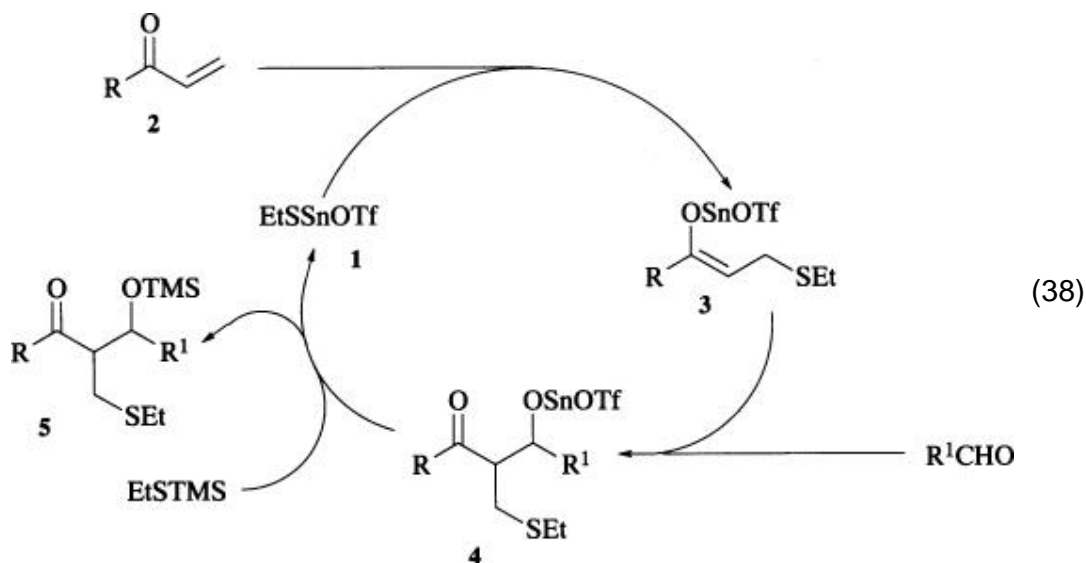
ketone **2** produces tin(II) enolate **3**, which in turn reacts with an aldehyde to give the aldol product **4** as its tin(II) alkoxide. In the next step, **4** reacts with the alkylthiotrimethylsilane to regenerate **1** along with the aldol product in the form of its trimethylsilyl ether **5**. The driving force for this reaction may be attributed to the difference in the relative bond strengths of tin(II)–sulfur and silicon–sulfur bonds.

2.2.1.1.2. Imines (Schiff bases) as Acceptors
Imines (Schiff bases) are one of the most promising classes of compounds for the synthesis of nitrogen-containing molecules such as amino sugars, amino acids, and β -lactams. (79-82) In spite of efforts to employ imines for the preparation of these valuable natural products, (83-85) the low reactivity of imines compared to the corresponding carbonyl compounds and side reactions, (86) such as oligomerization or abstraction of the α -proton, are still problems in attempts to use imines as electrophiles for carbon–carbon bondforming reactions.

Tin(II) enolates of thioesters, formed in situ from tin(II) 2-methyl-2-propanethiolate and ketenes, react with imines in the presence of tin(II) triflate to give β -amino thioesters with high *anti* selectivity (Eq. 39). In the absence of

(39)

(55-89%) *anti:syn* = 81:19 - 96:4
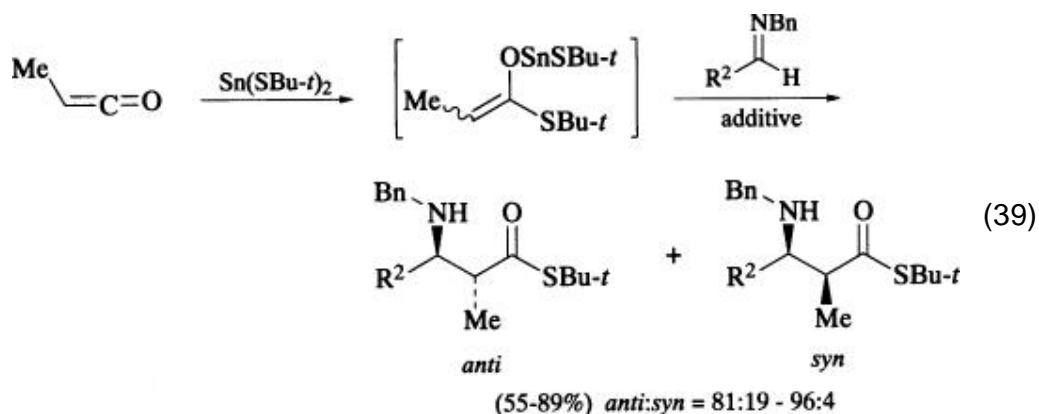
tin(II) triflate, this reaction is usually sluggish. Carbapenem antibiotic PS-5 is formally synthesized by this reaction (Eq. 40). (87)

I + II (60%) *anti:syn* = 88:12

(40)

(97%)   (84%)

known

PS-5
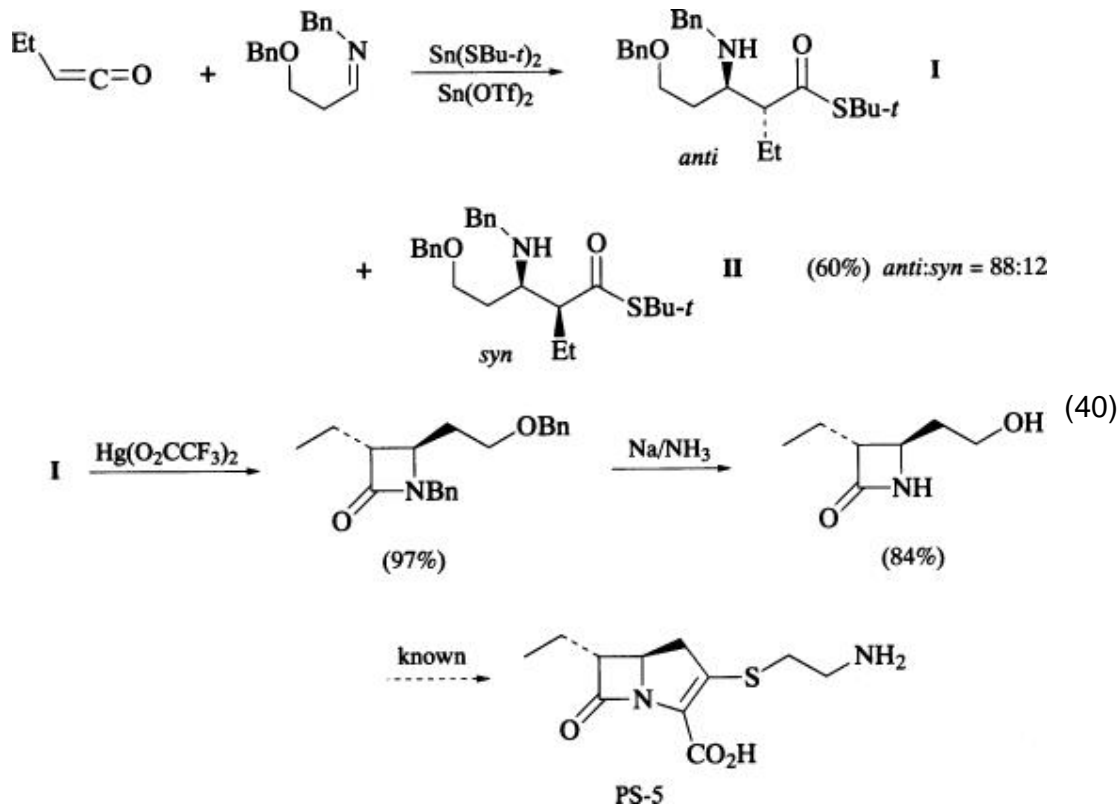
Tin(II) enolates of thioesters, generated from lithium enolates and tin(II) chloride, react smoothly with α -iminoesters to afford the corresponding β -amino thioesters in good yields with high diastereoselectivity. However, these enolates are less reactive than those prepared from lithium enolates and tin(II) triflate. (44)

The type of metal enolate has a dramatic effect on the addition to α -iminoesters. No adduct is obtained with lithium and magnesium enolates, probably because of decomposition of the α -iminoester under the strong basic conditions. Titanium and aluminum enolates react with α -iminoesters to give adducts in rather low yields. Tin(II) enolates afford *syn* isomers of β -amino thioesters in good yields with high stereoselectivity, while preferential formation of *anti* isomers is observed with titanium enolates. The best yield and very high *syn* stereoselectivity are achieved with the tin(II) enolate prepared from a lithium enolate and tin(II) chloride (Eq. 41).

(41)
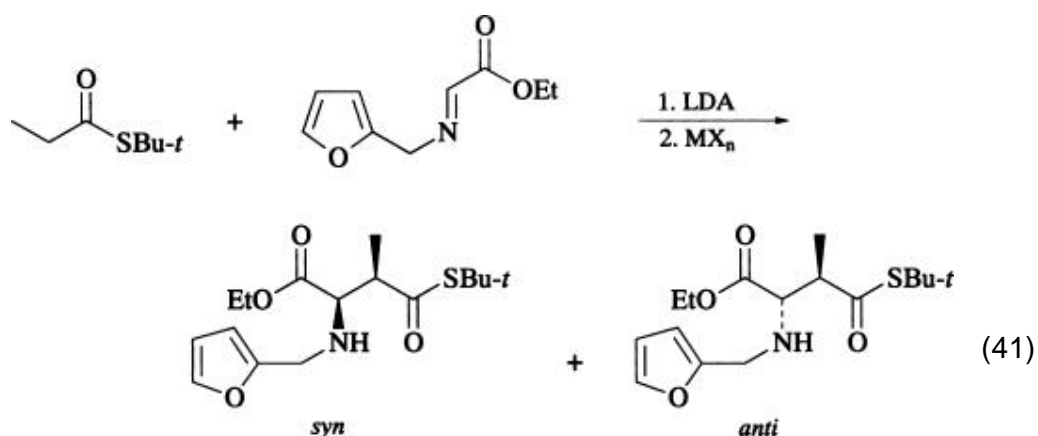
MX_n	Yield (%)	syn:anti
Li	(0)	—
$MgCl_2$	(0)	—
$TiCl_2(OPr\text{-}i)_2$	(30)	29:71
Et_2AlCl	(25)	50:50
$SnCl_2$	(72)	95:5
$Sn(OTf)_2$	(60)	80:20

2.2.1.1.3. Other Electrophiles as Acceptors

Tin(II) enolates formed from ketones and tin(II) triflate in the presence of *N*-ethylpiperidine react with dithioacetals in the presence of triphenylmethyl tetrafluoroborate (trityl tetrafluoroborate, $TrBF_4$) to afford γ -ketosulfides in good yields (Eq. 42). (88)

(42)
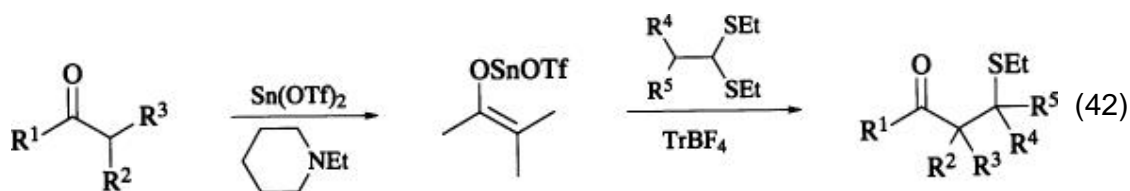
The addition of organometallic reagents to a quinone often affords complicated products because of undesirable side reactions. (89-91) For example, when Grignard reagents are employed, electron transfer from the anionic species to the quinone often predominates and the self-coupling product of the nucleophile is the major product. Also, it is often difficult to achieve selective 1,2 or 1,4 additions and mono- or diadditions of the nucleophile, though several successful results have recently been reported by using alkyllithium reagents, (92-96) trialkylboranes, (97-102) π -allyl Ni complexes, (103, 104) or allylstannanes, (105-109) which give either selective 1,2- or 1,4-addition products. However, addition of metal enolates derived from ketones or carboxylic acid derivatives has rarely been reported, probably because of competing side reactions.

Tin(II) enolates smoothly react with *p*-benzoquinone or its mono-*N*-tosylimino derivative to give 1,2-addition products in good yields. These can be reduced in situ to α -(*p*-hydroxy- or *p*-aminophenyl)carbonyl derivatives by addition of dichloromethylsilane and dimethylaminopyridine (Eq. 43). (110, 111) This is a novel addition-reduction reaction providing a convenient route for the synthesis of α -arylcarbonyl compounds.

(43)
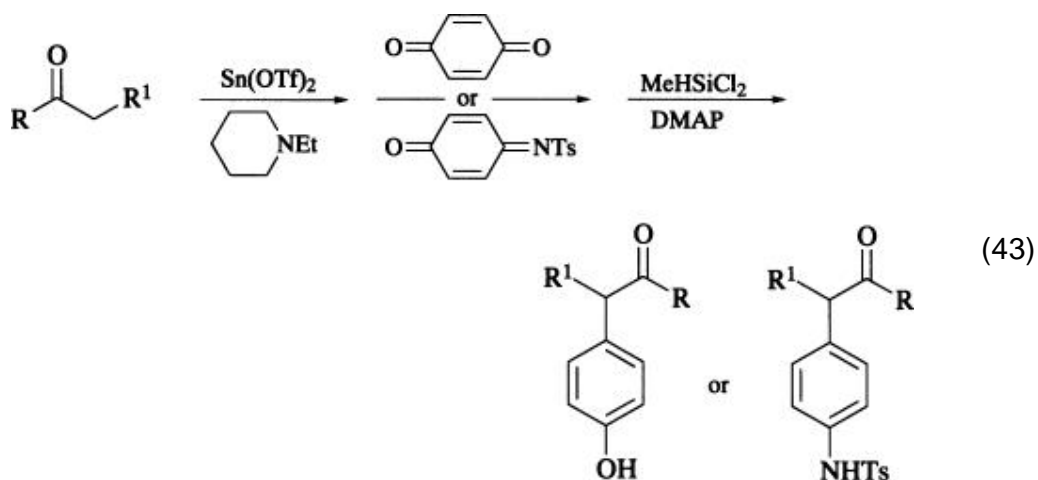
2.2.1.2. Michael Reactions

The Michael reaction is one of the most fundamental carbon–carbon bond forming reactions and it is widely employed in organic synthesis. (112-114) The reaction in which metal enolates behave as nucleophiles is of particular interest with great potential as a versatile method for the stereoselective synthesis of both acyclic and cyclic systems. Fruitful results have been reported in the Michael reaction of silyl enol ethers with α , β -unsaturated

carbonyl compounds by use of titanium tetrachloride, (115-119) trityl salts, (120-124) and other additives. (125-131) In the reaction between other metal enolates and α , β -unsaturated carbonyl compounds, however, the problems of competitive 1,2 addition along with some polymerization of enones limit the application of metal enolate nucleophiles in the Michael reaction. (132-152)

Though tin(II) enolates do not react with α , β -unsaturated ketones in the absence of an additive at –78°, the corresponding Michael adducts are obtained in good yields by using an equimolar amount of chlorotrimethylsilane as an activator (Eq. 44). (111, 153) Other silicon compounds, such as chlorodimethylsilane, dichlorodimethylsilane, and trimethylsilyl triflate, are also effective.

(44)

(56-85%) *anti:syn* = 95:5 - 8:92
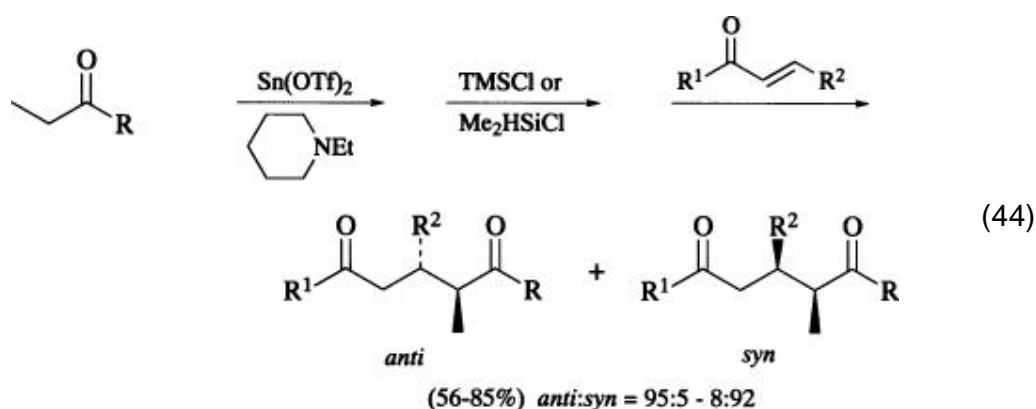
The tin(II) enolates of cyclic ketones react with β -nitrostyrene to afford 4-nitroketones with unprecedented *anti* selectivity (Eq. 45). (154)

(45)

(64-82%) *anti:syn* = 62:38 - >93:7
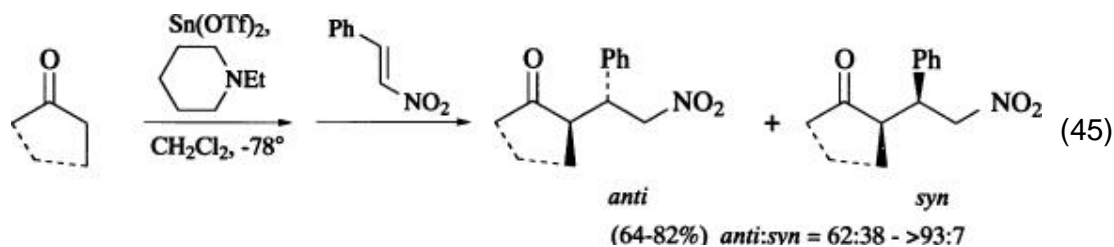
Tin(II) dienolates react exclusively at the γ carbon of acyclic α , β -unsaturated ketones in the Michael sense (Eq. 46). (41) It has been well established that enolate

(46)
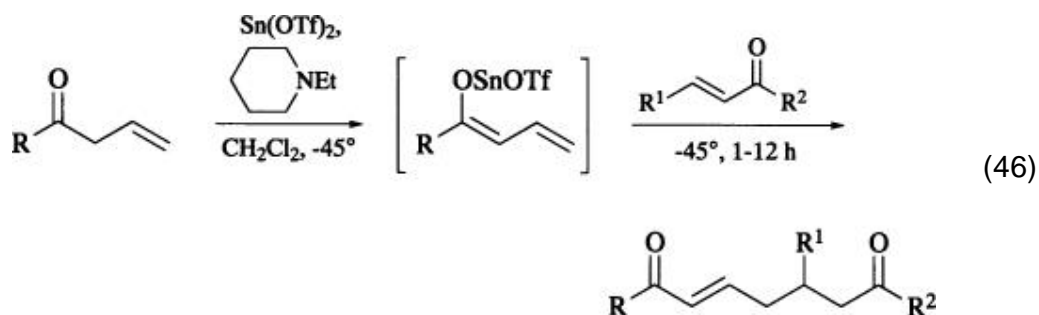
anions, notably lithium enolates of α , β -unsaturated carbonyl compounds, react predominantly at the α carbon. A series of silicon-directedγ -substitution reactions with a variety of electrophiles in the presence of a Lewis acid catalyst has been reported. (155-162)

In such reactions of dienolates, either acyclic 1,7-diketones or 2-cyclohexenol derivatives can be obtained in moderate to excellent yields by appropriate choice of reaction parameters. In the latter case, only a single cyclohexanol adduct is formed (Eq. 47). (41)

(47)
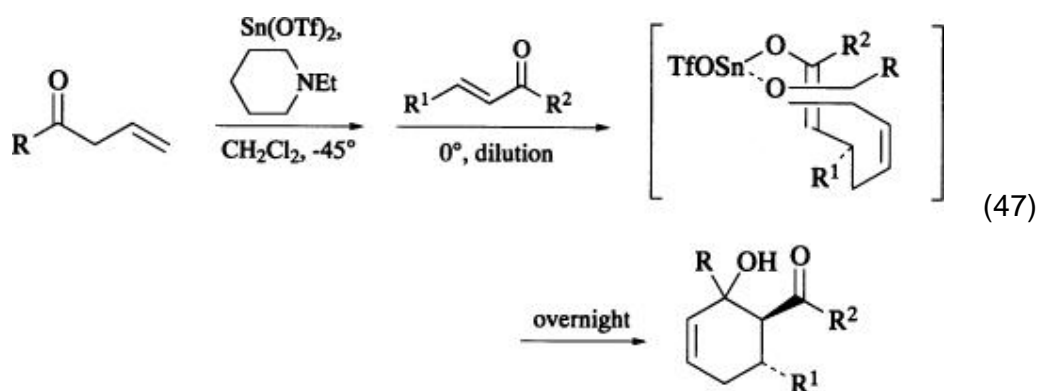
2.3. Asymmetric Reactions
2.3.1.1. Enantioselective Aldol Reactions
Divalent tin has vacant *d* orbitals to which amines, especially diamines, can easily coordinate. (163) Using this property of tin(II), a highly enantioselective cross-aldol reaction between ketones and aldehydes is accomplished by using a chiral diamine derived from (*S*)-proline as a ligand to a tin(II) enolate (Eq. 48). (164) Thus the tin(II) enolate formed from propiophenone and tin(II) triflate in the presence of *N*-ethylpiperidine is treated with diamine **6** and then with benzaldehyde at –78° to give the cross-aldol product in 65% yield with an optical purity of 60%. The optical purity can be improved to 65% by conducting the reaction at –95°. Screening of reaction conditions reveals that the chiral diamine forms a 1:1 complex with the tin(II) enolate. The structure of the chiral

diamine strongly influences the enantioselectivity, and the aldol product is obtained in up to 80% ee when chiral diamine **7** is employed as a ligand.

In the cross-aldol reaction of aromatic ketones with aromatic aldehydes, good to high ee is achieved by employing diamine **7** as a chiral ligand. With aliphatic aldehydes, proper choice of the chiral ligand affords the cross-aldol products in high optical purity. (36)

The enantioselectivity achievable in the cross-aldol reaction of aliphatic ketones with aldehydes is rather low (up to 50% ee) when chiral diamine **6** or **10** is employed. However, the tridentate ligand **11** is most effective for this reaction, and 70–80% ee is realized in the reaction of aldehydes with the tin(II) enolate of *tert*-butyl ethyl ketone. (36)

The asymmetric aldol reaction of 3-acetylthiazolidine-2-thione with achiral aldehydes is also successfully carried out via tin(II) enolates by using chiral diamine **7** as a ligand, (165) and the aldol-type adducts are obtained in high yields (Eq. 49). The enantioselectivities obtained in this reaction are high because the tin(II) enolate of 3-acetylthiazolidine-2-thione is almost completely fixed by coordination of the thiazolidine–thione part to tin(II). As described in the previous

Chiral diamines

$$
R^1\text{-C(=O)-CH}_2\text{CH}_3 \xrightarrow[\text{CH}_2\text{Cl}_2,\ -78°]{\text{Sn(OTf)}_2,\ \text{NEt}} \xrightarrow{\text{chiral diamine}} \xrightarrow{R^2\text{CHO}} R^1\text{-C(=O)-CH(CH}_3)\text{-CH(OH)-}R^2
$$
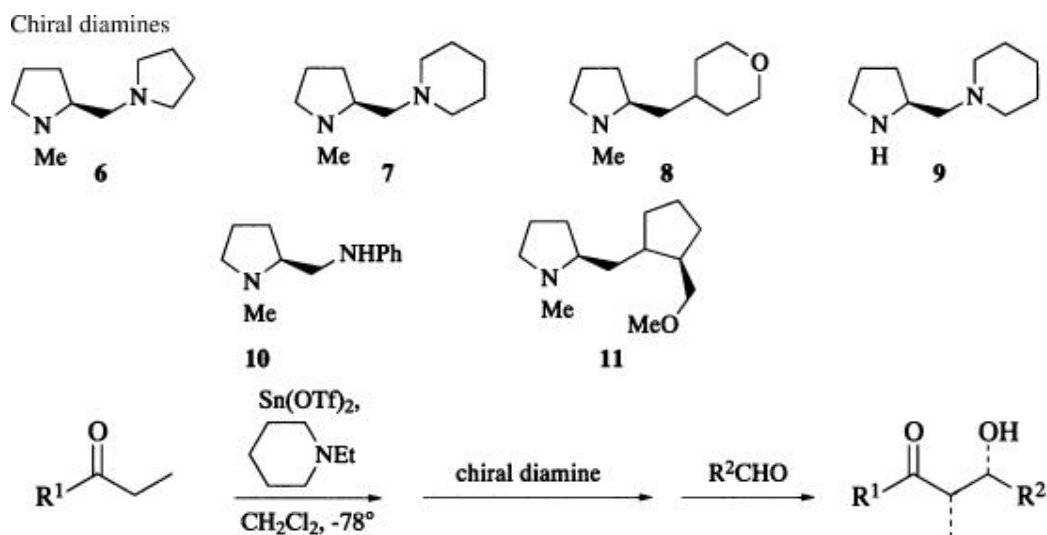
(48)

R^1	R^2	Chiral diamine	R^{2}CHO added at	Yield (%)	syn:anti	ee (%) of syn
Ph	Ph	6	-78°	(66)	6:1	60
Ph	Ph	6 (0.5 eq)	-78°	(74)	6:1	30
Ph	Ph	6 (2.0 eq)	-78°	(61)	6:1	60
Ph	Ph	6	-95°	(66)	6:1	65
Ph	Ph	6	-95° to 25°	(75)	1:2	0
Ph	Ph	6	-95°	(66)	6:1	65
Ph	Ph	7	-95°	(74)	6:1	80
Ph	Ph	8	-95°	(56)	6:1	50
Ph	Ph	9	-95°	(72)	6:1	75
Ph	Ph	10	-95°	(66)	20:1	20
Ph	Ph	7	-78°	(66)	6:1	60
Ph	Ph	7 (0.5 eq)	-78°	(74)	6:1	30
Ph	Ph	7 (2.0 eq)	-78°	(61)	6:1	60
Ph	Ph	7	-95°	(66)	6:1	65
Ph	Ph	7	-95° to rt	(75)	1:2	0
Ph	i-Pr	10	-95°	(69)	>20:1	75
Ph	t-Bu	7	-95°	(57)	100:0	90
t-Bu	R	11	-78°	(—)	—	70-80

(49)

~90% ee
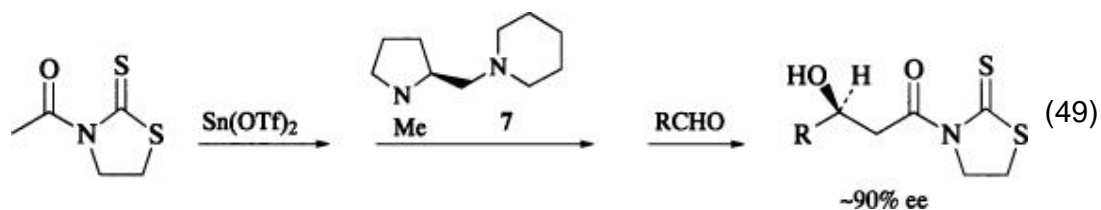
section, the adduct is easily converted to a β-hydroxy aldehyde or β-hydroxy carboxylic acid derivative, and thus this method is useful for the preparation of a variety of optically active compounds.

A highly enantioselective synthesis of 2-substituted malates is achieved by application of this reaction. The tin(II) enolate of 3-acetylthiazolidine-2-thione reacts with α -ketoesters to afford the aldol-type products generally in greater than 95% ee (Eq. 50). (166)

(50)

>95% ee
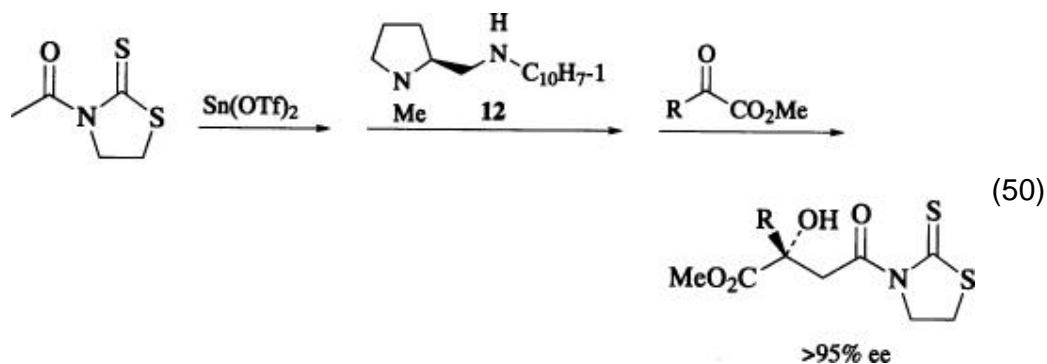
In the reaction of 3-(2-benzyloxyacetyl)thiazolidine-2-thione with aldehydes, up to 94% ee is observed in the *anti* adduct by employing chiral diamine **7** (Eq. 51). (73)

(51)

87-94% ee
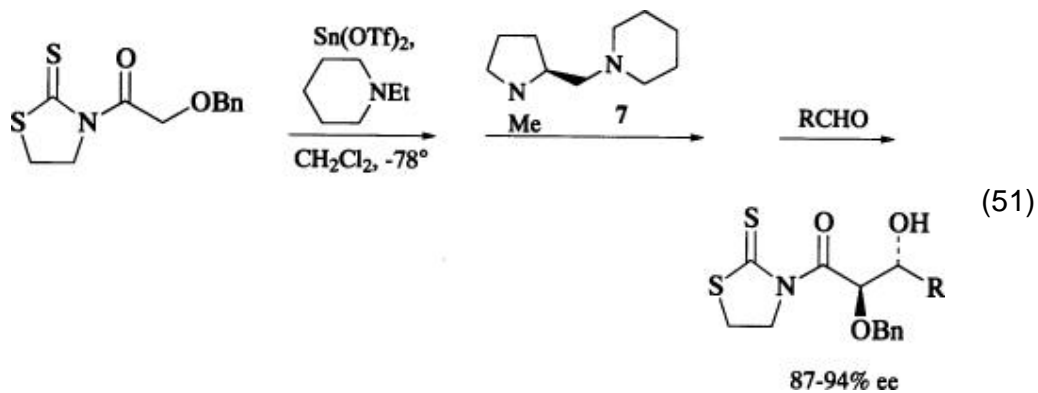
2.3.1.2. Enantioselective Michael Reactions
The asymmetric Michael reaction of tin(II) enolates is achieved in moderate to high enantioselectivities by using the coordination of chiral diamine ligands to the intermediate tin(II) enolate. Trimethylsilyl triflate (TMSOTf) is used as an activator of α , β -unsaturated ketones. The reactions do not proceed in the absence of TMSOTf. The tin(II) enolate of 3-propanoyl-1,3-oxazolidin-2-one or methyl dithioacetate reacts with benzalacetone in the presence of a chiral diamine and TMSOTf to give the Michael adduct in good yield with good enantioselectivity (Eq. 52). (78, 167)

The catalytic asymmetric Michael reaction of tin(II) enethiolates forms 5-oxodithioesters in high yields with moderate to good enantioselectivities by employing catalytic amounts of tin(II) triflate and chiral diamine **12** (Eq. 53). (78, 168) The catalytic cycle of Eq. 54 is postulated.

(52)

(44-82%) 15-70% ee

(53)
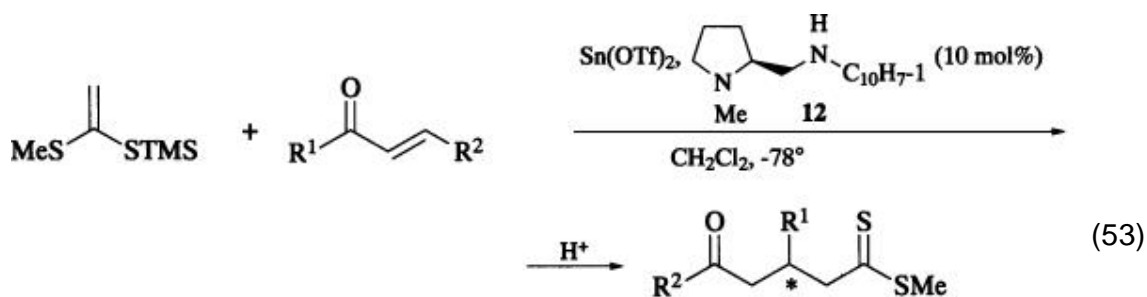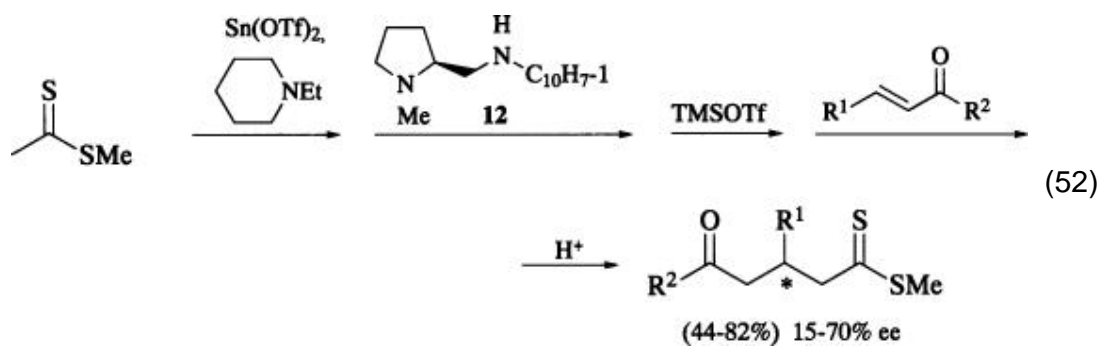
R¹	R²	Yield (%)	%ee	%ee (1 eq of **12**)
Me	Ph	(80)	70	70
Me	1-furyl	(82)	60	60
Ph	Ph	(79)	40	40

$$(54)$$
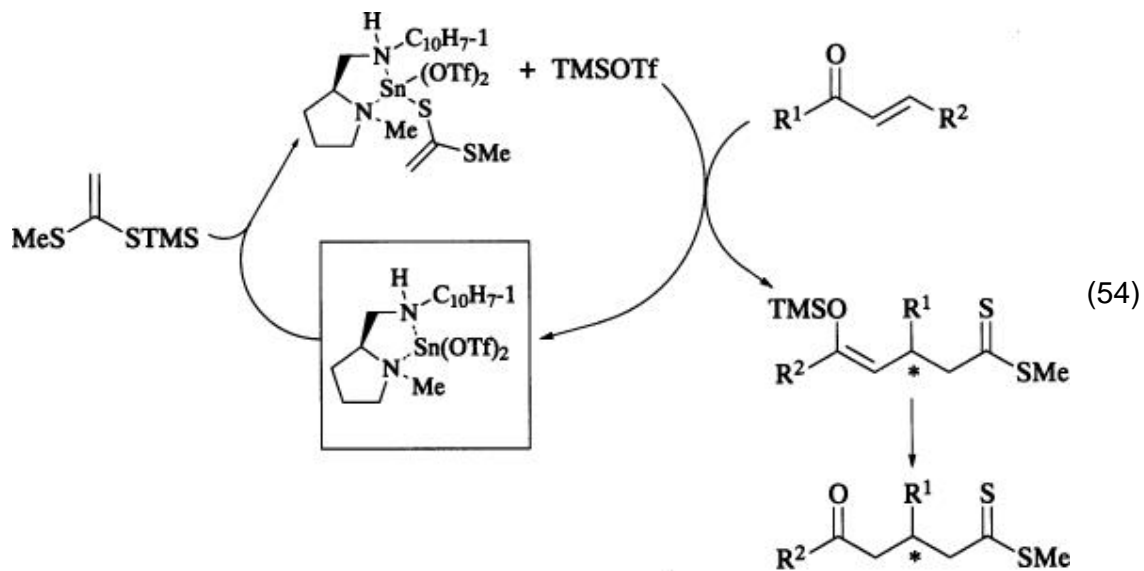
2.3.1.3. Asymmetric Sulfenylation

In the presence of a chiral diamine, the reaction of tin(II) enolates of ketones or 3-acyl-2-oxazolidones with thiosulfonates proceeds smoothly to give β-keto sulfides in high enantioselectivities. These products can be easily converted to optically active epoxides or allylic alcohols (Eq. 55). (169)

$$(55)$$
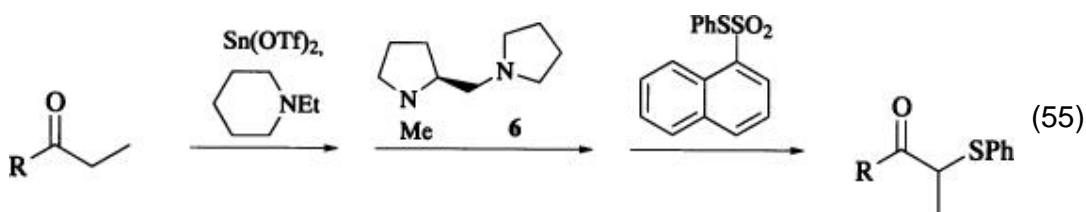
2.3.2. Diastereoselective Reactions

2.3.2.1.1. Aldol Reaction of Chiral Aldehydes or Imines

There are several examples of the reaction of tin(II) enolates with 2,3-O-isopropylidene-D-glyceraldehyde, 4-O-benzyl-2,3-O-isopropylidene-L-threose, their derivatives. In most cases, selectivities are good to high, and they are clearly explained by the Felkin–Anh model. (170-172) For example, 4-O-benzyl-2,3-O-isopropylidene-L-threose reacts with the tin(II) enolate prepared from ethyl bromoacetate and metallic tin to give predominantly the *anti* adduct (Eq. 56). This selectivity is reasonably explained

$$(58\%) \quad syn:anti = 13:87$$
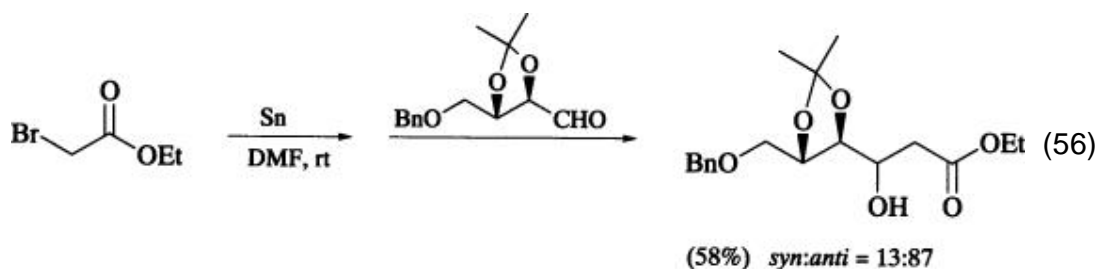
by the model shown in Fig. 1; the - CH$_2$OBn group, being away from the reaction site, has little effect on the reaction path. (173)

Figure 1.
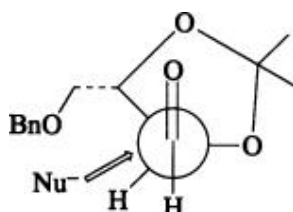
This reaction provides a convenient method for the preparation of monosaccharides. Some biologically important sugars, such as methyl D-glucosaminate (75) and 2-amino-2-deoxy-D-arabinitol (64) are synthesized by this reaction (Eqs. 57 and 58).

(57)

D-glucosaminate

(58)

2-amino-2-deoxy-D-arabinitol pentaacetate
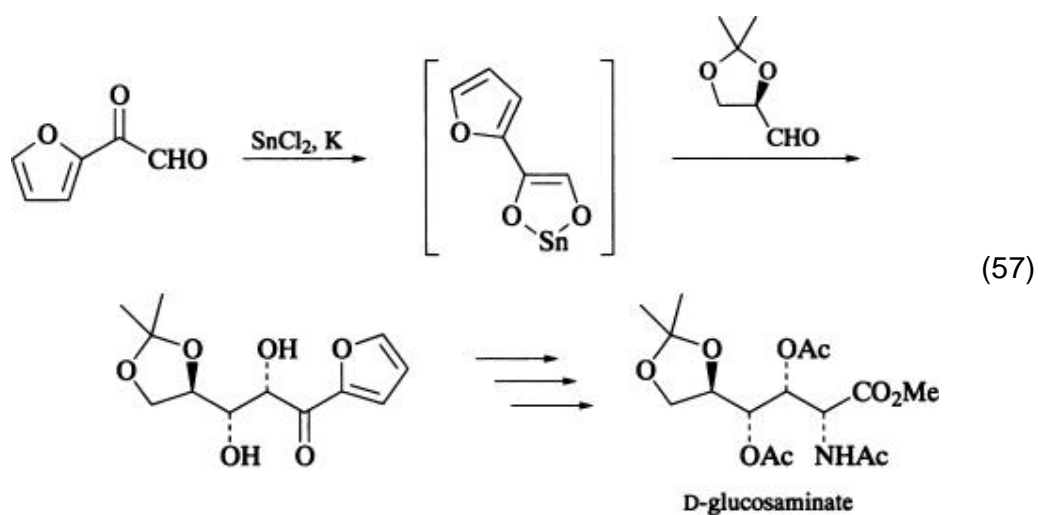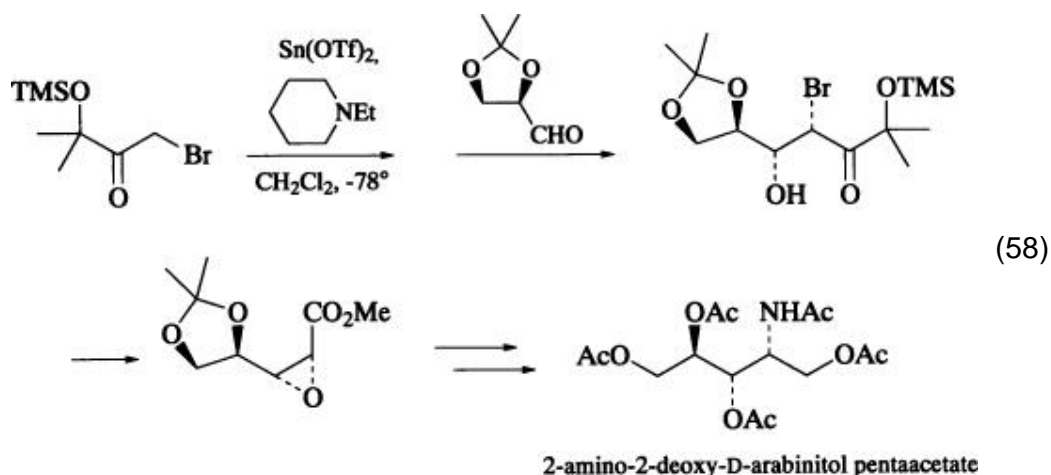
The asymmetric addition of tin(II) enolates derived from thioesters to α
-iminoesters having a chiral auxiliary on the nitrogen atom proceeds smoothly
to afford *syn*- β -amino acid derivatives, which are in turn converted to optically
active *cis*-substituted β -lactams (Eq. 59). (174)

2.3.2.1.2. Aldol Reactions of Chiral Tin(II) Enolates
Highly efficient internal asymmetric induction is achieved in the aldol reaction
of tin(II) enolates generated from 3-amino-substituted
pentanoylthiazolidine-2-thiones. This reaction is successfully applied to the
formal total synthesis of thienamycin (Eq. 60). (175)

(78-85%) 67:33 - 95:5

(59)

(60)
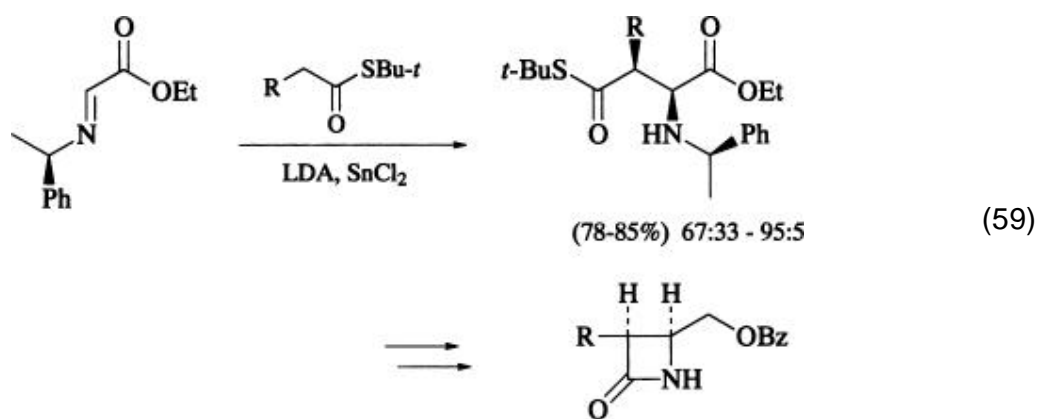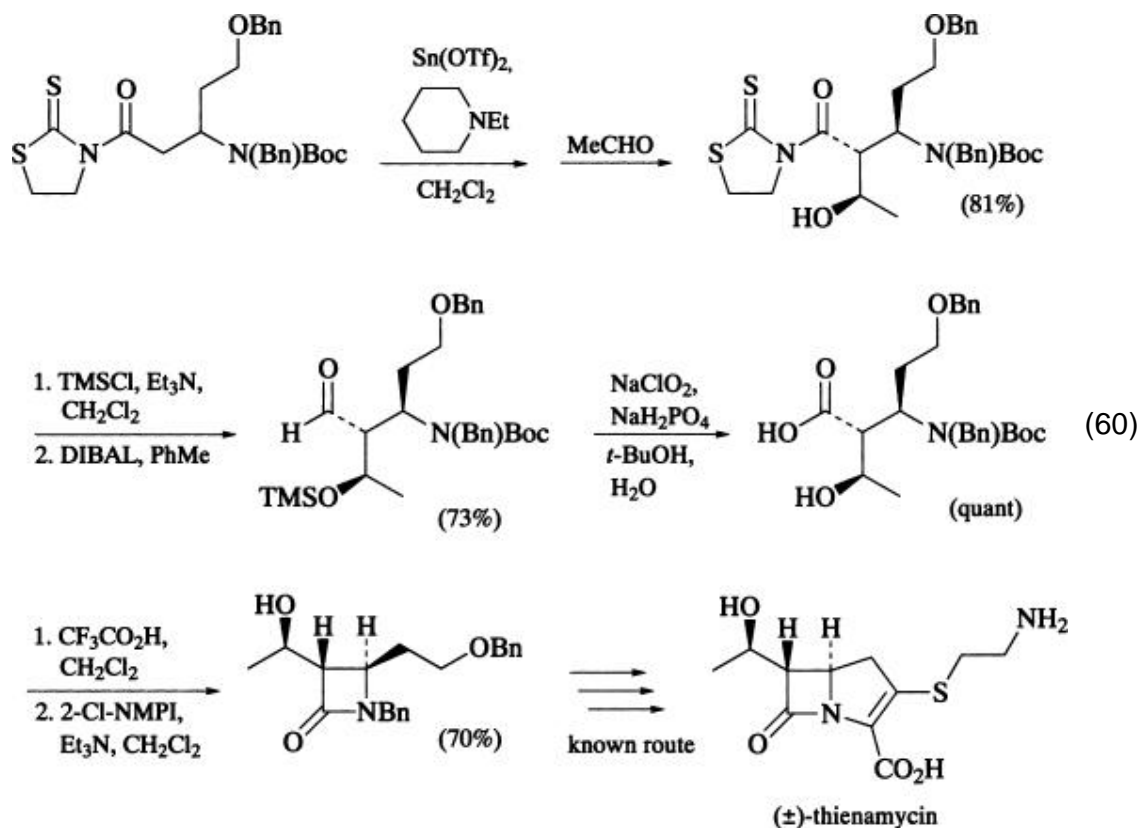
Several examples of the reaction of tin(II) enolates of chiral amides or imides with aldehydes are reported. Though these reactions require a tedious procedure for the attachment and removal of chiral auxiliaries, they are synthetically useful because diastereoselectivities are generally high and chiral sources can be recovered.

Tin(II) enolates of chiral 3-acetyloxazolidine-2-thiones react stereoselectively with aldehydes to give the corresponding adducts in good yields (Eq. 61). High diastereoselectivities are explained by a cyclic transition state which involves

(61)
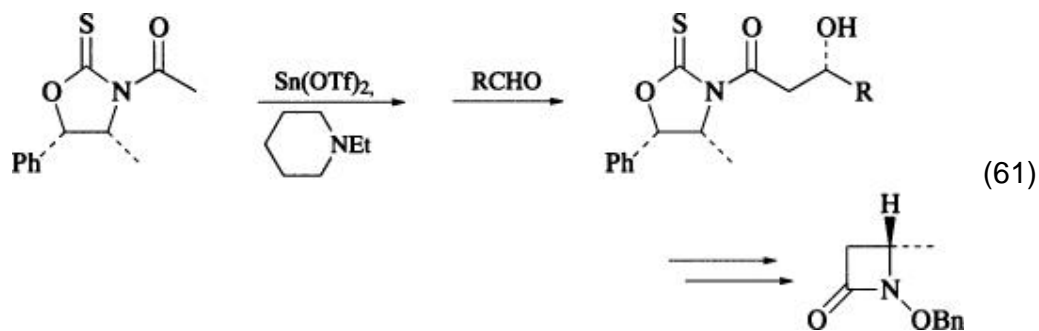
chelation of the thione portion of the chiral auxiliary as shown in Fig. 2. (38) This transition state contrasts remarkably with that of the aldol reaction of boron enolates of chiral 3-acyloxazolidine-2-ones with aldehydes (176) (see the next section). This reaction is applied to the synthesis of a chiral azetidinone (Eq. 61). (38)

Figure 2.
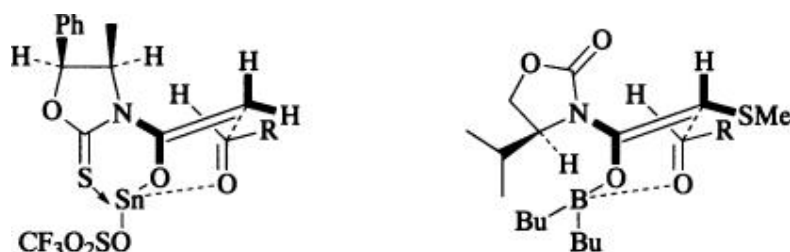
When 3-acylthiazolidine-2-thiones are employed as enolate components instead of 3-acyloxazolidine-2-thiones, superior diastereoselectivities are obtained. Diastereocontrolled aldol reactions between tin(II) enolates, prepared from 3-acetylthiazolidine-2-thiones, tin(II) triflate, and *N*-ethylpiperidine, and α , β -unsaturated aldehydes are successfully carried out to give the corresponding adducts in good yields (Eq. 62). (55) This reaction is applied to the synthesis of the chiral Geissman–Waiss lactones **13** (Eq. 63). (177)

(62)

(63)

13
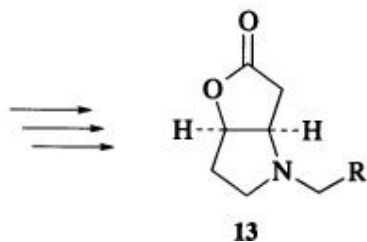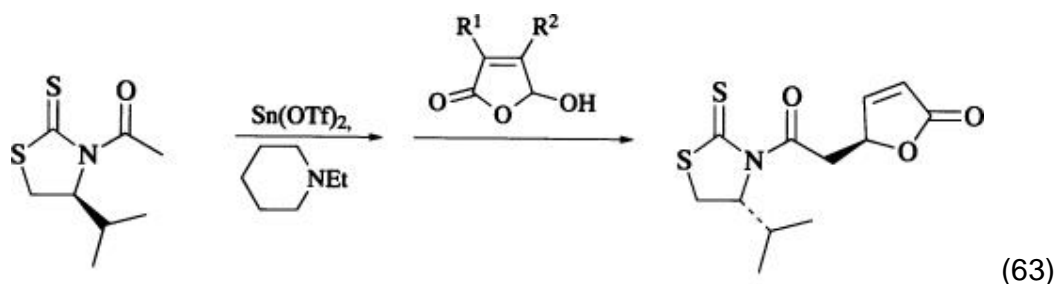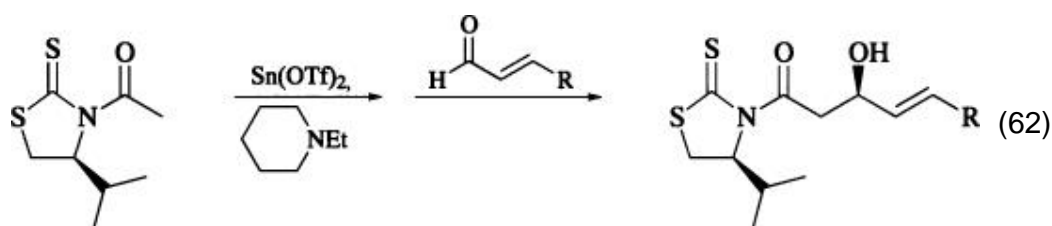
The aldol reaction of tin(II) enolates of chiral 3-acyloxazolidine-1-ones with aldehydes gives lower diastereoselectivities than those obtained in the reactions discussed above. Benzyl cis- α , β -epoxycarboxylates are prepared by a modified Darzens procedure by using the aldol reaction of chiral α -haloimidates with aldehydes (Eq. 64). (39) The selectivities of this reaction are improved when the tin(II)

$$(64)$$
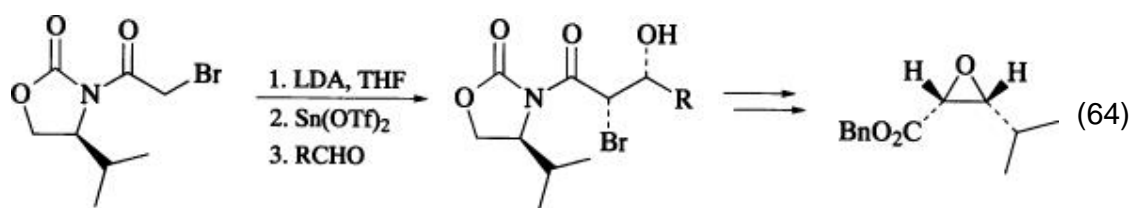
enolates are prepared by the metal exchange reaction of lithium enolates with tin(II) triflate.

Cysteine-derived thiazolidinethiones serve as efficient chiral auxiliaries in tin(II)-mediated aldol reactions (Eq. 65). These chiral auxiliaries are easily removed

$$(65)$$
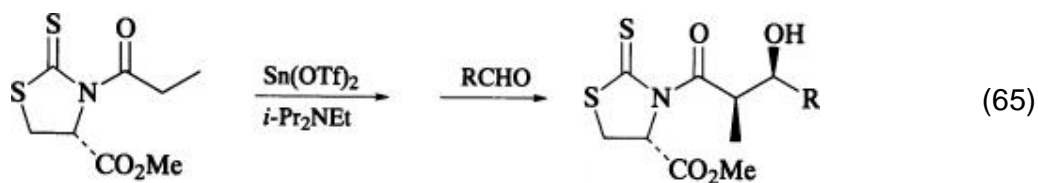
and recovered by methanolysis or hydroxaminolysis. (178) It is remarkable that the diastereofacial preference of the chiral 3-acylthiazolidine-2-thione is opposite to that of 3-acyloxazolidine-2-thiones or 3-acylthiazolidine-2-thiones. The sense of the selectivity in this reaction is the same as that obtained in the reaction of boron enolates, and higher selectivity is observed when using the boron enolate.

A chiral glycine synthon, as its derived tin(II) enolate, undergoes a highly syn diastereoselective aldol reaction with aldehydes to give the corresponding adducts in high yields. The utility of these intermediates is demonstrated by their subsequent transformation to enantiomerically pure N-methyl- β -hydroxy amino acids (Eq. 66). (179)

(66)
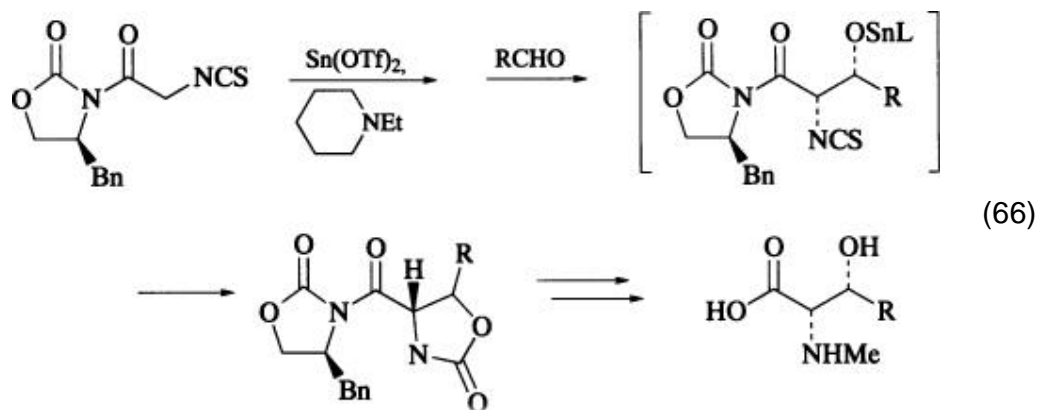
The tin(II) enolate generated by the action of $SnCl_2$– $LiAlH_4$ on an (α-bromoisobutanoyl)oxazolidinone reacts with benzaldehyde or a conjugated (Z)-enal to yield oxazinedione derivatives with excellent diastereoselectivities (Eq. 67). (180) Neooxazolomycin, a novel oxazole polyene lactam–lactone antitumor antibiotic, is synthesized by use of this reaction as one of key steps (Eq. 68). (181)

Tin(II) azaenolates are prepared from chiral 1,3-oxazolidines and react with aldehydes to afford aldol-type adducts in high yields with high diastereoselectivities (Eq. 69). (46, 182)

(67)

(69%) 97:3

(68)

Neooxazolomycin

(69)

R = Me (59-65%)
58-86% ee
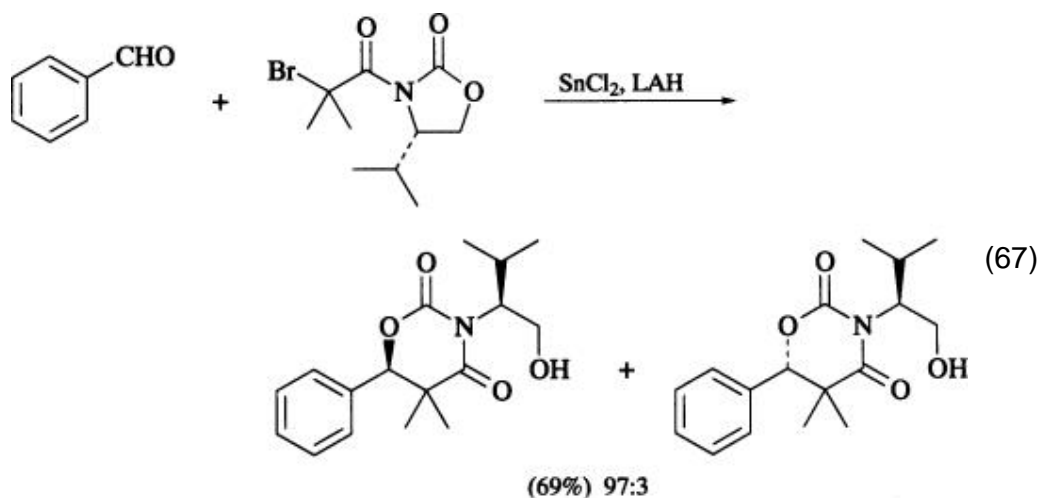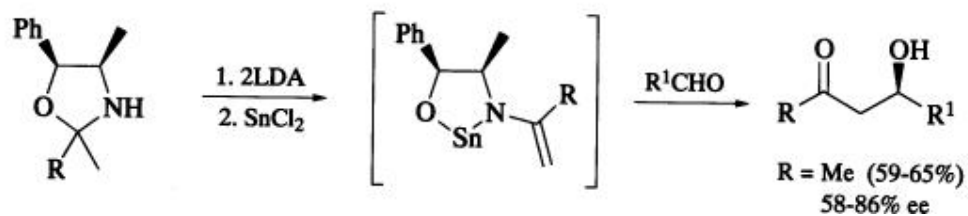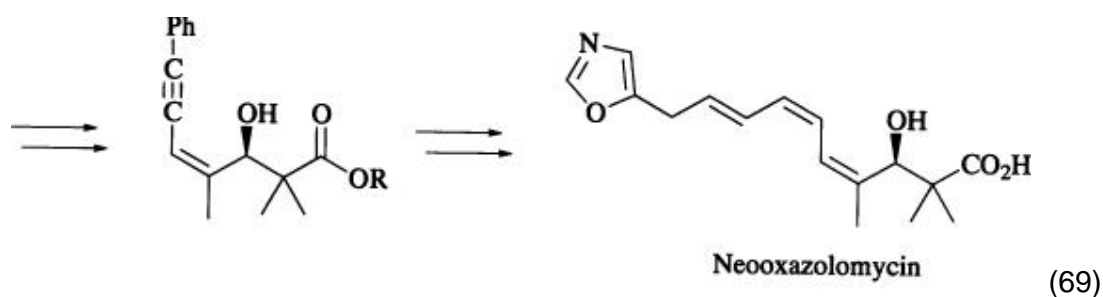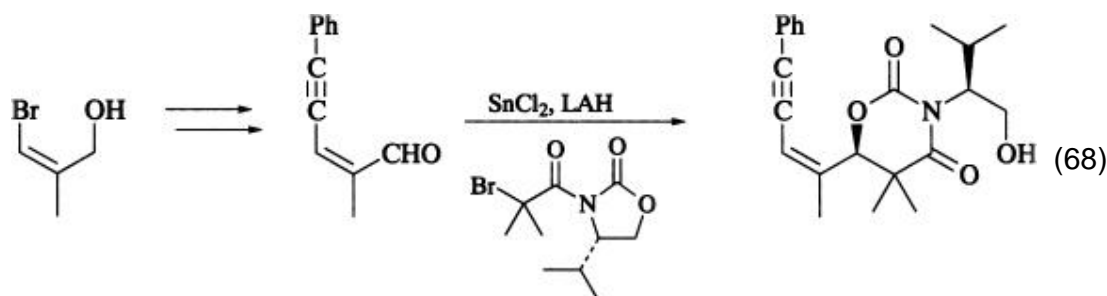
Highly diastereoselective aldol-type alkylation is carried out by employing tin(II) enolates derived from chiral 3-acylthiazolidine-2-thiones and 4-acetoxy-2-azetidinones. These tin(II) enolates also react with optically active 2-azetidinones in a highly stereoselective manner to give the corresponding adducts in high yield (Eq. 70). (183)

(70)
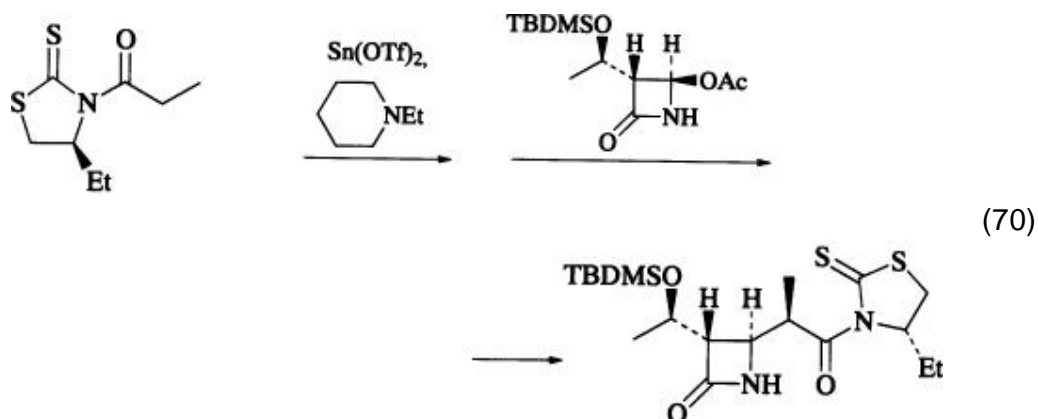
The same level of diastereoselectivity is attained by using the tin(II) enolate of 3-acyloxazolidine-2-one in the presence of zinc bromide as an activator of the azetidinone (Eq. 71). (184) The corresponding boron enolate gives better selectivity in this reaction.

(71)
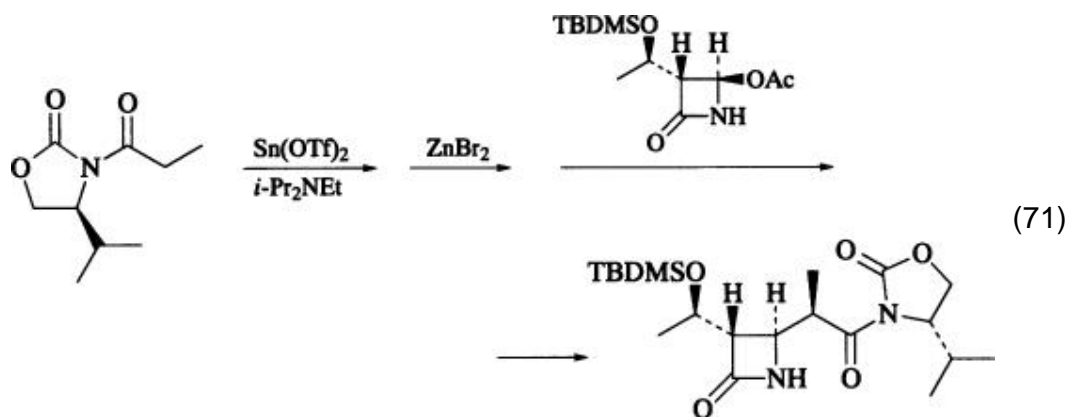
These reactions provide a new approach to the construction of chiral carbapenem precursors. (185-187)

A general method for the enantioselective synthesis of bicyclic alkaloids with a nitrogen atom ring juncture involves the aldol-type alkylation of tin(II) enolates with cyclic acyl imines followed by reductive annulation of the resultant cyclic imines (Eq. 72). (+)-Epilupinine (14) is synthesized by this methodology. (188, 189)

(72)

14
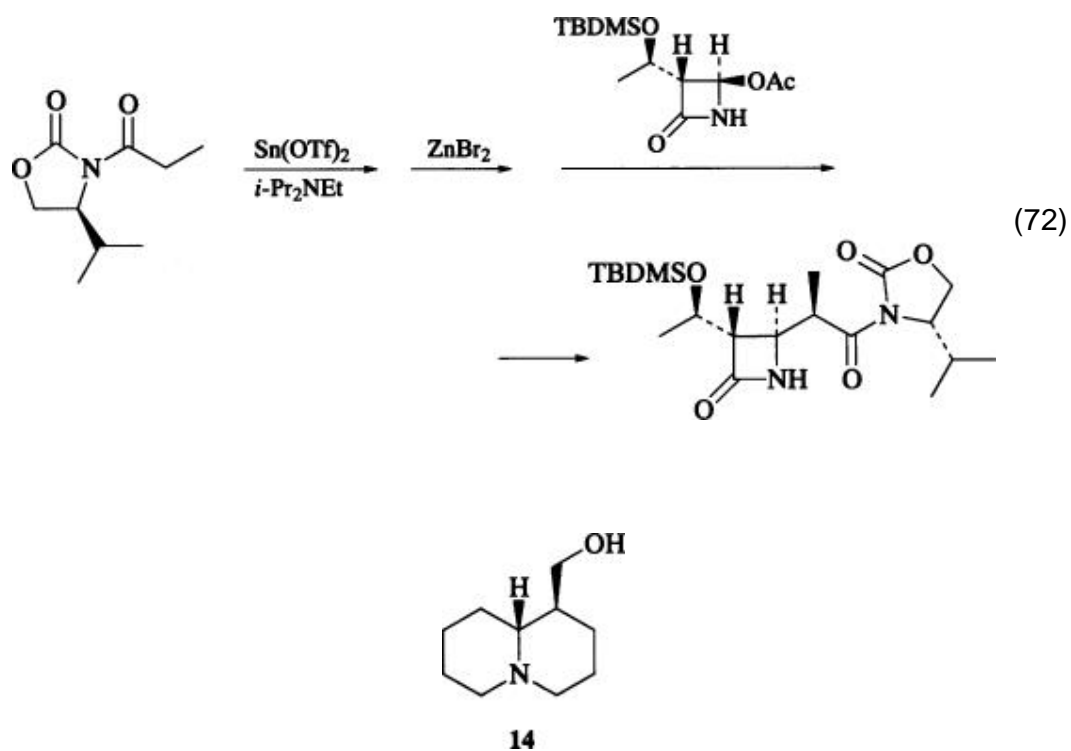
The β -methylcarbapenem key intermediate **15** is prepared by this aldol-type alkylation of the tin(II) enolate generated in situ from the bromoketone and metallic tin with the azetidinone (Eq. 73). (190)

(73)

15
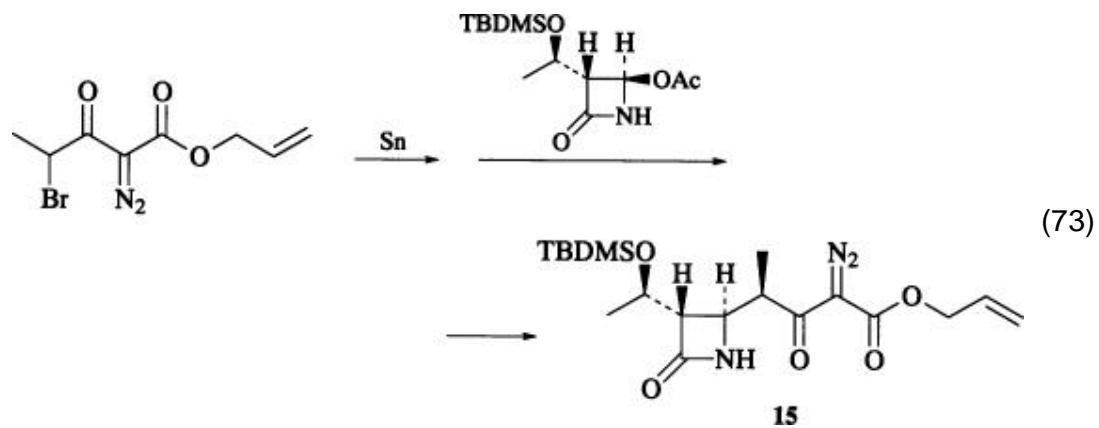
3. Comparison with Other Metal Enolates

Tin(II) enolates are easily prepared under extremely mild conditions compared to other metal enolates. Although lithium enolates are commonly employed, their use is restricted because of their strong basicity. For example, the formation of lithium enolates of β -alkoxy carbonyl compounds fails because β eliminations rapidly follow deprotonations of the α protons under the strongly basic conditions. Enolate formation using the tin(II) triflate method is quite effective in these cases. The tin(II) enolates are smoothly generated from 3-acetylthiazolidine-2-thione with β -alkoxy functionality by treatment with tin(II) triflate in the presence of *N*-ethylpiperidine. These enolates react with aldehydes to afford aldol-type products in high yields (Eq. 74). (74)

(74)
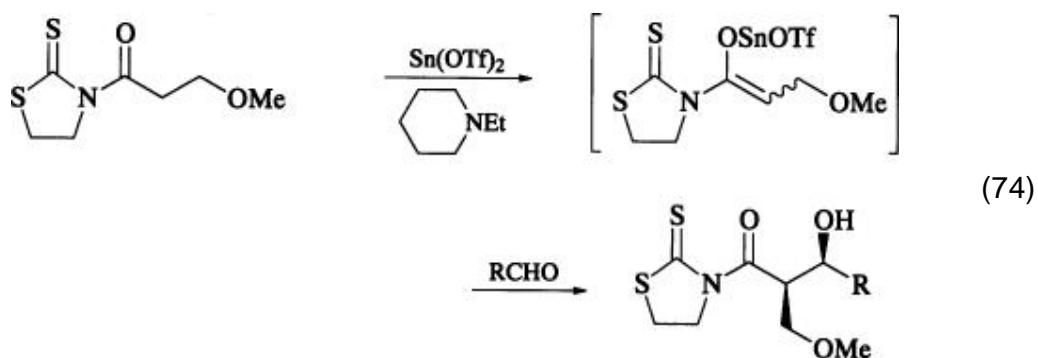
Tin(II) enolates are also generated from 3-(3-aminopropanoyl)thiazolidine-2-thiones and they react smoothly with aldehydes to give aldol-type adducts with high *syn* selectivity. These aldol-type adducts are stereospecifically converted to β -lactam derivatives with hydroxy side chains (Eq. 75). (74, 191)

(75)
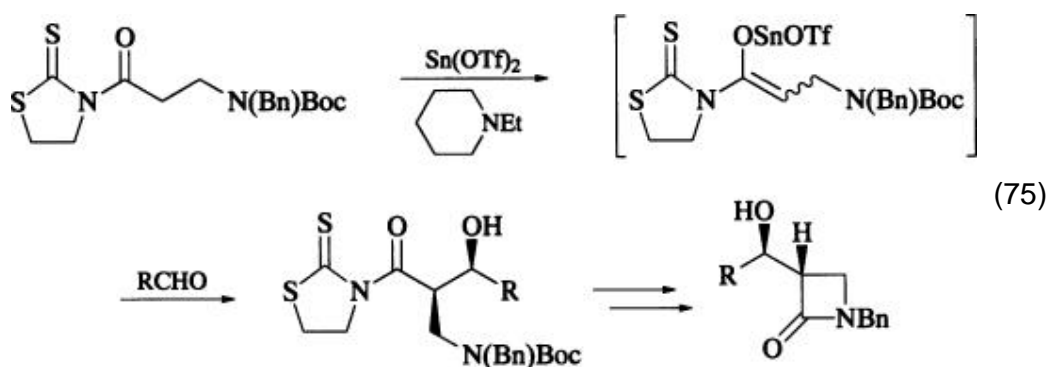
Enolate formation from active esters sometimes gives disappointing results owing to easy elimination of the ester groups to form ketenes. For example, attempts to generate the lithium enolate from 3-acetylthiazolidine-2-thione under standard conditions fail because of ketene formation (Eq. 76). On the other hand,

(76)
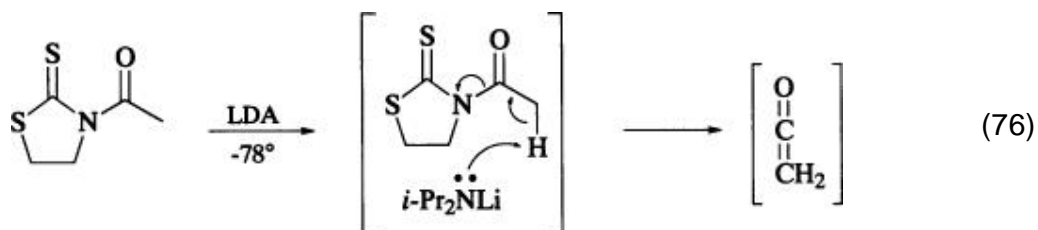
the tin(II) enolates of 3-acylthiazolidine-2-thiones are easily prepared by treatment with tin(II) triflate and *N*-ethylpiperidine and react with electrophiles such as aldehydes, ketones, and α , β -unsaturated carbonyl compounds (Eq. 77). (36, 72)

(77)
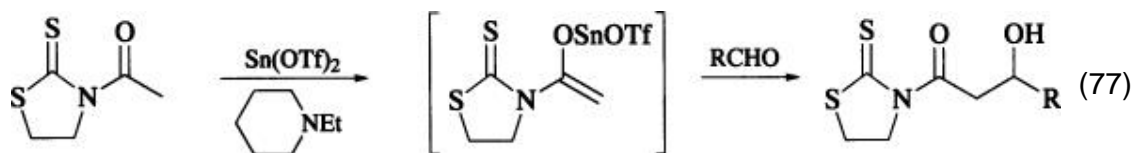
It is interesting that tin(II) and tin(IV) enolates have quite different properties in preparation, reactivity, and selectivity. Tin(IV) enolates sometimes exist as an equilibrium mixture of *C*-stannyl and *O*-stannyl enolates, and their behavior is rather similar to that of silicon enolates.

In the aldol reaction of tin(IV) enolates with aldehydes, the stereoselectivities depend on the reaction temperature, (17, 18, 192, 193) and *anti* aldol adducts predominate at low temperature (Eq. 78). On the other hand, the reaction of tin(II) enolates proceeds with excellent *syn* selectivity at –78° (Eq. 79). (26, 36)

-78°, 20:80
45°, 77:23

(78)

$$\tag{79}$$
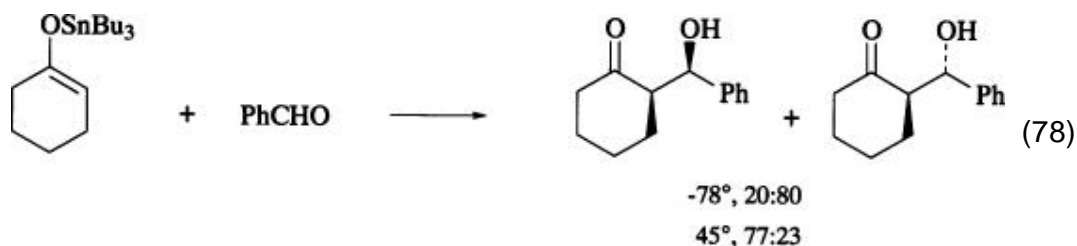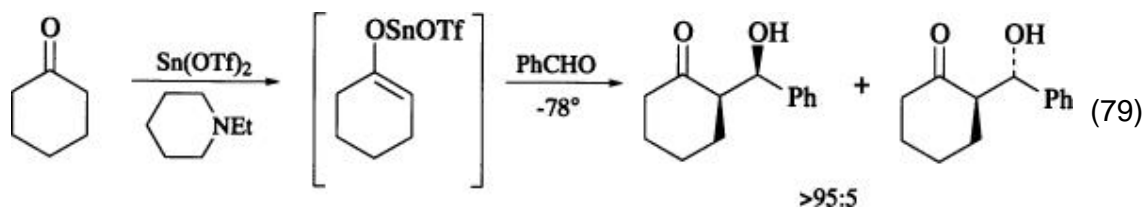
Boron enolates can also be prepared by using dialkylboryl triflate and a tertiary amine (usually Hünig's base) under mild conditions. (53, 54) While tin(II) triflate is a white solid and can be stored for a long time under argon, dibutylboryl triflate, which is the most commonly used dialkylboryl triflate, is a liquid at room temperature and can be distilled. It is usually used as a stock solution in an appropriate solvent (e.g., dichloromethane).

One of the most striking differences between tin(II) and boron enolates is their reactivity toward ketones as acceptors. While the reaction of boron enolates with ketones proceeds sluggishly, tin(II) enolates generated from ketones react smoothly with another ketone to give ketone–ketone cross-coupling adducts in high yields. (52)

The higher reactivity of tin(II) enolates than boron enolates is also observed in the reaction of sterically hindered ketones with aldehydes. The boron enolate generated from the chiral N-isobutyryloxazolidinone reacts with benzaldehyde to give the oxazinedione as a 92:8 diastereomeric mixture in 23% yield. When the lithium enolate from the same oxazolidinone is treated with benzaldehyde, the opposite stereoselection is observed in better yield. On the other hand, the tin(II) enolate generated from α -bromoisobutyryloxazolidinone **16** reacts with benzaldehyde to give oxazinediones **17** and **18** (69%) in a 97:3 ratio (Eq. 80). (180, 181)

Tin(II) and boron enolates generally give better selectivities than other metal enolates. The sense of the selectivities depends strongly on the combination of metals and substrates, and even opposite selectivity is sometimes observed between tin(II) and boron enolates. Thus the tin(II) enolate derived from the 3-acyloxazolidine-2-thione reacts smoothly with aldehydes to give adducts in high

(80)

X	Reagent	Yield (%)	(R,S)/(S,S)
H	Bu₂BOTf, i-Pr₂NEt	(23)	92:8
H	LDA	(64)	13:87
Br	SnCl₂, LiAlH₄	(69)	97:3
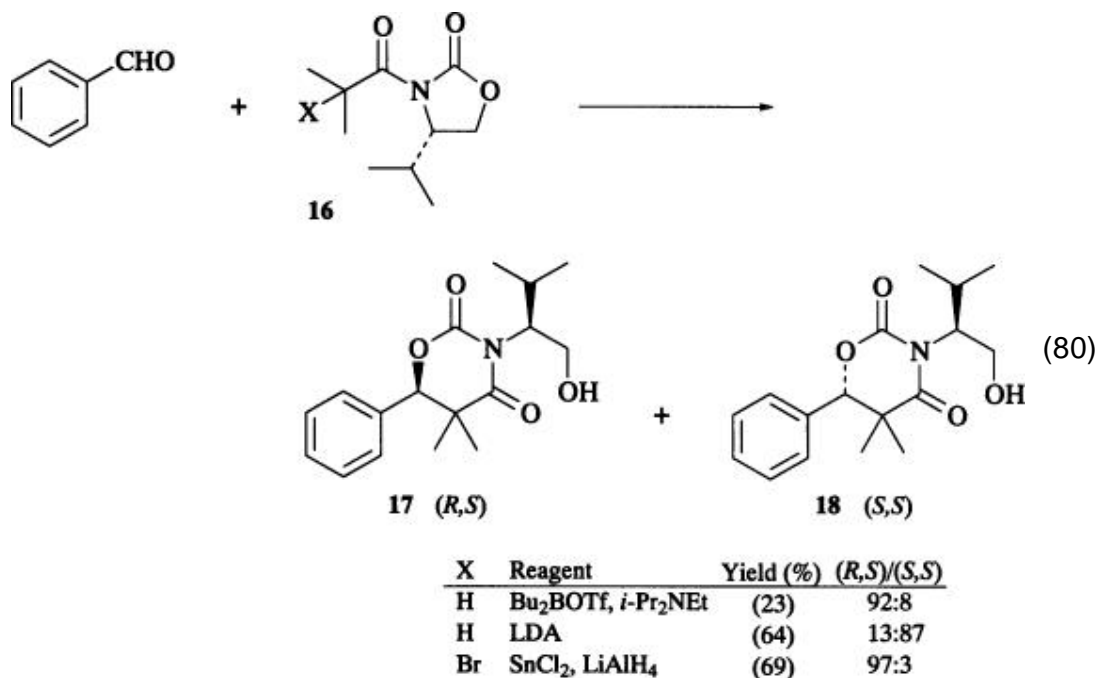
yields (Eq. 81). (38, 176, 177) The high selectivities obtained in these cases are opposite to those obtained in the reaction of the boron enolates derived from 3-acyloxazolidine-2-ones (Eq. 82). (55) These selectivities can be explained by the chelation and nonchelation models (Fig. 3).

(81)

(82)
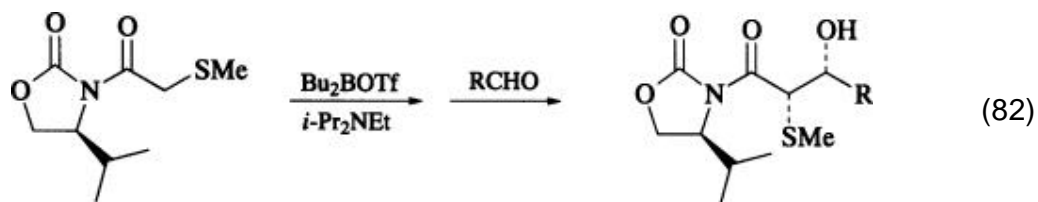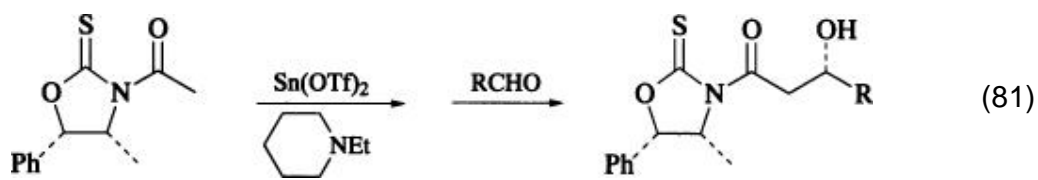
Figure 3.
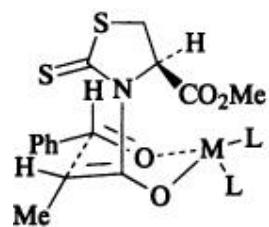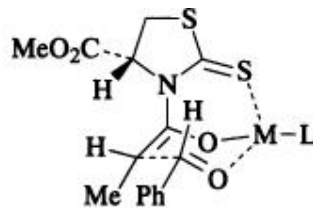
Nonchelation model | Chelation model

On the other hand, similar selectivities are observed with tin(II) and boron enolates in the reaction of cysteine-derived thiazolidinethione enolates with aldehydes (Eq. 83). (178) These selectivities are explained by the nonchelation model.

$$ \tag{83} $$
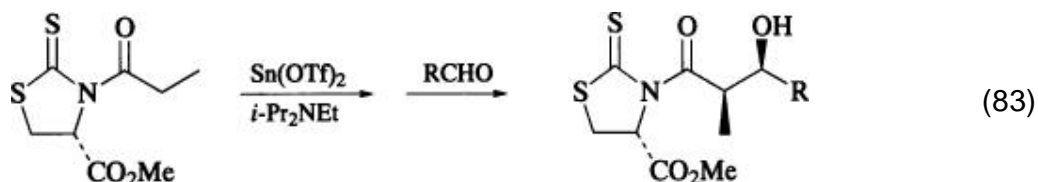
A remarkable contrast in selectivities is observed between tin(II) and titanium(IV) β -keto imide-derived enolates with aldehydes (Eq. 84). (194)

$$ \tag{84} $$
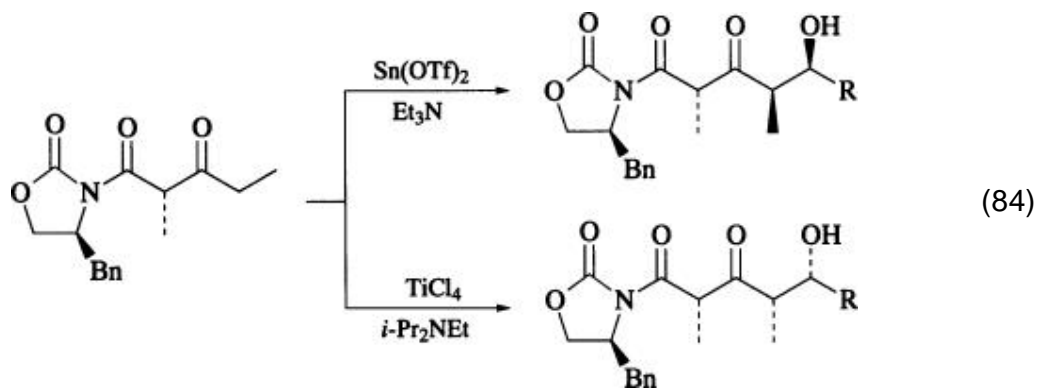
Effects of different metal enolates are observed in the reaction of η ^{5}-CpFe(PPh$_3$)COCOCH$_3$ with benzaldehyde (Eq. 85). (195)

MX	Yield (%)	I:II
Et$_2$AlCl	(81)	3.5:1
TiCl(OPr-i)$_3$	(75)	1:1
MgBr$_2$	(69)	1.1:1
SnCl$_2$	(66)	1:13.3
Sn(OTf)$_2$	(38)	1:1.9
Cp$_2$ZrCl$_2$	(39)	1:4.8

(85)
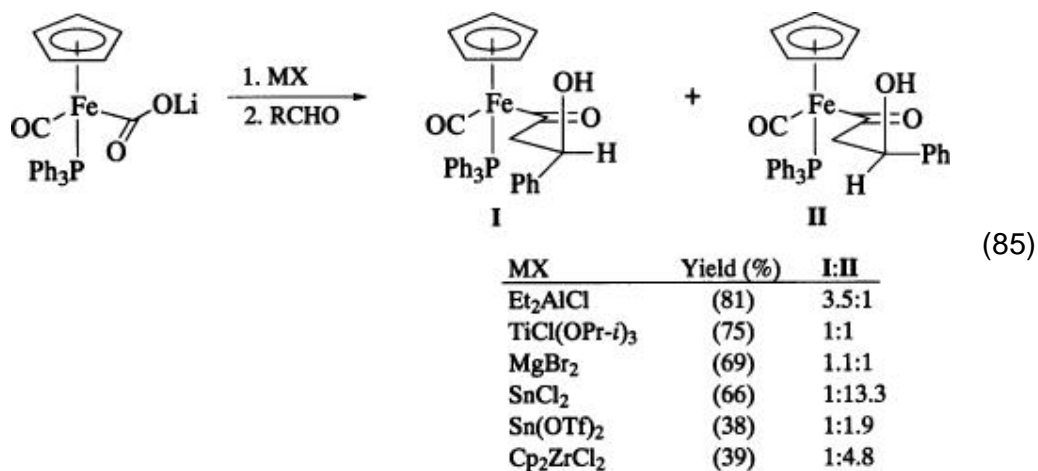
Finally, it is noteworthy that tin(II) enolates can be coordinated by up to three ligands such as amines, thus differing from other metal enolates. Good results are obtained in the asymmetric aldol reaction of tin(II) enolate with chiral diamine ligands derived from (S)-proline. Chiral tin(II) Lewis acids have recently been developed by using these properties of tin(II) metal, and several useful asymmetric reactions have been developed. (196-216)

4. Experimental Procedures

4.1.1.1. Tin Powder
Commercially available tin powder was added to about twice its weight of 10% aqueous sodium hydroxide solution and the mixture was shaken vigorously for 10 minutes. The powder was then washed with water until the washings showed no alkalinity to litmus, rinsed with methanol, and dried in vacuo at 130° for an hour. (42, 217)

4.1.1.2. Tin(II) Chloride
Commercially available anhyd. tin(II) chloride was thoroughly dried before use by heating in vacuo at ca. 120° for an hour. (25)

4.1.1.3. Tin(II) Triflate [Sn(OTf)$_2$] (36)
A modification of the procedure of Aubke et al. (218) was employed. Excess trifluoromethanesulfonic acid (40 g, 26.7 mmol) was added with vigorous stirring to anhydrous SnCl$_2$ (16 g, 8.4 mmol). Gaseous HCl was evolved in an exothermic reaction. To ensure complete reaction, the mixture was heated at 80° for 48 hours. After removal of essentially all volatile products in vacuo, the resultant white solid was washed with dry ether (50 mL × 3) to remove the last traces of acid. After drying in vacuo with warming (ca. 100°) for several hours, the powdery white solid tin(II) triflate was used as such without further purification. Tin(II) triflate is stored under Ar over P$_2$O$_5$. If the activity becomes low, the old tin(II) triflate must be rewashed with ether and dried in vacuo. *Note: Preparation and all handling of Sn(OTf)$_2$ should be carried out under an inert atmosphere in the strict absence of moisture.*
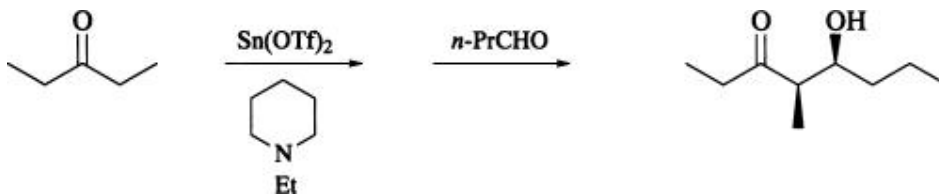
4.1.1.4. syn-5-Hydroxy-4-methyl-3-octanone [Tin(II) Triflate Promoted Aldol Reaction between a Ketone and an Aldehyde] (26, 36)
To a suspension of tin(II) triflate (0.458 g, 1.1 mmol) and *N*-ethylpiperidine (0.138 g, 1.2 mmol) in CH$_2$Cl$_2$ (2 mL) was added dropwise 3-pentanone (0.086 g, 1.0 mmol) in CH$_2$Cl$_2$ (2 mL) at –78° under argon with stirring. At this point, the suspension became a solution. After the mixture was stirred for 30 minutes, *n*-butyraldehyde (0.093 g, 1.3 mmol) in CH$_2$Cl$_2$ (2 mL) was added dropwise at –78°. The mixture was allowed to stand for 2.5 hours, then added to a vigorously stirred pH 7 phosphate buffer– CH$_2$Cl$_2$ mixture at 0°. After

separation of the organic layers, the aqueous layer was extracted with CH_2Cl_2 (three times), then the combined organic layers were dried over Na_2SO_4. After concentration in vacuo, the resultant oil was purified by flash column chromatography (hexane–Et_2O, 4:1) to yield 5-hydroxy-4-methyl-3-octanone (0.136 g, 86%, *syn:anti* = > 91:9). IR (neat) 3450, 1705 cm^{-1}; 60 MHz ^{1}H NMR (CCl_4) δ 0.88–1.56 (m, 13H), 2.4–2.7 (m, 3H), 3.6 (m, 1H), 3.85 (m, 1H); 270 MHz ^{1}H NMR ($CDCl_3$) δ 3.89 (m, *J* = 3 Hz, *syn*) and 3.65 (m, *J* = 7 Hz, *anti*).
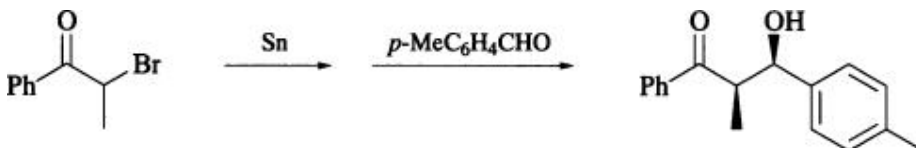
4.1.1.5. syn-3-Hydroxy-2-methyl-1-phenyl-3-(p-tolyl)-1-propanone (Metallic Tin) (42)

A solution of α -bromopropiophenone (212 mg, 1.0 mmol) in CH_2Cl_2 (2 mL) was added dropwise to metallic tin (131 mg, 1.1 mmol) in DMF (2 mL) with stirring under Ar at 0°. The resulting mixture was stirred vigorously at this temperature for 35 minutes. At this point, most of the metallic tin had disappeared and a dark green slurry resulted. The mixture was cooled to –78° and a solution of *p*-tolualdehyde (96 mg, 0.8 mmol) in CH_2Cl_2 (2 mL) was added slowly over 20 minutes. The reaction mixture was stirred for 2 hours at –78°, then pH 7 phosphate buffer was added. After removal of the precipitate by filtration, the organic layer was extracted with ether, and the extract was dried over $MgSO_4$. 3-Hydroxy-2-methyl-1-phenyl-3-(*p*-tolyl)-1-propanone (201 mg, 99%, *syn:anti* = 92:8) was isolated by preparative TLC on silica gel (hexane:Et_2O = 4:1); IR (neat) 3450, 1670, 1450, 1220, 970, 700, 680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.15 (d, 3H), 2.3 (s, 3H), 3.85 (m, 2H), 4.9 (d, trace, *anti*, *J* = 7.5 Hz), 5.1 (d, 1H, *syn*, *J* = 3 Hz), 7.55–7.0 (m, 7H), 8.0–7.75 (m, 2H).
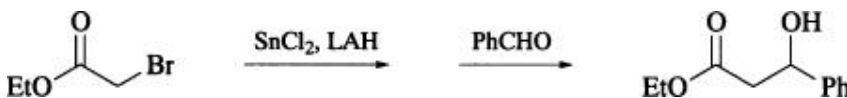
4.1.1.6. Ethyl 3-Hydroxy-3-phenylpropionate (SnCl₂–LAH) (25)

Lithium aluminum hydride (19 mg; 0.5 mmol) was added portionwise to anhydrous tin(II) chloride (190 mg; 1.0 mmol) suspended in THF (1 mL) under argon. A spontaneous exothermic reaction occurred and a dark gray material was deposited. To this suspension were added dropwise at room temperature

ethyl bromoacetate (100 mg; 0.6 mmol) dissolved in THF (1 mL), followed by benzaldehyde (53 mg; 0.5 mmol) dissolved in THF (1 mL), and the mixture was stirred for 2 hours at this temperature. Water was added to the reaction mixture and then the THF was removed under reduced pressure. The organic materials were extracted with ether and the extract was dried over MgSO$_4$. Ethyl 3-hydroxy-3-phenylpropionate (81 mg, 83%) was isolated by preparative TLC on silica gel. NMR (CDCl$_3$) δ 1.17 (t, 3H, J = 7 Hz), 2.55 (d, 2H, J = 7 Hz), 3.23-3.70 (broad, 1H), 4.03 (q, 2H, J = 7 Hz), 4.93 (t, 1H, J = 7 Hz), 7.15 (s, 5H). IR (neat) 3450, 1720 cm^{-1}.
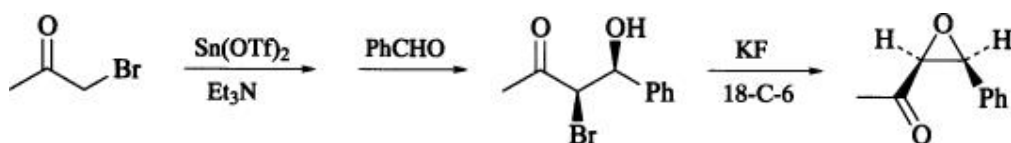
4.1.1.7. cis-3,4-Epoxy-4-phenyl-2-butanone (Synthesis of an α , β -Epoxyketone) (36, 59)
To a suspension of tin(II) triflate (355 mg, 0.85 mmol) and Et$_3$N (110 mg, 1.09 mmol) in 2 mL of THF was added dropwise bromoacetone (87 mg, 0.64 mmol) in THF (2 mL) at –78° under Ar with stirring. After the mixture was stirred for 30 minutes, benzaldehyde (108 mg, 1.02 mmol) in THF (2 mL) was added dropwise and the mixture was stirred for another 30 minutes at –78°. The reaction was quenched with 10% aqueous citric acid and the organic materials were extracted with ether (three times) and dried over Na$_2$SO$_4$. After evaporation of the solvent, the resultant crude adduct in DMF (2 mL) was added dropwise to a suspension of KF (136 mg, 2.34 mmol) and dicyclohexyl-18-crown-6 (914 mg, 2.46 mmol) in DMF (2 mL) at room temperature under Ar with stirring. After the mixture was stirred for 12 hours, the reaction was quenched with pH 7 phosphate buffer and the organic materials were extracted with ether (three times). The combined organic extracts were washed with brine and dried over Na$_2$SO$_4$. After evaporation of the solvent, the resultant oil was purified by silica gel column chromatography (hexane–Et$_2$O = 8:1) to afford 3,4-epoxy-4-phenyl-2-butanone in 72% yield (*cis*:*trans* = 70:30). IR (neat) 1715, 700 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ for *cis* isomer, 1.77 (s, 3H), 3.72 (d, 1H, J = 5 Hz), 4.25 (d, 1H, J = 5 Hz), 3.93 (d, 1H, J = 2 Hz), 7.26 (s, 5H); for *trans* isomer, 2.13 (s, 1H), 3.42 (d, 1H, J = 2 Hz), 3.93 (d, 1H, J = 2 Hz), 7.26 (s, 5H).
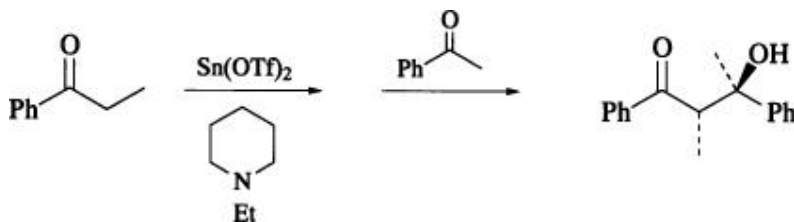
4.1.1.8. anti-3-Hydroxy-2-methyl-1,3-diphenylbutan-1-one (Cross Aldol Reaction between Ketones) (52)

To a suspension of tin(II) triflate (1.458 g, 1.1 mmol) and N-ethylpiperidine (0.138 g, 1.2 mmol) in CH_2Cl_2 (2 mL) was added dropwise propiophenone (0.134 g, 1.0 mmol) in CH_2Cl_2 (2 mL) at 0° under Ar with stirring. After the mixture had been stirred for 15 minutes, acetophenone (0.156 g, 1.3 mmol) in CH_2Cl_2 (1 mL) was added dropwise at 0°. The mixture was allowed to stand for 1 hour, then pH 7 phosphate buffer was added. After separation of the organic layer, the aqueous layer was extracted with CH_2Cl_2 (three times), and the combined organic extracts were dried over Na_2SO_4. After evaporation under reduced pressure, the resultant oil was purified by preparative TLC (hexane–Et_2O = 9:1) to yield crystalline anti-3-hydroxy-2-methyl-1,3-diphenylbutan-1-one (0.151 g, 60%). IR (neat) 3480, 1660 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.35 (d, J = 7 Hz, 3H), 1.45 (s, 3H), 4.0 (q, J = 7 Hz, 1H), 4.6 (s, 1H), 4.0–4.6 (m, 8H), 7.68–8.0 (m, 2H).
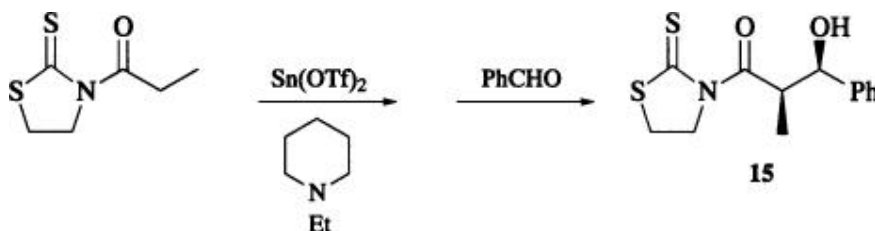
4.1.1.9. syn-3-(3-Hydroxy-2-methyl-3-phenylpropanoyl)thiazolidine-2-thione (Reaction of 3-Acylthiazolidine-2-thione with an Aldehyde) (36, 72)

To a CH_2Cl_2 suspension (2.0 mL) of tin(II) triflate (480 mg, 1.15 mmol) and N-ethylpiperidine (155 mg, 1.37 mmol) was added dropwise a CH_2Cl_2 solution (1.2 mL) of 3-propanoylthiazolidine-2-thione (163 mg, 0.93 mmol) at –78°. After further stirring at this temperature for 15 minutes, a CH_2Cl_2 solution (1.2 mL) of benzaldehyde (146 mg, 1.38 mmol) was added, and the mixture was further stirred for 20 minutes. The reaction was quenched with pH 7 phosphate buffer and the white precipitate was removed through Celite. The organic material was extracted with ether (three times), and the extracts were

dried over Na$_2$SO$_4$ and evaporated in vacuo. The residual oil was purified by silica gel column chromatography to afford 3-(3-hydroxy-2-methyl-3-phenylpropanoyl) thiazolidine-2-thione in 94% yield (*syn:anti* = 97:3). IR (neat) 3450, 1690 cm^{-1},^{1}H NMR (CDCl$_3$) δ 1.21 (d, 3H, *J* = 7 Hz), 2.77–3.17 (m, 3H), 4.00–4.25 (m, 2H), 4.63–4.97 (m, 2H), 7.33 (s, 5H).
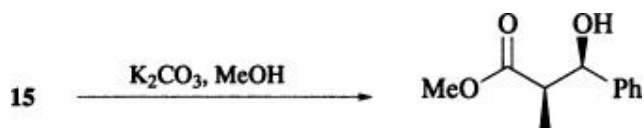
4.1.1.9.1. Conversion of the Aldol Adduct into Ester (36, 72)

To a MeOH solution (2 mL) of *syn*-3-(3-hydroxy-2-methyl-3-phenylpropanoyl)thiazolidine-2-thione (86 mg, 0.31 mmol) was added powdered K$_2$CO$_3$ (100 mg, 0.72 mmol) and the mixture was stirred for several minutes until the yellow color disappeared completely. A pH 7 phosphate buffer was added and the organic materials were extracted with ether. The extracts were dried over Na$_2$SO$_4$ and then evaporated in vacuo. The crude product was purified by silica gel TLC to afford the corresponding methyl ester (56 mg, 95%).

4.1.1.9.2. Conversion of the Aldol Adduct into Amide (36, 72)

To a CH$_2$Cl$_2$ solution (2 mL) of *syn*-3-(3-hydroxy-2-methyl-3-phenylpropanoyl)thiazolidine-2-thione (90 mg, 0.32 mmol) was added a CH$_2$Cl$_2$ solution of benzylamine (101 mg, 0.94 mmol) at room temperature. The yellow color disappeared immediately, and pH 7 phosphate buffer was added. The organic materials were extracted with AcOEt and the extracts were dried over Na$_2$SO$_4$. After evaporation of the solvent, the crude product was purified by silica gel TLC to afford the corresponding amide (77 mg, 90%).
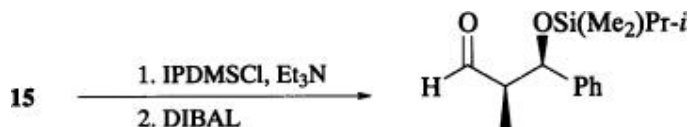
4.1.1.9.3. Conversion of the Aldol Adduct into Aldehyde (36, 72)

The hydroxy function of the adduct was protected by reaction with isopropyldimethylsilyl chloride (2 equiv), and Et₃N (2 equiv) in CH_2Cl_2 at 0° overnight (87%).

To a toluene solution (1.0 mL) of this protected compound (82 mg, 0.22 mmol) was added a toluene solution (0.80 mL, 1.83 mL/mmol) of DIBAL at –78° and the mixture was further stirred for 10 minutes at –78°. The reaction was quenched with pH 7 phosphate buffer solution (0.2 mL) and Na_2SO_4 was added as a drying agent. After removal of the precipitate through Celite, the solvent was evaporated in vacuo and the residual oil was purified by silica gel column chromatography to afford *syn*-3-isopropyldimethylsiloxy-2-methyl-3-phenylpropanal in 75% yield.
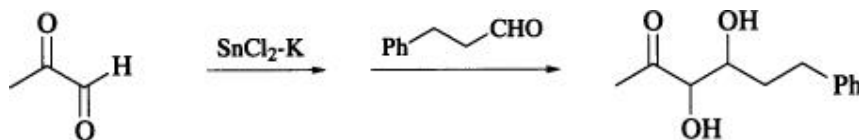
4.1.1.10. 3,4-Dihydroxy-6-phenyl-2-hexanones [Tin(II) Enediolate] (75)

A THF suspension of tin(II) chloride (1.52 g, 8 mmol) and metallic potassium (313 mg, 8 mmol) was stirred at room temperature for 1 hour under Ar and was then refluxed carefully for another 30 minutes. After the suspension had been cooled to 0° in an ice bath, a THF solution (2 mL) of 3-phenylpropanal (67.1 mg, 0.5 mmol) was added and a THF solution (8 mL) of fresh methylglyoxal (0.24 g, 3.3 mmol) was added dropwise. The reaction mixture was stirred at 0° overnight and poured into a phosphate buffer solution (pH 7, 20 mL). After filtration of insoluble materials, the organic materials of the filtrate were extracted with AcOEt and the extracts were dried over anhydrous MgSO₄. After evaporation of the solvent, the residue was purified by preparative TLC on silica gel (AcOEt:petroleum ether, 1:1.5) to give 3,4-dihydroxy-6-phenyl-2-hexanones (73.1 mg, 70%, *syn*:*anti* = 40:60). *syn*: ¹H NMR (CDCl₃) δ 1.67–2.50 (m, 3H), 2.21 (s, 3H), 2.57–3.00 (m, 2H), 3.17–4.30 (m, 3H), 7.23 (s, 5H); IR (NaCl) 3430, 1710 cm⁻¹. *anti*: ¹H NMR (CDCl₃) 1.45–1.92 (m, 2H), 2.12 (s, 3H), 2.18–2.41 (m, 1H), 2.55–2.93 (m,

2H), 3.55 (d, 1H, J = 5 Hz), 3.68–4.02 (m, 1H), 4.24 (dd, 1H, J = 3.3 Hz), 7.22 (s, 5H); IR (NaCl) 3430, 1710 cm^{-1}.
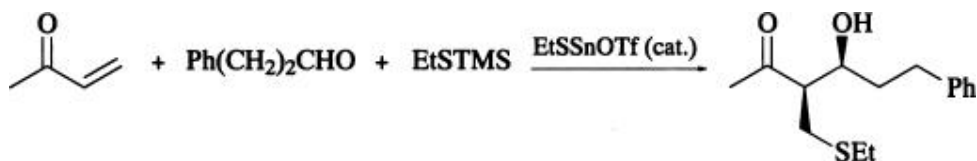
4.1.1.11. 3-Ethylthiomethyl-4-hydroxy-6-phenyl-2-hexanone [Preparation of α , β -Ethylthiomethyl Aldol with a Catalytic Amount of Tin(II) Enolate] (77, 78)

To a solution of ethanethiol (10 mg, 0.17 mmol) in THF (2 mL) was added *n*-butyllithium (1.54 M, 0.11 mL) in hexane at 0° under Ar. Tin(II) triflate (69 mg, 0.17 mmol) was added, and after 20 minutes, the mixture was cooled to –45°. Methyl vinyl ketone (118 mg, 1.68 mmol) in THF (1.5 mL) and 3-phenylpropanal (350 mg, 2.61 mmol) in THF (1.5 mL) were successively added to the mixture. The reaction mixture was stirred for 12 hours, then quenched with 10% aqueous citric acid, and the organic materials were extracted with CH_2Cl_2 (three times). To completely hydrolyze the trimethylsilyl ether group, the crude aldol product obtained after evaporation of the solvent was dissolved in methanol and to this solution was added citric acid. After stirring for 30 minutes, the reaction was quenched with pH 7 phosphate buffer. The organic layer was extracted with CH_2Cl_2 (three times) and the combined extracts were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by silica gel column chromatography to afford 3-ethylthiomethyl-4-hydroxy-6-phenyl-2-hexanone (336 mg, 75% yield, *syn:anti* = 90:10). IR (neat) 3450, 1750 cm^{-1}; ^{1}H NMR (CCl$_4$) δ 1.1 (t, 3H, J = 8 Hz), 1.3–1.7 (m, 2H), 1.9 (*syn*), 2.0 (*anti*) (s, 3H), 2.1–3.2 (m, 8H), 3.6 (brs, 1H), 7.0 (s, 5H). The diastereomeric ratio was determined by integration of the methyl signal. Relative stereochemistry was determined by ^{13}C NMR spectra. (108) ^{13}C NMR (CDCl$_3$) δ 70.97 (*syn*), 71.73 (*anti*).
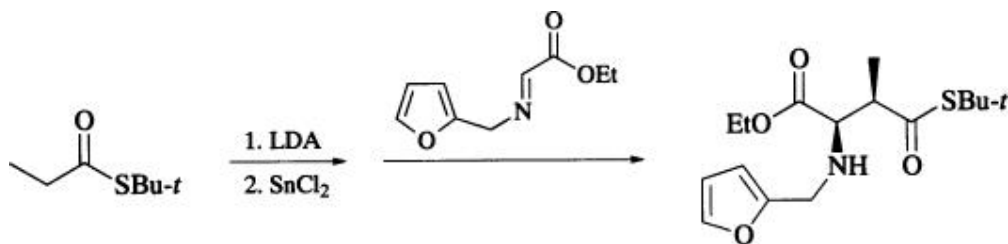
4.1.1.12. Ethyl 3-(tert-Butylthio)carbonyl-2-furfurylaminobutyrate [Reaction of a Tin(II) Thioester Enolate with an α-Iminoester] (44)

To a solution of lithium diisopropylamide (0.68 mmol) in dry ether (2 mL) under argon at –78° was added *tert*-butyl propanethioate (100 mg, 0.68 mmol) in dry ether (1.5 mL) over 5 minutes. After the mixture was stirred for 30 minutes, tin(II) chloride (156 mg, 0.82 mmol) was added as a powder and the mixture was stirred vigorously for another 30 minutes. To this mixture, ethyl *N*-furfuryliminoacetate (62 mg, 0.34 mmol) was added and the reaction mixture was stirred for 3 hours at –78°. The reaction was quenched by adding pH 7 phosphate buffer, the mixture was filtered through a Celite pad, and the product was extracted with AcOEt. The organic layer was washed with brine and dried over Na$_2$SO$_4$. After evaporation of the solvents, the crude product was purified by silica gel TLC (AcOEt–hexane) to afford ethyl 3-(*tert*-butylthio)carbonyl-2-furfurylaminobutyrate (92 mg, 82% yield, *syn*/*anti* = 95:5).
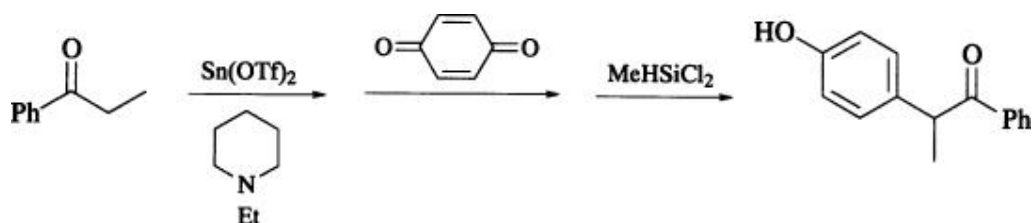
4.1.1.13. 4-(1-Benzoylethyl)phenol [Addition-reduction Reaction of a Tin(II) Enolate with 1,4-Benzoquinone] (110, 111)
Propiophenone (0.44 mmol) in CH$_2$Cl$_2$ (1 mL) was added dropwise at –78° to a stirred mixture of tin(II) triflate (0.55 mmol) and *N*-ethylpiperidine (0.61 mmol) in CH$_2$Cl$_2$ (1 mL). The resulting mixture was stirred at –78° for 40 minutes. 1,4-Benzoquinone (0.19 mmol) in CH$_2$Cl$_2$ (2 mL) was added dropwise at –78° to the yellow-green suspension, and stirring was continued for 30 minutes, after which dichloromethylsilane (0.97 mmol in 2 mL of CH$_2$Cl$_2$) and dimethylaminopyridine (0.44 mmol in 2 mL of CH$_2$Cl$_2$) were added dropwise in quick succession. Stirring was continued at –78° until preparative TLC (50% ethyl acetate/hexane) showed consumption of all the intermediate (ca. 30 minutes). The reaction was then quenched with 10% aqueous citric acid solution (10 mL) and the resulting two-phase mixture was extracted with CH$_2$Cl$_2$ (3 × 10 mL). The combined extracts were dried (MgSO$_4$), filtered, and evaporated under reduced pressure to give an oily residue which was purified by preparative TLC on silica gel using 30% ethyl acetate/hexane as eluant to give the desired phenol (0.16 mmol, 83%) as a colorless oil, which slowly solidified on standing: mp. 89–90° (recrystallized from chloroform/hexane). IR (KBr) 3400, 1660, 1605, 1590, 1570, 1505, 1220, 730 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.5 (d, 3H, *J* = 7 Hz), 4.6 (q, 1H, *J* = 7 Hz), 6.7 (d, 2H, *J* = 7 Hz), 7.1 (d, 2H, *J* = 7 Hz), 7.4 (m, 3H), 7.8–8.0 (m, 2H).
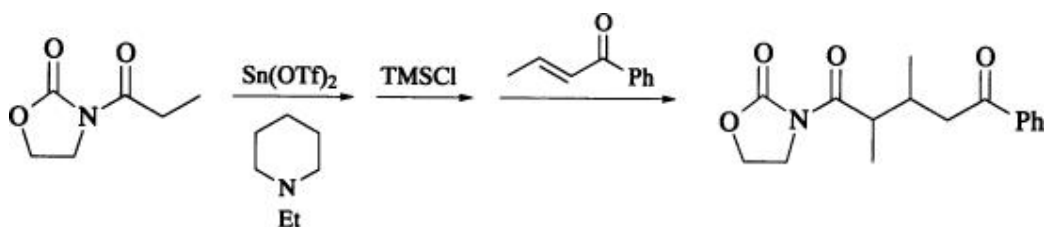
4.1.1.14. 3-(2,3-Dimethyl-5-oxo-5-phenylpentanoyl)-1,3-oxazolidin-2-one [Reaction of a Tin(II) Enolate with an α, β -Unsaturated Ketone in the Presence of TMSCl] (111, 153)

Tin(II) triflate (343 mg, 0.82 mmol) was cooled to –78° and *N*-ethylpiperidine (116 mg, 1.03 mmol) in CH_2Cl_2 (2 mL) was added dropwise. After 10 minutes, a solution of 3-propanoyl-1,3-oxazolidin-2-one (97 mg, 0.67 mmol) in dichloromethane (1.5 mL) was added dropwise with stirring to the yellow-green suspension, and stirring was continued at –78° for 1 hour. Phenyl propenyl ketone (77 mg, 0.53 mmol) and TMSC1 (107 mg, 0.99 mmol) were added successively to the mixture, and after stirring for 2 hours the reaction was quenched at –78° with 10% citric acid (10 mL). Dichloromethane (10 mL) was added and the organic and aqueous phases were separated. The aqueous phase was extracted with CH_2Cl_2 (10 mL × 3) and the combined organic layers were dried ($MgSO_4$), filtered, and evaporated under reduced pressure. To completely hydrolyze the trimethysilyl ether, the residue was dissolved in methanol and citric acid was added. After stirring for 1 hour the reaction was quenched with pH 7 phosphate buffer. The organic layer was extracted with dichloromethane (10 mL × 3) and the combined extracts were dried ($MgSO_4$). After evaporation of the solvent, the crude product was purified by preparative TLC to afford white crystalline 3-(2,3-dimethyl-5-oxo-5-phenylpentanoyl)-1,3-oxazolidin-2-one (120 mg, 79%). IR(KBr) 2970, 1760, 1680, 1380, 1240, 760, 690 cm^{-1}; ^{1}H NMR($CDCl_3$) δ 0.9–1.3 (m, 6H), 2.4–3.3 (m, 3H), 3.6–4.5 (m, 5H), 7.2–7.6 (m, 3H), 7.8–8.1 (m, 2H).
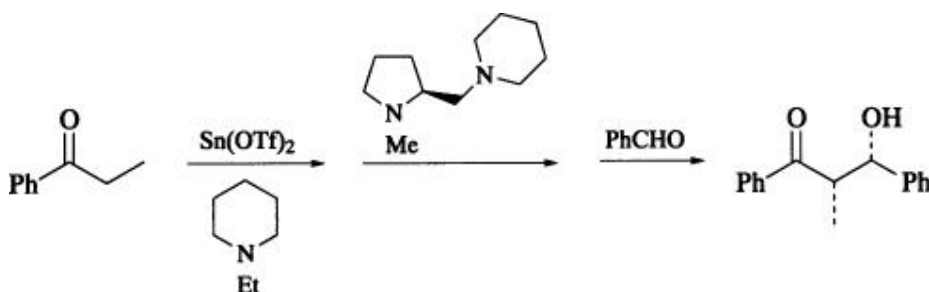
4.1.1.15. 3-Hydroxy-2-methyl-1,3-diphenyl-1-propanone [Enantioselective Cross Aldol Reaction of a Ketone and an Aldehyde] (36, 164)

To a suspension of tin(II) triflate (296 mg, 0.71 mmol) and *N*-ethylpiperidine (95 mg, 0.84 mmol) in CH_2Cl_2 (2 mL) was added dropwise propiophenone (78 mg, 0.58 mmol) in CH_2Cl_2 (1.5 mL) at –78° under Ar. After the mixture was stirred for 30 minutes, (*S*)-1-methyl-2-[(piperidin-1-yl)methyl]pyrrolidine (158 mg, 0.87 mmol) in CH_2Cl_2 (1.5 mL) was added dropwise, and the mixture was stirred for 5 minutes at –78°. The mixture was cooled to –95°, and then benzaldehyde (91 mg, 0.86 mmol) in CH_2Cl_2 (1.5 mL) was added dropwise. The mixture was further stirred for 30 minutes at the same temperature, then quenched with pH 7 phosphate buffer. The organic layer was extracted with ether (three times) and the combined extracts were dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by silica gel TLC to afford 3-hydroxy-2-methyl-1,3-diphenyl-1-propanone (103 mg, 74%). The optical purity of the product was determined by measurement of the ^1H and ^{19}F NMR spectra of the MTPA ester (80% ee). (219)
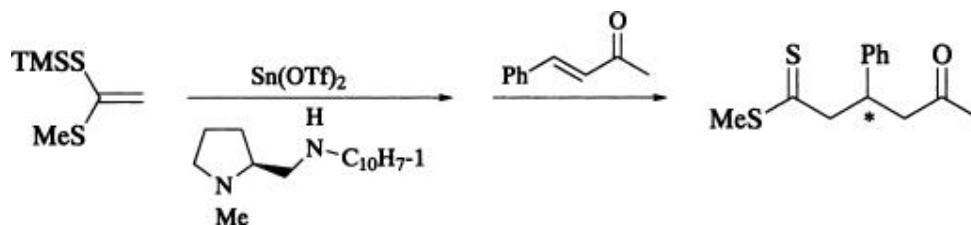
4.1.1.16. 5-Oxo-3-phenylhexanedithioate [Catalytic Asymmetric Michael Reaction of a Tin(II) Enethiolate] (78, 168)

To a CH_2Cl_2 suspension (2 mL) of tin(II) triflate (38 mg, 0.09 mmol), benzalacetone (0.93 mmol), and (*S*)-1-methyl-2-[(*N*-1-naphthylamino)methyl]pyrrolidine (23 mg, 0.10 mmol) under Ar was added a CH_2Cl_2 solution (1 mL) of 4-phenyl-3-buten-2-one (136 mg, 0.93 mmol) at –78°. To this mixture was slowly added a CH_2Cl_2 solution (2 mL) of vinylthiosilane (199 mg, 1.11 mmol) over 4 hours. The mixture was stirred for 1 hour at this temperature, 10% aqueous citric acid was added, and the organic materials were extracted with CH_2Cl_2 (three times). The combined extracts were washed with 4% aqueous $NaHCO_3$ (twice) and brine successively, and the organic phase was dried with anhydrous $MgSO_4$. After evaporation of the solvent, the residue was dissolved in methanol (10 mL), citric acid (800 mg, 4.16 mmol) was added, and the mixture was stirred for 1 hour at room temperature. To the mixture was added pH 7 phosphate buffer, the organic materials were extracted with CH_2Cl_2 (three

times), and the combined extracts were dried over anhydrous $MgSO_4$. After evaporation of the solvent, the crude product was purified by silica gel TLC to afford methyl 5-oxo-3-phenylhexanedithioate (187 mg, 80% yield, 70% ee). IR (neat) 1675, 1255 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.9 (s, 3H), 2.4 (s, 3H), 2.7 (d, 2H, J = 7 Hz), 3.2 (d, 2H, J = 7 Hz), 3.6–4.1 (m, 1H), 7.1 (s, 5H).
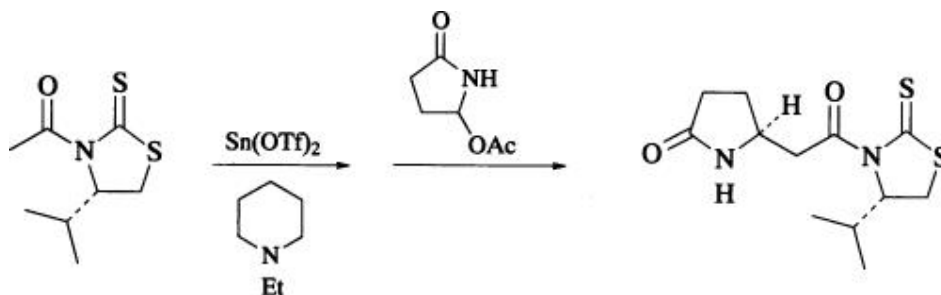
4.1.1.17. 3-[(5-Oxo-2(S)-pyrrolidinyl)acetyl]-4(S)-isopropyl-1,3-thiazolidine-2-t hione [Alkylation of a Chiral Tin(II) Enolate] (188, 189)

Tin(II) triflate (1.08 g, 2.59 mmol) was dissolved in dry THF (6 mL) under Ar at room temperature. To the solution cooled to –50° in a dry ice–acetonitrile bath were added successively *N*-ethylpiperidine (0.41 ml, 2.99 mmol) and 3-acetyl-4(*S*)-isopropyl-1,3-dithiazolidine-2-thione (0.406 g, 2.0 mmol) in dry THF (1.8 mL), and the mixture was then stirred for 3 hours between –50 and –40° to form the tin(II) enolate. To this enolate was added a 1.0 M solution of 5-acetoxy-2-pyrrolidinone (3.0 mmol) in dry THF at –5°, and the mixture was then stirred for 2 hours between –5 and 0°. The reaction mixture was poured into a mixture of phosphate buffer solution (pH 7.0, 50 mL) and AcOEt (50 mL) with vigorous stirring. After the precipitate was filtered through Celite and washed with AcOEt (3 × 50 mL), the combined filtrate was washed with brine and then submitted to workup to provide a crude product. A sample of the crude product was submitted to HPLC analysis (column, Diasil 5 C 184.6 mm i.d. × 25 cm; eluant, CH$_3$CN – H$_2$O , 9:1; flow rate, 1.0 mL/min; detection, UV 305 nm) to determine diastereomeric excess (94% de). Flash column chromatography of the crude product (elution with 67% AcOEt in CHCl$_3$) afforded the pure product, 3-([5-oxo-2(*S*)-pyrrolidinyl]acetyl)-4(*S*)-isopropyl-1,3-thiazolidine-2-thione (67%). IR (CH$_3$Cl) 3340, 1690, (br), 1255, 1175 cm^{-1}; ^{1}H NMR (100 MHz, CDCl$_3$) δ 0.98 and 1.06 (d, 6H, J = 6.8 Hz), 1.68–2.08 (m, 1H), 2.18–2.60 (m, 4H), 3.04 (dd, 1H, J = 11.5, 1.5 Hz), 3.18 (dd, 1H, J = 17.8, 9.8 Hz), 3.57 (dd, 1H, J = 11.5, 8.0 Hz), 3.78 (dd, 1H, J = 17.8, 3.5 Hz), 3.96–4.28 (m, 1H), 5.20 (ddd, 1H, J = 8.0, 6.0, 1.5 Hz), 6.28 (brs, 1H).

5. Tabular Survey

The seven tables include all examples of the reaction found in the literature through the middle of 1991. Entries in each table are arranged in order of increasing number of carbon atoms in the donor carbonyl compound.

The following abbreviations are used in the tables:

Ac	acetyl
Bn	benzyl
Boc	*tert*-butoxycarbonyl
Bz	benzoyl
Cbz	benzyloxycarbonyl
de	diastereomeric excess
18-C-6	dicyclohexyl-18-crown-6
DEIPS	diethylisopropylsilyl
ee	enantiomeric excess
IPDMS	isopropyldimethylsilyl
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
NEPIP	*N*-ethylpiperidine
NMMOR	*N*-methylmorpholine
Py	pyridine
TBDMS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl (triflyl)
TMS	trimethylsilyl
TrBF$_4$	trityl tetrafluoroborate
Ts	*p*-toluenesulfonyl

Table I. Aldol Reaction with Achiral Substrates; No or Simple Diastereoselection

View PDF

Table II. Michael Reaction with Achiral Substrates; No or Simple Diastereoselection

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Table III. Enantioselective Aldol Reaction

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Table IV. Enantioselective Michael Reaction

View PDF

Table V. Enantioselective Sulfenylation

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Table VI. Diastereoselective Aldol Reaction

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Table VII. Diastereoselective Aldol Alkylation

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TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION
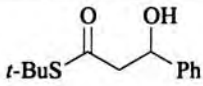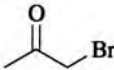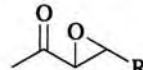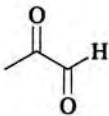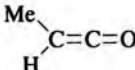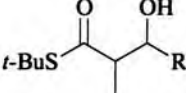
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C₂ $CH_2=C=O$	$Sn(SBu\text{-}t)_2$	PhCHO	(75)	43
C₃ (1-bromoacetone)				
	$Sn(OTf)_2$, NEPIP, KF, 18-C-6	PhCHO	R = Ph, (72) 70/30	59
	"	$Ph(CH_2)_2CHO$	R = $Ph(CH_2)_2$, (65) 73/27	59
	$Sn(OTf)_2$, Et₃N	$(EtO)_2(O)PCH_2CHO$	R = $CH_2P(O)(OEt)_2$, (63) 60/40	60
	"	$(EtO)_2(O)P\diagdown CHO$	R = $CH(Me)P(O)(OEt)_2$, (43) 67/33	60
	"	$(EtO)_2(O)P\diagdown CHO$	R = $C(Me)_2P(O)(OEt)_2$, (30) 100/0	60
(pyruvaldehyde)				75
	$SnCl_2$, K	$Ph(CH_2)_2CHO$	R = $Ph(CH_2)_2$, (70) 43/57	
	"	$BnO(CH_2)_3CHO$	R = $BnO(CH_2)_3$, (80) 16/84	
	"	$n\text{-}C_7H_{15}CHO$	R = $n\text{-}C_7H_{15}$, (55) 33/67	
	"	$p\text{-}ClC_6H_4CHO$	R = $p\text{-}ClC_6H_4$, (54) 25/75	
(methylketene)				43

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
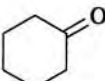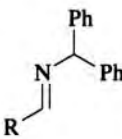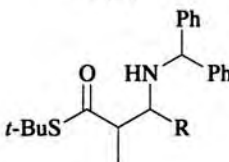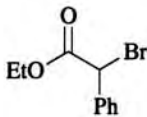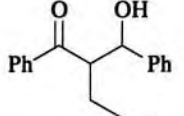
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	$Sn(SBu\text{-}t)_2$	PhCHO	R = Ph, (98) 90/10	
	"	$Ph(CH_2)_2CHO$	R = $Ph(CH_2)_2$, (89) 97/3	
	"	$i\text{-}PrCHO$	R = $i\text{-}Pr$, (78) 93/7	
	"	$t\text{-}BuCHO$	R = $t\text{-}Bu$, (72) 90/10	
				43
	$Sn(SBu\text{-}t)_2$	(cyclohexanone)	$R^1, R^2 = \text{-}(CH_2)_6\text{-}$, (78)	
	"	PhCOMe	$R^1 = Ph, R^2 = Me$, (77) 70/30	
	"	$Ph(CH_2)_2COMe$	$R^1 = Ph(CH_2)_2, R^2 = Me$, (69) 58/42	
	"	EtO_2CCOMe	$R^1 = CO_2Et, R^2 = Me$, (96) 19/81	
	"	$MeCO(CH_2)_8CHO$	$R^1 = MeCO(CH_2)_8, R^2 = H$ -100°, (67) -45°, (81)	
		(imine)		87
	$Sn(OTf)_2$	"	R = Ph, (89) 96/4	
	"	"	R = PhCH=CH, (60) 81/19	
	$SnBr_2$	"	R = PhCH=CH, (55) 84/16	

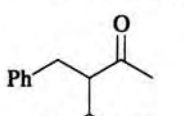TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
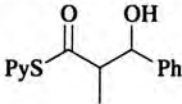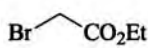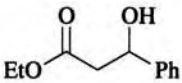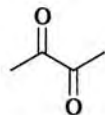
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)$_2$	"	R = *i*-Pr, (83) 92/8	
	"	"	R = Ph(CH$_2$)$_2$, (65) 92/8	
C$_4$	Sn(SPy)$_2$	PhCHO	(89) 93/7	43
Br⌢CO$_2$Et	Sn	PhCHO	(84)	25
	SnCl$_2$, K	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (95) 50/50	48
	SnCl$_2$, K, C$_6$F$_6$	"	R = Ph(CH$_2$)$_2$, (86) 75/25	48
	SnCl$_2$, K	*n*-C$_8$H$_{17}$CHO	R = *n*-C$_8$H$_{17}$, (78) 50/50	48
	SnCl$_2$, K, C$_6$F$_6$	"	R = *n*-C$_8$H$_{17}$, (70) 75/25	48
	SnCl$_2$, K	*i*-PrCHO	R = *i*-Pr, (83) 67/33	48
	"	BnOCH$_2$CHO	R = CH$_2$OBn, (77) 67/33	48

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
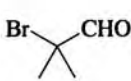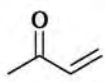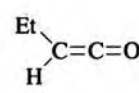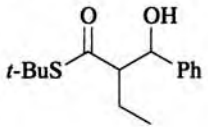
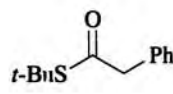| Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
Br⌢CHO				
	SnCl$_2$, K	PhCHO	R = Ph, (64)	76
	"	*p*-ClC$_6$H$_4$CHO	R = *p*-ClC$_6$H$_4$, (71)	76
	"	*p*-BrC$_6$H$_4$CHO	R = *p*-BrC$_6$H$_4$, (70)	76
	"	*n*-C$_{11}$H$_{23}$CHO	R = *n*-C$_{11}$H$_{23}$, (65)	76
	"	BnO(CH$_2$)$_3$CHO	R = (CH$_2$)$_3$OBn, (74)	76
	EtSSnOTf	PhCHO	R = Ph, (68) 95/5	77, 78
	"	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (75) 90/10	77, 78
Et⌒C=C=O / H	Sn(SBu-*t*)$_2$	PhCHO	(90) >95/5	43

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	"	Ph N—CHPh_(imine) R	t-BuS—C(=O)...HN—CHPh₂, R (60) 12/88	87
C₅ (2-bromopropanoate EtO, Br)	Sn	PhCHO	EtO—C(=O)—CH(Me)—CH(OH)Ph (81) 55/45	25
Br—CH₂CH=CH—CO₂Me	Sn	PhCHO	MeO—C(=O)—... vinyl, CH(OH)Ph (85) 57/43	25
3-pentanone	Sn(OTf)₂, NEPIP	PhCHO	R = Ph, (77) 87/13	26, 36
	"	*i*-PrCHO	R = *i*-Pr, (73) 93/7	26, 36
	"	*n*-PrCHO	R = *n*-Pr, (86) >91/9	26, 36

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)₂, NEPIP	Ph—C(=O)—CH₃ (acetophenone)	O, OH, Ph, Me product (45) 13/87	52
	Sn(OTf)₂, NEPIP	1,4-benzoquinone, MeHSiCl₂	product (4-OH phenyl) (68)	110, 111
	Sn(OTf)₂, NEPIP	quinone NTs imide, MeHSiCl₂	product (4-NTs phenyl) (68)	110, 111
2-bromo-3-pentanone (O, Br)	Sn		O, OH product	
	Sn	PhCHO	R = Ph, (70) 91/9	42
	"	*i*-PrCHO	R = *i*-Pr, (65) 91/9	42
	"	*n*-PrCHO	R = *n*-Pr, (77) 92/8	42

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
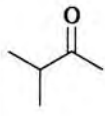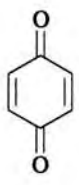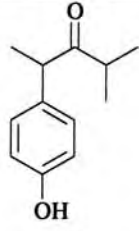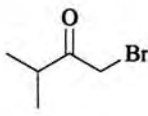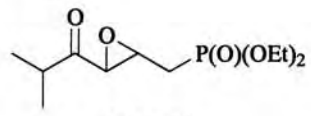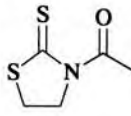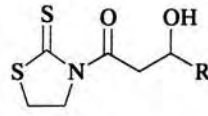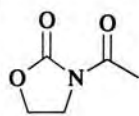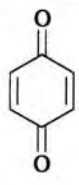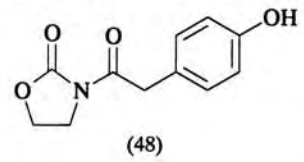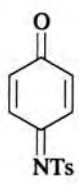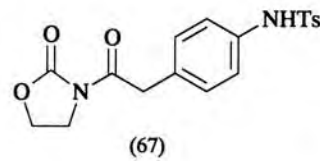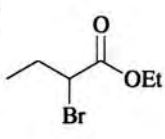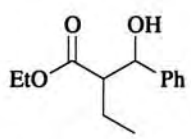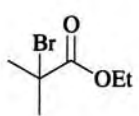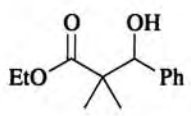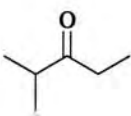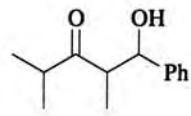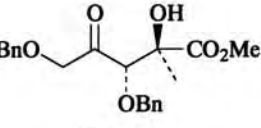
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)₂, NEPIP	, MeHSiCl₂	(65)	110, 111
	Sn(OTf)₂, Et₃N	(EtO)₂(O)PCH₂CHO	(46) 75/25	60
	Sn(OTf)₂, NEPIP	PhCHO	R = Ph, (90)	36, 37
	"	Ph(CH₂)₂CHO	R = Ph(CH₂)₂, (88)	36, 37
	"	*i*-PrCHO	R - *i*-Pr, (94)	36, 37

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)₂, NEPIP	, MeHSiCl₂	(48)	110, 111
	Sn(OTf)₂, NEPIP	, MeHSiCl₂	(67)	110, 111
C₆ 	Sn	PhCHO	(81) 57/43	25
	Sn	PhCHO	(95)	25
	Sn(OTf)₂, NEPIP	PhCHO	(72) 91/9	26, 36

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
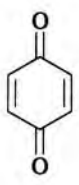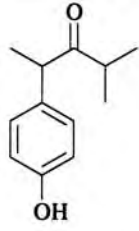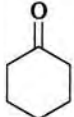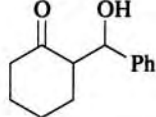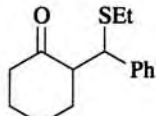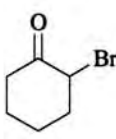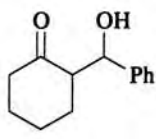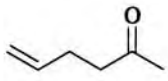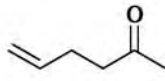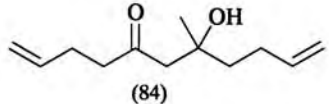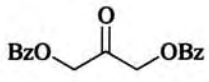
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)₂, NEPIP	(1,4-benzoquinone), MeHSiCl₂	(70)	110, 111
(cyclohexanone)	Sn(OTf)₂, NEPIP	PhCHO	(41) >95/5	26, 36
	Sn(OTf)₂ , NEPIP	PhCH(SEt)₂	−45°, (78) 77/23; −78°, (87) 87/13	88
(2-bromocyclohexanone)	Sn	PhCHO	(28) 94/6	42
(hex-5-en-2-one)	Sn(OTf)₂, NMMOR	(hex-5-en-2-one)	(84)	52

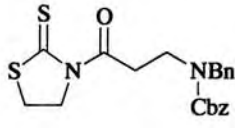TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
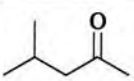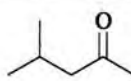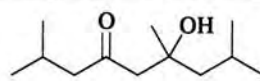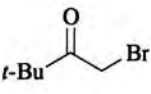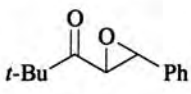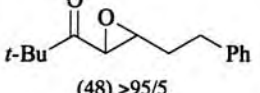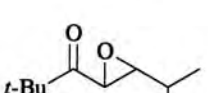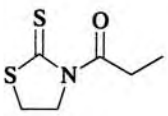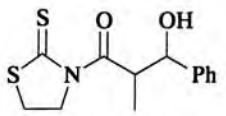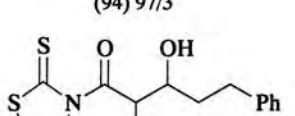
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
(4-methylpentan-2-one)	Sn(OTf)₂, NMMOR	(4-methylpentan-2-one)	(76)	52
t-Bu—C(O)—CH₂Br	Sn(OTf)₂, NEPIP, KF, 18-C-6	PhCHO	(64) >95/5	59
	Sn(OTf)₂, NEPIP, KF, 18-C-6	Ph(CH₂)₂CHO	(48) >95/5	59
	Sn(OTf)₂, NEPIP, KF, 18-C-6	*i*-PrCHO	(47) >95/5	59
(3-propionyl-1,3-thiazolidine-2-thione)	Sn(OTf)₂, NEPIP	PhCHO	(94) 97/3	36, 37
	Sn(OTf)₂, NEPIP	Ph(CH₂)₂CHO	(91) >97/3	36, 37

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
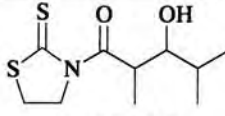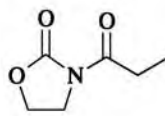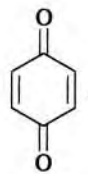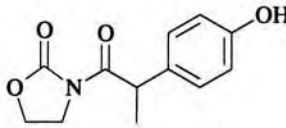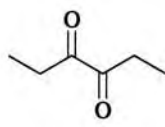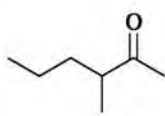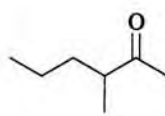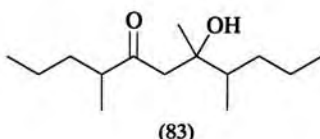
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)$_2$, NEPIP	*i*-PrCHO	(95) >97/3	36, 37
	Sn(OTf)$_2$, NEPIP	, MeHSiCl$_2$	(71)	110, 111
	Sn	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (92) 67/33	48
	Sn, C$_6$F$_6$	"	R = Ph(CH$_2$)$_2$, (87) 80/20	48
	Sn	*n*-C$_8$H$_{17}$CHO	R = *n*-C$_8$H$_{17}$, (86) 67/33	48
	Sn, C$_6$F$_6$	"	R = *n*-C$_8$H$_{17}$, (81) 75/25	48
C$_7$	Sn(OTf)$_2$, NMMOR		(83)	52

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
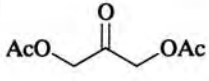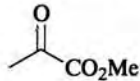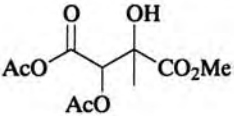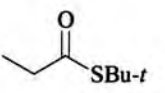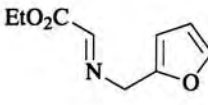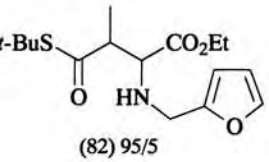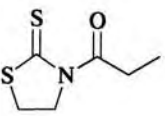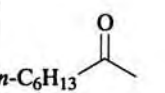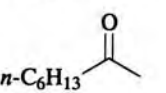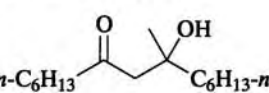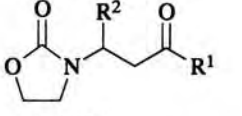
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
AcO OAc	Sn(OTf)$_2$, NEPIP	CO$_2$Me	0°, (45) 85/15 −78°, (37) 71/29	58
SBu-*t*	LDA, SnCl$_2$	EtO$_2$C	(82) 95/5	44
	Sn(OTf)$_2$, NEPIP	PhCHO	R = Ph, (95) 25/75	74
	"	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (82) 84/16	74
	"	*n*-C$_5$H$_{11}$CHO	R = *n*-C$_5$H$_{11}$, (77) 85/15	74
	"	*i*-PrCHO	R = *i*-Pr, (68) 67/33	74
	"	PhCH=CHCHO	R = PhCH=CH, (73) 50/50	74
C$_8$ *n*-C$_6$H$_{13}$	Sn(OTf)$_2$, NMMOR	*n*-C$_6$H$_{13}$	*n*-C$_6$H$_{13}$ C$_6$H$_{13}$-*n* (82)	52

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
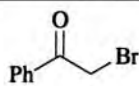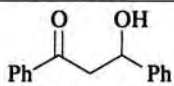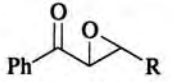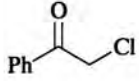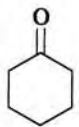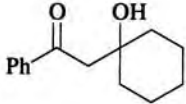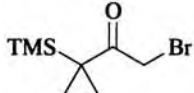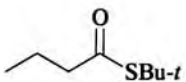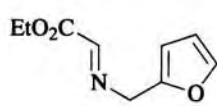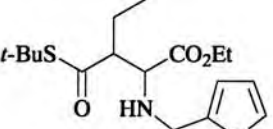
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
Ph—C(O)—CH2Br	Sn	PhCHO	Ph—C(O)—CH2—CH(OH)—Ph (63)	42
	Sn(OTf)2, NEPIP, KF, 18-C-6	Ph(CH2)2CHO	R = Ph(CH2)2, (80) 66/34	59
	"	*i*-PrCHO	R = *i*-Pr, (80) 65/35	59
Ph—C(O)—CH2Cl	Sn(OTf)2, NEPIP	cyclohexanone	Ph—C(O)—CH2—C(OH)(cyclohexane) (87)	52
TMS—C(CH3)2—C(O)—CH2Br	Sn(OTf)2, NEPIP	PhCHO	R = Ph, (70) >95/5	66
	"	Ph(CH2)2CHO	R = Ph(CH2)2, (83) >95/5	66
	"	*n*-C11H23CHO	R = *n*-C11H23, (79) >95/5	66
CH3CH2CH2—C(O)—SBu-*t*	LDA, SnCl2	EtO2C—CH=N—CH2-(2-furyl)	*t*-BuS—C(O)—CH(Et)—CH(CO2Et)—NH—CH2-(2-furyl) (61) 95/5	44

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
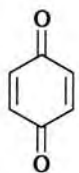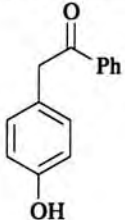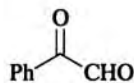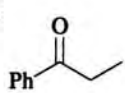
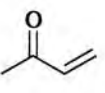| Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
Ph—C(O)—CH3	Sn(OTf)2, NEPIP	1,4-benzoquinone, MeHSiCl2	4-hydroxyphenyl—CH2—C(O)—Ph (65)	110, 111
Ph—C(O)—CHO	SnCl2, K	Ph(CH2)2CHO	R = Ph(CH2)2, (73) 50/50	76
	"	*n*-C8H17CHO	R = *n*-C8H17, (68) 67/33	76
C9 Ph—C(O)—CH2CH3	Sn(OTf)2, NEPIP	PhCHO	R = Ph, (71) >95/5	26, 36
	"	*i*-PrCHO	R = *i*-Pr, (80) 91/9	26, 36
	"	*n*-PrCHO	R = *n*-Pr, (79) 86/14	26, 36

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
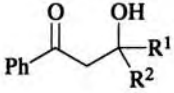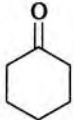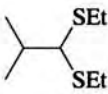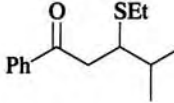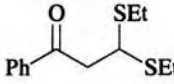
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)$_2$, NEPIP	cyclohexanone	R^{1}R^2 = (CH$_2$)$_5$, (83)	52
	"	cyclopentanone	R^{1}R^2 = (CH$_2$)$_4$, (75)	52
	"	EtCOEt	R^1 = R^2 = Et, (80)	52
	"	PhCOMe	R^1 = Ph, R^2 = Me, (60) 0/100	52
	"	*i*-PrCOMe	R^1 = *i*-Pr, R^2 = Me, (69) 50/50	52
	"	*i*-BuCOMe	R^1 = *i*-Bu, R^2 = Me, (69) 50/50	52
	"	Ph(CH$_2$)$_2$COMe	R^1 = Ph(CH$_2$)$_2$, R^2 = Me, (78) 50/50	52
	Sn(OTf)$_2$, NEPIP		(64) 56/44	88
	Sn(OTf)$_2$, NEPIP	CH(SEt)$_3$	(80)	88

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
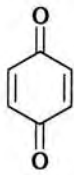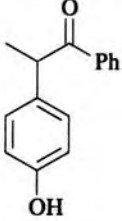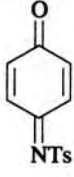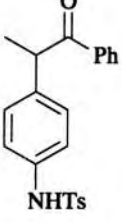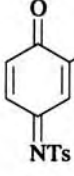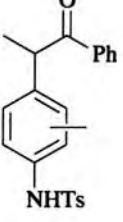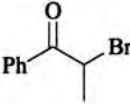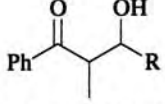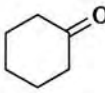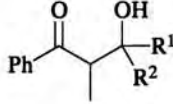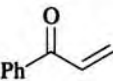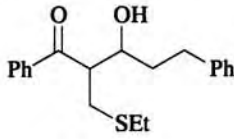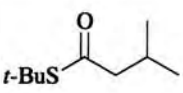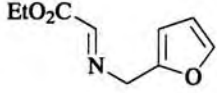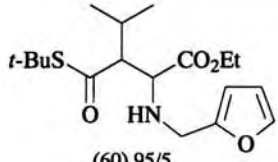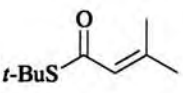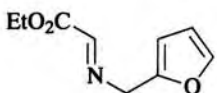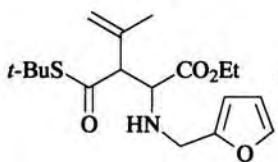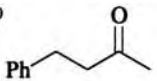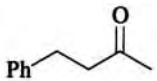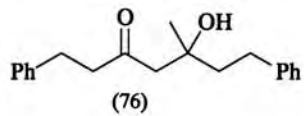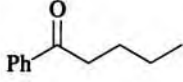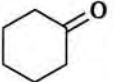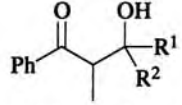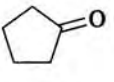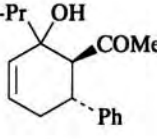
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)$_2$, NEPIP	, MeHSiCl$_2$	(83)	110, 111
	Sn(OTf)$_2$, NEPIP	, MeHSiCl$_2$	(77)	110, 111
	Sn(OTf)$_2$, NEPIP	, MeHSiCl$_2$	(59)	110, 111

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TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn	PhCHO	R = Ph, (93) 93/7	42
	"	p-MeC$_6$H$_4$CHO	R = p-MeC$_6$H$_4$, (99) 92/8	42
	"	p-ClC$_6$H$_4$CHO	R = p-ClC$_6$H$_4$, (91) 92/8	42
	"	n-PrCHO	R = n-Pr, (85) 91/9	42
	"	i-BuCHO	R = i-Bu, (72) 92/8	42
	Sn		R^{1}R^2 = (CH$_2$)$_5$, (88)	42
	"	BnCOBn	R^1 = R^2 = Bn, (44)	42
	EtSSnOTf	Ph(CH$_2$)$_2$CHO	(73) 84/16	77, 78

TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	LDA, SnCl$_2$		(60) 95/5	44
	LDA, SnCl$_2$		(60)	44
C$_{10}$	Sn(OTf)$_2$, NMMOR		(76)	52
	Sn(OTf)$_2$, NEPIP		R^{1}R^2 = (CH$_2$)$_5$, (87)	52
	"		R^{1}R^2 = (CH$_2$)$_4$, (76)	52
	"	PhCOMe	R^1 = Ph, R^2 = Me, (41) 0/100	52
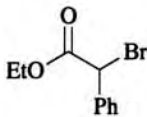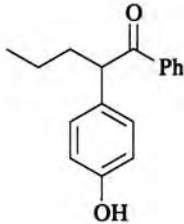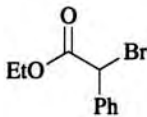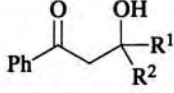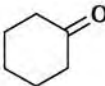
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)$_2$, NEPIP	, MeHSiCl$_2$	(83)	110, 111
	Sn	p-ClC$_6$H$_4$CHO	R = p-ClC$_6$H$_4$, (88) 80/20	25
	"	p-MeC$_6$H$_4$CHO	R = p-MeC$_6$H$_4$, (93) 77/23	25
	"	1-C$_{10}$H$_7$CHO	R = 1-C$_{10}$H$_7$, (93) 77/23	25
	"	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (91) 71/29	25
	"	PhCH=CHCHO	R = PhCH=CH, (83) 79/21	25
	Sn	BnCOBn	R^1 = R^2 = Bn, (80)	25
	"		R^{1}R^2 = (CH$_2$)$_5$, (96)	25
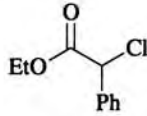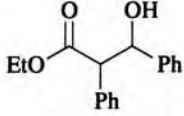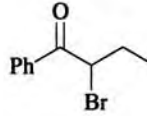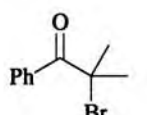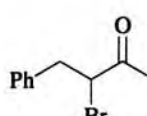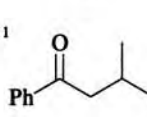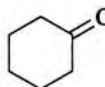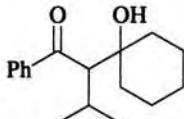
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn	PhCHO	(88) 59/41	25
	Sn	PhCHO	(96)	42
	Sn	PhCHO	R = Ph, (92)	42
	"	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (94)	42
	"	PhCH=CHCHO	R = PhCH=CH, (91)	42
	Sn	PhCHO	(82)	42
C$_{11}$	Sn(OTf)$_2$, NEPIP		(48)	52

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Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C$_{12}$ (thiazolidinethione-CO-CH$_2$CH$_2$Ph)			(thiazolidinethione-CO-CH(CH$_2$CH$_2$Ph)-CH(OH)R)	
	Sn(OTf)$_2$, NEPIP	PhCHO	R = Ph, (88) >97/3	36, 37
	"	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (95) >97/3	36, 37
t-BuS-CO-CH$_2$Ph	LDA, SnCl$_2$	EtO$_2$C-CH=N-CH$_2$-(furan)	*t*-BuS-CO-CH(CH$_2$Ph)-CH(CO$_2$Et)-NH-CH$_2$-(furan) (68) 93/7	44
t-BuCO$_2$-CH$_2$-CO-CH$_2$-O$_2$CBu-*t*	Sn(OTf)$_2$, NEPIP	CH$_3$-CO-CO$_2$Me	*t*-BuCO$_2$-CH$_2$-CO-CH(O$_2$CBu-*t*)-C(OH)(CH$_3$)(CO$_2$Me) 0°, (68) 64/36 -78°, (55) 82/18	58
C$_{14}$ Ph-CO-CHBr-Ph (CHPh)	Sn	PhCHO	Ph-CO-CH(Ph)-CH(OH)-Ph (82)	42

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C$_{15}$ Ph-CO-CH$_2$-O$_2$CPh			Ph-CO-CH(O$_2$CPh)-C(OH)(R^1)(R^2)	
	Sn(OTf)$_2$, NEPIP	cyclohexanone	R^{1}R^2 = (CH$_2$)$_5$, (86)	52
	"	cyclopentanone	R^{1}R^2 = (CH$_2$)$_4$, (78)	52
	"	PhCOMe	R^1 = Ph, R^2 = Me, 0°, (85) 30/70 -78°, (48) >95/5	52
	Sn(OTf)$_2$, NEPIP	1,4-benzoquinone, MeHSiCl$_2$	Ph-CH$_2$-CH(CO-Ph)(C$_6$H$_4$-4-OH) (66)	110, 111
C$_{17}$ BnO-CH$_2$-CO-CH$_2$-OBn	Sn(OTf)$_2$, NEPIP	CH$_3$-CO-CO$_2$Me	BnO-CH$_2$-CO-CH(OBn)-C(OH)(CH$_3$)(CO$_2$Me) (63) 74/26	58
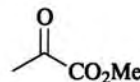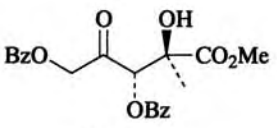
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
BzO—∥O—OBz	Sn(OTf)$_2$, NEPIP	CH$_3$COCO$_2$Me	BzO, O, OH, CO$_2$Me, OBz (93) 85/15	58
thiazolidinethione—NBn—Cbz			thiazolidinethione—OH—R—NBn—Cbz	
	Sn(OTf)$_2$, NEPIP	PhCHO	R = Ph, (94) 90/10	74
	"	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (96) 95/5	74
	"	n-C$_5$H$_{11}$CHO	R = n-C$_5$H$_{11}$, (98) 95/5	74
	"	i-PrCHO	R = i-Pr, (98) 95/5	74
	"	MeCHO	R = Me, (99) 95/5	74

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TABLE I. ALDOL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
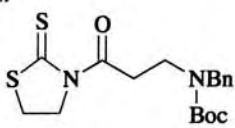
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C$_{21}$ thiazolidinethione—NBn—Boc			thiazolidinethione—OH—R—NBn—Boc	
	Sn(OTf)$_2$, NEPIP	PhCHO	R = Ph, (83) 90/10	74
	"	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (99) 95/5	74
	"	n-C$_5$H$_{11}$CHO	R = n-C$_5$H$_{11}$, (99) 95/5	74
	"	MeCHO	R = Me, (97) 95/5	74

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TABLE II. MICHAEL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION
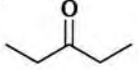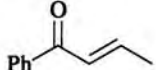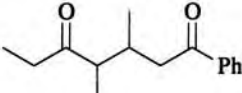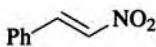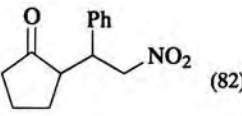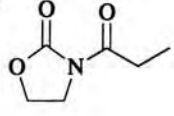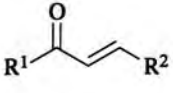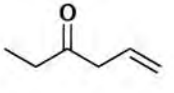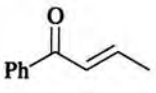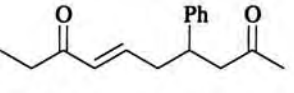
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C₅	Sn(OTf)₂, NEPIP	(Me₂HSiCl)	(72)	110, 111
	Sn(OTf)₂, NEPIP	Ph⌐NO₂	(82) 30/70	154
C₆	Sn(OTf)₂, NEPIP			111, 153
			R¹ = Me, R² = Ph, Me₂HSiCl (77) 92/8	
			Me₃SiCl (78) 29/71	
			R¹ = Me, R² = Me, Me₂HSiCl (56) 5/95	
			Me₃SiCl (56) 29/71	
			R¹ = Ph, R² = Me, Me₂HSiCl (85) 25/75	
			R¹R² = (CH₂)₃ Me₃SiCl (84) 38/62	
	Sn(OTf)₂, NEPIP	Ph	−45°, (60)	41

TABLE II. MICHAEL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)
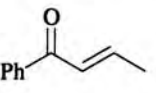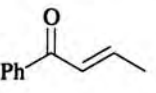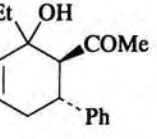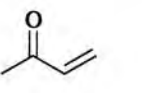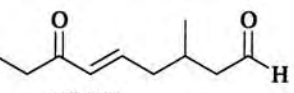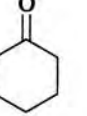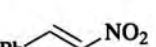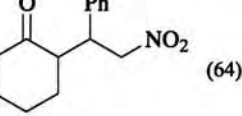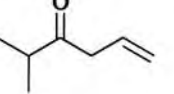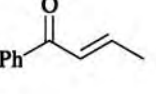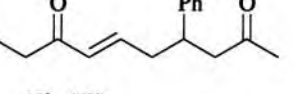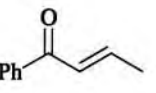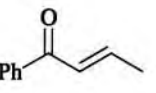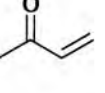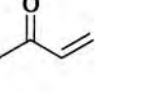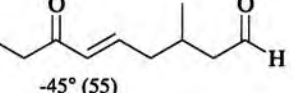
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)₂, NEPIP	Ph	−45 to 0°, (52)	41
	Sn(OTf)₂, NEPIP		−45° (38)	41
	Sn(OTf)₂, NEPIP	Ph⌐NO₂	(64) <7/93	154
C₇	Sn(OTf)₂, NEPIP	Ph	−45°, (72)	41
	Sn(OTf)₂, NEPIP	Ph	−45 to 0°, (66)	41
	Sn(OTf)₂, NEPIP		−45° (55)	41

TABLE II. MICHAEL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C8	Sn(OTf)2, NEPIP		-45°, (83)	41
	Sn(OTf)2, NEPIP		-45 to 0°, (73)	41
	Sn(OTf)2, NEPIP		-45° (75)	41
	Sn(OTf)2, NEPIP		-45°, (81)	41
	Sn(OTf)2, NEPIP		-45 to 0°, (70)	41

TABLE II. MICHAEL REACTION WITH ACHIRAL SUBSTRATES; NO OR SIMPLE DIASTEREOSELECTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	Sn(OTf)2, NEPIP		-45°, (71)	41
	Sn(OTf)2, NEPIP		-45 to 0°, (72)	41
C9	Sn(OTf)2, NEPIP	, TMSCl	(54)	111, 153
	Sn(OTf)2, NEPIP		(67) 24/76	154
C10	Sn(OTf)2, NEPIP		(76) 38/62	154

TABLE III. ENANTIOSELECTIVE ALDOL REACTION
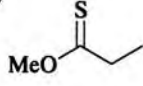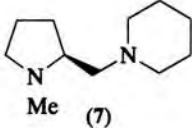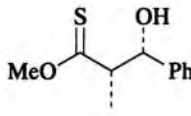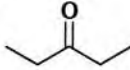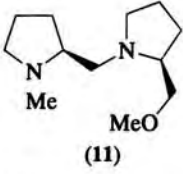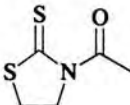
Starting Material	Acceptor	Chiral Ligand	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C₄	PhCHO	(7)	(73) 78/22, 90% ee	78
C₅				
	PhCHO	7	R = Ph, (54) 75/25, 45% ee	36
	PhCHO	(11)	R = Ph, (60) 75/25, 55% ee	36
	p-MeOC₆H₄CHO	7	R = *p*-MeOC₆H₄, (69), 89/11, 50% ee	36
	PhCHO	7	R = Ph, (79), 65% ee	36, 165
	i-PrCHO	7	R = *i*-Pr, (63), > 90% ee	36, 165
	Ph(CH₂)₂CHO	7	R = Ph(CH₂)₂, (76), 90% ee	36, 165

TABLE III. ENANTIOSELECTIVE ALDOL REACTION (*Continued*)
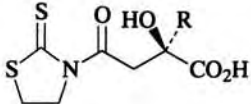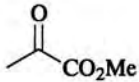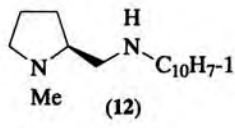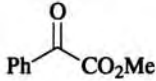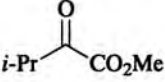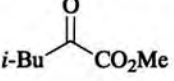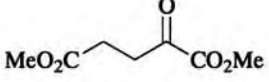
Starting Material	Acceptor	Chiral Ligand	Product(s) and Yield(s) (%), *syn/anti*	Refs.
	C₆H₁₁CHO	7	R = C₆H₁₁, (81), 88% ee	36, 165
	EtCHO	7	R = Et, (70), 90% ee	36, 165
	n-C₅H₁₁CHO	7	R = *n*-C₅H₁₁, (65), 90% ee	36, 165
	12	R = Me, (74), 85% ee	166
	12	R = Ph, (78), >95% ee	166
	12	R = *i*-Pr, (75), >95% ee	166
	12	R = *i*-Bu, (65), >95% ee	166
	12	R = MeO₂C(CH₂)₂, (80), >95% ee	166

TABLE III. ENANTIOSELECTIVE ALDOL REACTION (*Continued*)
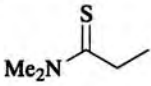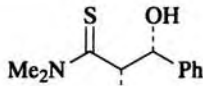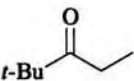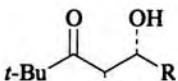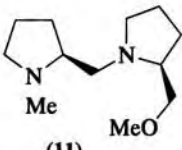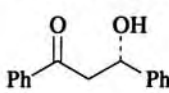
Starting Material	Acceptor	Chiral Ligand	Product(s) and Yield(s) (%), *syn/anti*	Refs.
(thioamide structure, Me$_2$N)	PhCHO	7	(product structure) (93), 92/8, 85% ee	78
(ketone structure, *t*-Bu)			(product structure, *t*-Bu, R)	
	PhCHO	7	R = Ph, (22), >95/5, 53% ee	36
	PhCHO	**7**	R = Ph, (29), >95/5, 80% ee	36
	Ph(CH$_2$)$_2$CHO	7	R = Ph(CH$_2$)$_2$, (35), >95/5, 53% ee	36
	Ph(CH$_2$)$_2$CHO	11	R = Ph(CH$_2$)$_2$, (40), >95/5, 70% ee	36
	p-ClC$_6$H$_4$CHO	11	R = *p*-ClC$_6$H$_4$, (30), >95/5, 80% ee	36
	p-MeOC$_6$H$_4$CHO	11	R = *p*-MeOC$_6$H$_4$, (24), >95/5, 77% ee	36
C$_8$ (PhCOCH$_3$)	PhCHO	7	(product structure, Ph, Ph) (35), 75% ee	36, 164

(chiral ligand **11** structure with Me, MeO groups)

TABLE III. ENANTIOSELECTIVE ALDOL REACTION (*Continued*)
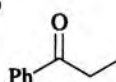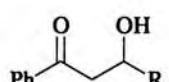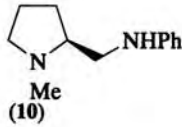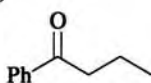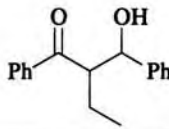
Starting Material	Acceptor	Chiral Ligand	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C$_9$ (Ph ketone structure)			(product structure, Ph, R)	
	PhCHO	7	R = Ph, (74), 85/15, 80% ee	36, 164
	p-MeC$_6$H$_4$CHO	7	R = *p*-MeC$_6$H$_4$, (72), 89/11, 80% ee	36, 164
	p-ClC$_6$H$_4$CHO	7	R = *p*-ClC$_6$H$_4$, (72), 85/15, 85% ee	36, 164
	p-MeOC$_6$H$_4$CHO	7	R = *p*-MeOC$_6$H$_4$, (78), 89/11, 80% ee	36, 164
	i-PrCHO	(ligand **10**, NHPh)	R = *i*-Pr, (69), >95/5, 75% ee	36, 164
	t-BuCHO	10	R = *t*-Bu, (57), 100/0, 90% ee	36, 164
	C$_6$H$_{11}$CHO	10	R = C$_6$H$_{11}$, (24), >95/5, 77% ee	36, 164
C$_{10}$ (Ph ketone structure)	PhCHO	7	(product structure, Ph, Ph) (72), 83/17, 75% ee	36, 164
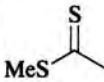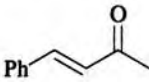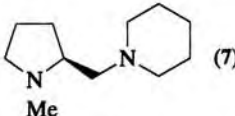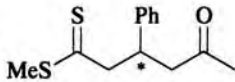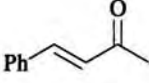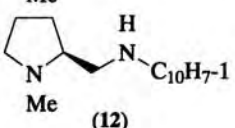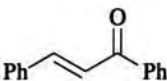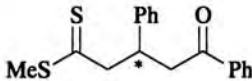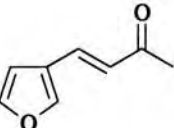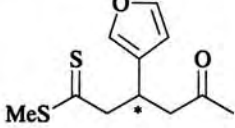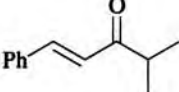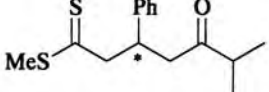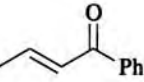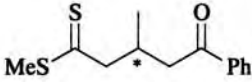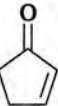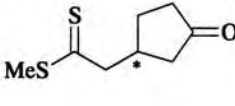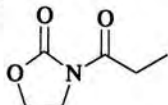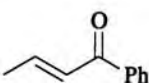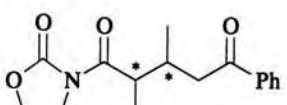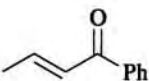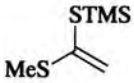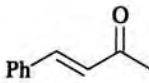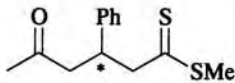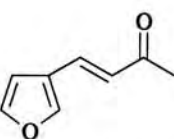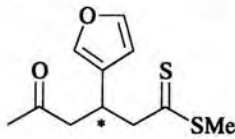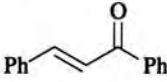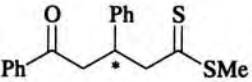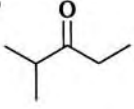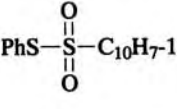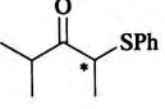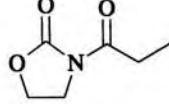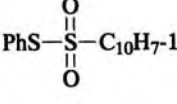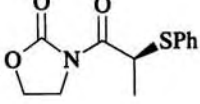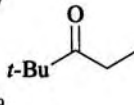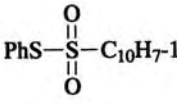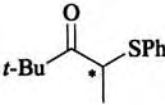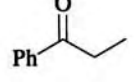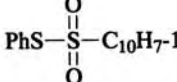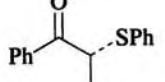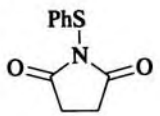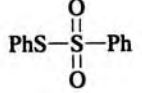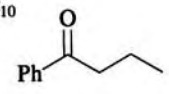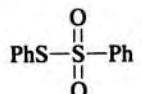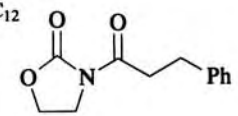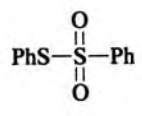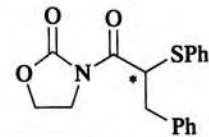
(chiral ligand **10** structure with Me, NHPh groups)
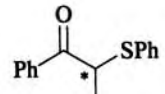
TABLE IV. ENANTIOSELECTIVE MICHAEL REACTION[a]

Starting Material	Acceptor	Chiral Ligand	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C₃ MeS–C(=S)–CH₃	Ph–CH=CH–C(=O)–CH₃	(7)	(73), 26% ee	167
	Ph–CH=CH–C(=O)–CH₃	(12)	" (82), 70% ee	167
	Ph–CH=CH–C(=O)–Ph	12	(75), 40% ee	167
	furyl–CH=CH–C(=O)–CH₃	12	(79), 60% ee	167
	Ph–CH=CH–C(=O)–CH(CH₃)₂	12	(79), 60% ee	167
	CH₃–CH=CH–C(=O)–Ph	12	(62), 15% ee	167
	2-cyclopentenone	12	(44), 30% ee	167

TABLE IV. ENANTIOSELECTIVE MICHAEL REACTION (*Continued*)

Starting Material	Acceptor	Chiral Ligand	Product(s) and Yield(s) (%), *syn/anti*	Refs.
C₆ 3-propionyl-oxazolidin-2-one	CH₃–CH=CH–C(=O)–Ph	7	(70), >95/5, 80% ee (*syn*)	167
	CH₃–CH=CH–C(=O)–Ph	12	" (72), >95/5, 93% ee (*syn*)	167
MeS–C(STMS)=CH₂	Ph–CH=CH–C(=O)–CH₃	Sn(OTf)₂ (10 mol%) + 12	(80), 70% ee	78,168
	furyl–CH=CH–C(=O)–CH₃	Sn(OTf)₂ (10 mol%) + 12	(82), 60% ee	78,168
	Ph–CH=CH–C(=O)–Ph	Sn(OTf)₂ (10 mol%) + 12	(79), 40% ee	78,168

[a] The absolute configurations at * were not determined.

TABLE V. ENANTIOSELECTIVE SULFENYLATION[a]

Starting Material	Acceptor[b]	Product(s) and Yield(s) (%)
C6	PhS—S—C10H7-1 (with two O)	(72), 50% ee
	PhS—S—C10H7-1 (with two O)	(93), 81% ee
C7 *t*-Bu	PhS—S—C10H7-1 (with two O)	*t*-Bu (52), 70% ee
C9 Ph	PhS—S—C10H7-1 (with two O)	Ph (78), 85% ee
	PhSCl	" (63), 54% ee
		" (27), 60% ee
	PhS—S—Ph (with one O)	" (58), 75% ee
C10 Ph	PhS—S—Ph (with one O)	Ph (80), 75% ee
C12	PhS—S—Ph (with one O)	(91), 82% ee

[a] The absolute configurations at * were not determined.
[b] All reactions were carried out with Sn(OTf)2, NEPIP, and chiral diamine **7**.
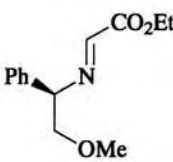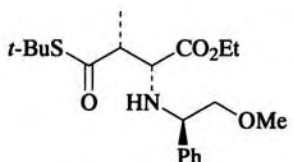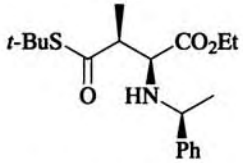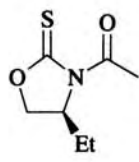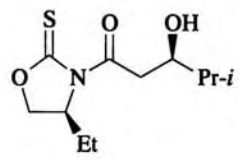
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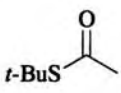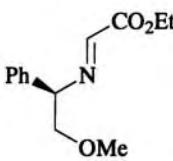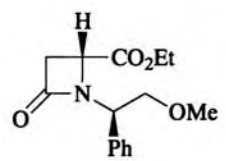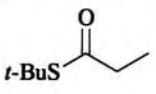TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION
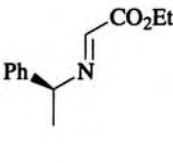
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
C$_6$	LDA, SnCl$_2$		(52), 92/8	174
C$_7$	LDA, SnCl$_2$		(85), 75/25	174
	LDA, Sn(OTf)$_2$	"	" (81), 67/33	174
	LDA, SnCl$_2$		(78), 91/9	174
	Sn(OTf)$_2$, NEPIP	i-PrCHO	(60), 91/9	38

TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
	Sn(OTf)$_2$, NEPIP	Ph~CHO	(77), 93/7	38
	Sn(OTf)$_2$, NEPIP	CHO	(74), 93/7	38
	Sn(OTf)$_2$, NEPIP	CHO	(74), 89/11	38
C$_8$ *t*-BuS	LDA, SnCl$_2$	Ph—N=—CO$_2$Et	(78), 95/5	174

TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
Et	Sn(OTf)$_2$, NEPIP	PhCHO	(74), 86/14	38
Pr-*i*	Sn(OTf)$_2$, NEPIP	Ph~CHO	(81), 97/3	38
	Sn(OTf)$_2$, NEPIP	CHO	(70), 97/3	38
Pr-*i*	Sn(OTf)$_2$, NEPIP	R^1 R^2 / O OH	R^1 = R^2 = H (86), >99/1	177
			R^1 = H, R^2 = Me (85), 99/1	177
			R^1 = H, R^2 = Et (90), 99/1	177

TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)
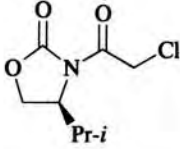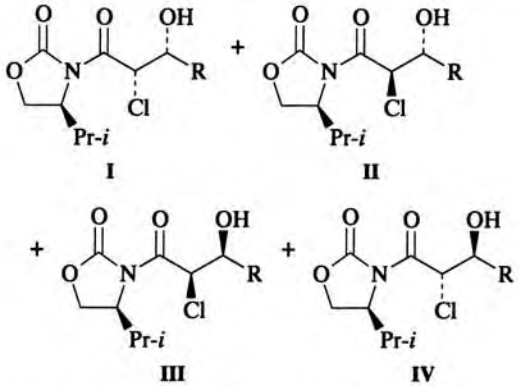
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
			$R^1 = H, R^2 = n\text{-Pr}$ (85), >99/1	177
			$R^1 = H, R^2 = i\text{-Pr}$ (93), 99/1	177
			$R^1 = H, R^2 = Ph$ (81), 99/1	177
			$R^1 = R^2 =$ (87), 99/1	177
			$R^1 = R^2 = (CH_2)_4$ (90), 99/1	177

I   II

III   IV

	Sn(OTf)$_2$, NEPIP	$n\text{-}C_5H_{11}CHO$	R = $n\text{-}C_5H_{11}$, (84), **I/II/III/IV** = 50/25/6/19	39
	LDA, SnCl$_2$	$n\text{-}C_5H_{11}CHO$	R = $n\text{-}C_5H_{11}$, (84), **I/II/III/IV** = 73/12/6/9	39
	Sn(OTf)$_2$, NEPIP	$i\text{-BuCHO}$	R = $i\text{-Bu}$, (68), **I/II/III/IV** = 61/21/9/9	39
	LDA, SnCl$_2$	$i\text{-BuCHO}$	R = $i\text{-Bu}$, (73), **I/II/III/IV** = 78/11/4/7	39
	Sn(OTf)$_2$, NEPIP	$i\text{-PrCHO}$	R = $i\text{-Pr}$, (64), **I/II/III/IV** = 50/25/10/15	39
	LDA, SnCl$_2$	$i\text{-PrCHO}$	R = $i\text{-Pr}$, (77), **I/II/III/IV** = 74/18/4/4	39

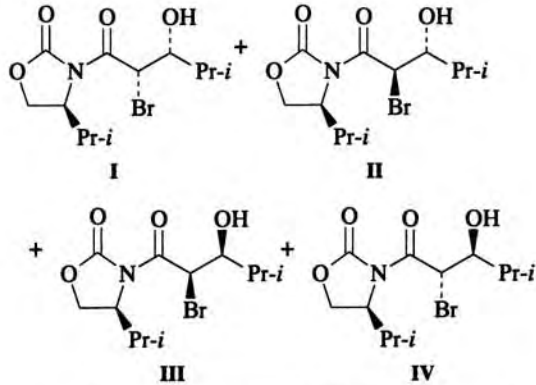TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
			I II III IV	
	LDA, SnCl$_2$	$i\text{-PrCHO}$	R = $i\text{-Pr}$, (65), **I/II/III/IV** = 80/14/3/3	39
	Sn(OTf)$_2$, $i\text{-Pr}_2$NEt	PhCHO	(71), 86/14	178
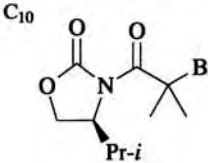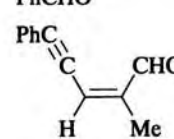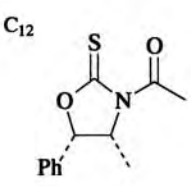
C$_9$

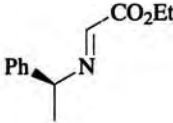| | LDA, SnCl$_2$ | | (79), 95/5 | 174 |

TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)

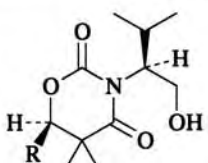| Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
C$_{10}$				
	SnCl$_2$, LAH	PhCHO	R = Ph, (69), 97/3	180
		PhC≡C–CH=C(Me)CHO	R = PhC≡C–CH=C(Me), (76), >99.5/0.5	180, 181
C$_{12}$				
	Sn(OTf)$_2$, NEPIP	MeCHO	R = Me, (62), 76/24	38
	Sn(OTf)$_2$, NEPIP	*i*-PrCHO	R = *i*-Pr, (68), 89/11	38
	Sn(OTf)$_2$, NEPIP	*i*-BuCHO	R = *i*-Bu, (64), 82/18	38

TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)
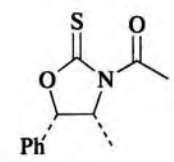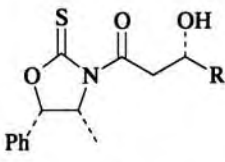
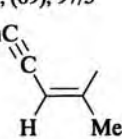| Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
	LDA, SnCl$_2$	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (59), 58% ee	46
	"	*n*-PrCHO	R = *n*-Pr, (60), 58% ee	46
	"	Et$_2$CHCHO	R = Et$_2$CH, (60), 69% ee	46
	"	C$_6$H$_{11}$CHO	R = C$_6$H$_{11}$, (65), 73% ee	46
	"	*t*-BuCHO	R = *t*-Bu, (65), 86% ee	46
	Sn(OTf)$_2$, NEPIP	*i*-PrCHO	(65), 83.7/16.3	38
C$_{13}$				
	Sn(OTf)$_2$, NEPIP	MeCHO	R = Me, (75), 91/9	179
	"	*i*-PrCHO	R = *i*-Pr, (92), 99/1	179
	"	PhCHO	R = Ph, (91), 99/1	179

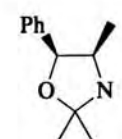TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)
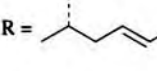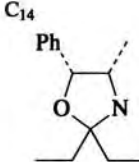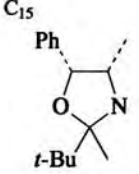
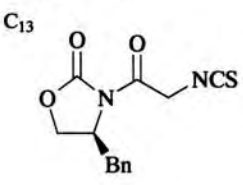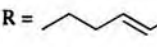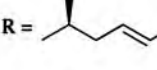| Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
	Sn(OTf)$_2$, NEPIP	CHO	R = (81), 93/7	179
	Sn(OTf)$_2$, NEPIP	CHO	R = (71), 97/3	179
	Sn(OTf)$_2$, NEPIP	CHO	R = (73), 94/6	179
C$_{14}$				
	LDA, SnCl$_2$	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (77), 87/13, 92% ee (*syn*)	182
	"	EtCHO	R = Et, (61), 88/12, 95% ee (*syn*)	182
	"	C$_6$H$_{11}$CHO	R = C$_6$H$_{11}$, (75), 90/10, 92% ee (*syn*)	182
C$_{15}$	"	*t*-BuCHO	R = *t*-Bu, (56), 86/14, >95% ee (*syn*)	182
t-Bu				
	LDA, SnCl$_2$	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (64), 85% ee	46
	"	C$_6$H$_{11}$CHO	R = C$_6$H$_{11}$, (54), 84% ee	46
	"	*t*-BuCHO	R = *t*-Bu, (56), >95% ee	46

TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)
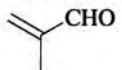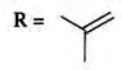
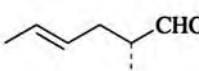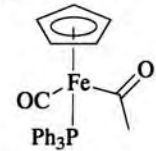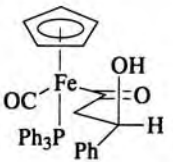| Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
C$_{16}$				
	LDA, SnCl$_2$	PhCHO	(66), 93/7	195
	LDA, SnBr$_2$	"	(33), 92/8	195
	LDA, Sn(OTf)$_2$	"	(38), 66/34	195
Bn			Bn	
	Sn(OTf)$_2$, Et$_3$N	EtCHO	R = Et, (71), 79/21	194
	"	*i*-PrCHO	R = *i*-Pr, (83), 95/5	194
	"	PhCHO	R = Ph, (85), 89/11	194
	"	CHO	R = , (77), 95/5	194

TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
C$_{17}$				
	LDA, SnCl$_2$	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (68), 70% ee	46
	"	*n*-PrCHO	R = *n*-Pr, (69), 76% ee	46
	"	C$_6$H$_{11}$CHO	R = C$_6$H$_{11}$, (64), 77% ee	46
	"	*t*-BuCHO	R = *t*-Bu, (66), 93% ee	46
C$_{19}$				
	Sn(OTf)$_2$, NEPIP	Ph(CH$_2$)$_2$CHO	R = Ph(CH$_2$)$_2$, (91), >98/2	175
	"	PhCHO	R = Ph, (99), >98/2	175
	"	*n*-C$_5$H$_{11}$CHO	R = *n*-C$_5$H$_{11}$, (91), >98/2	175
	"	*n*-PrCHO	R = *n*-Pr, (98), >98/2	175
	"	MeCHO	R = Me, (98), >98/2	175

TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)
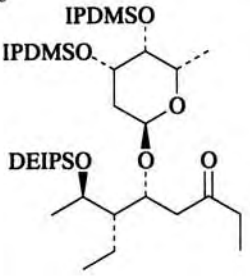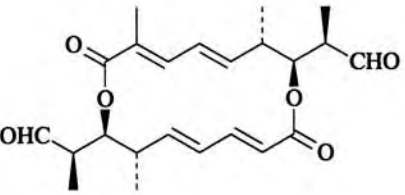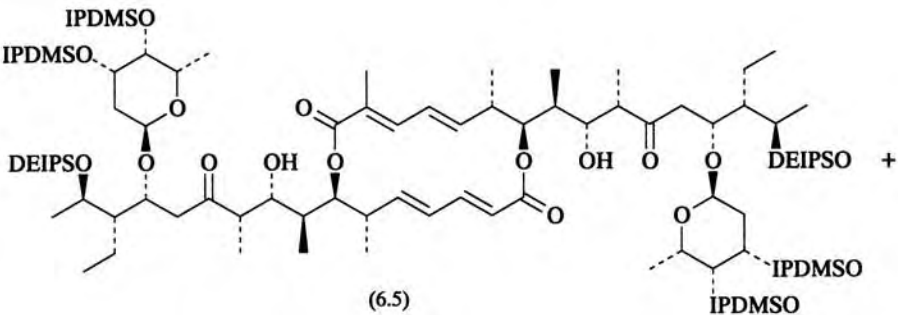
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.
C$_{33}$	Sn(OTf)$_2$, NEPIP			220

(6.5)

TABLE VI. DIASTEREOSELECTIVE ALDOL REACTION (*Continued*)
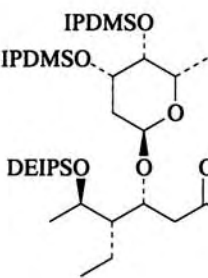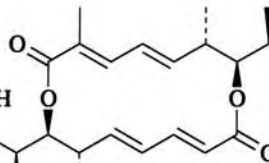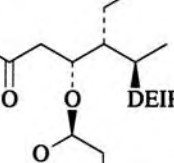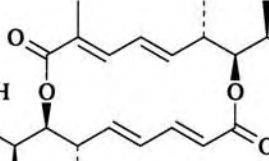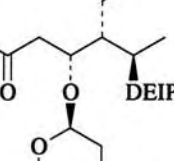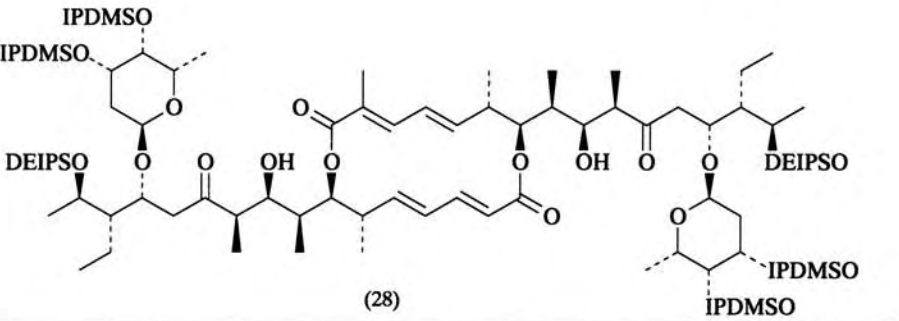
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), diastereomer ratio	Refs.

(21)

(28)

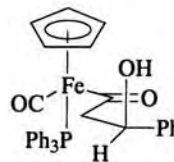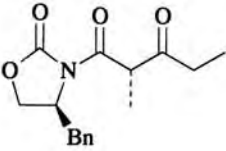## TABLE VII. DIASTEREOSELECTIVE ALDOL ALKYLATION
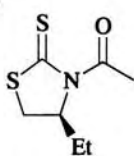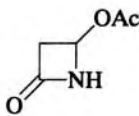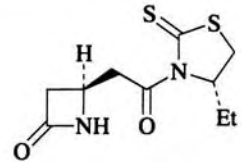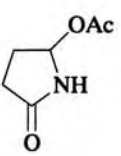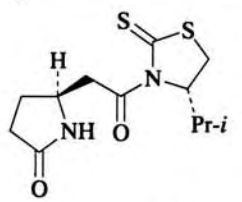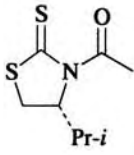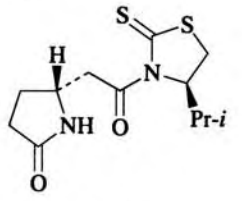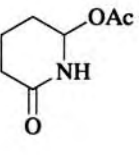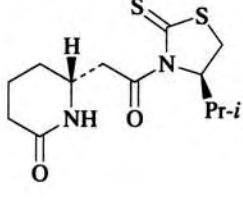
	Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C_7		Sn(OTf)$_2$, NEPIP		(82), 95/5	183
C_8		Sn(OTf)$_2$, NEPIP		(67), >97/3	189
		Sn(OTf)$_2$, NEPIP		(66), >97/3	189
		Sn(OTf)$_2$, NEPIP		(63), >98/2	189

TABLE VII. DIASTEREOSELECTIVE ALDOL ALKYLATION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Sn(OTf)$_2$, NEPIP		(96), 98/2	186
	Sn, I$_2$ (cat.), AgBF$_4$ (5 mol%)		(75-80), 75/25	190
C$_9$	Sn(OTf)$_2$, *i*-Pr$_2$NEt, ZnBr$_2$		+ 59/41	184

TABLE VII. DIASTEREOSELECTIVE ALDOL ALKYLATION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Sn(OTf)$_2$, *i*-Pr$_2$NEt, ZnBr$_2$		(80), 92/8	184
	Sn(OTf)$_2$, NEPIP		(55), 97/3	187
	Sn(OTf)$_2$, NEPIP		(55), 97/3	187
C$_{10}$	Sn(OTf)$_2$, NEPIP		(64), >99/1	188, 189

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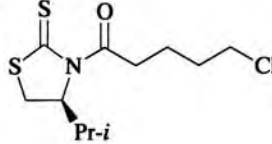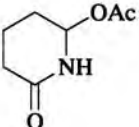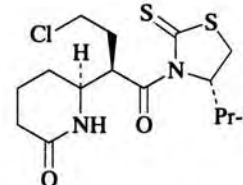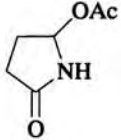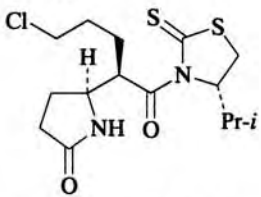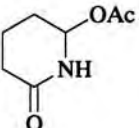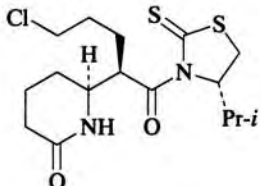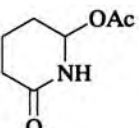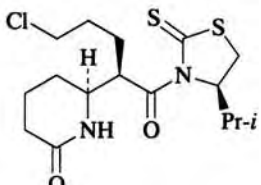
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TABLE VII. DIASTEREOSELECTIVE ALDOL ALKYLATION (*Continued*)

Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Sn(OTf)$_2$, NEPIP		(57), >98/2	188, 189
C$_{11}$	Sn(OTf)$_2$, NEPIP		(72), >99/1	188, 189
	Sn(OTf)$_2$, NEPIP		(73), >96/4	188, 189
	Sn(OTf)$_2$, NEPIP		(73), >96/4	189

TABLE VII. DIASTEREOSELECTIVE ALDOL ALKYLATION (*Continued*)
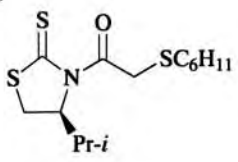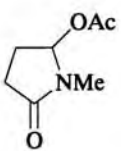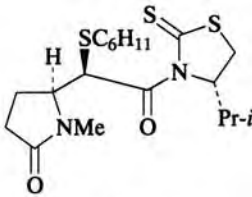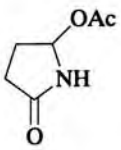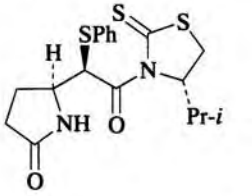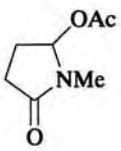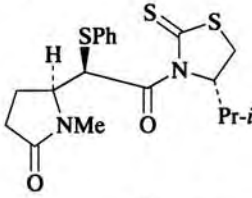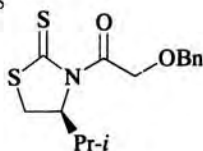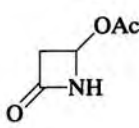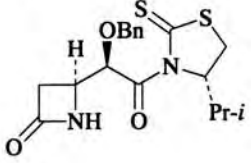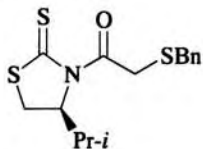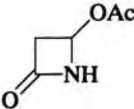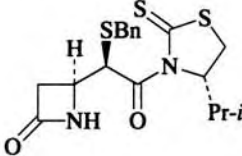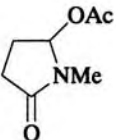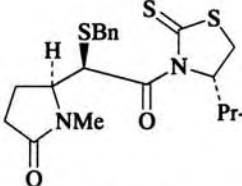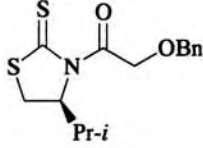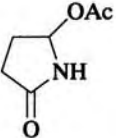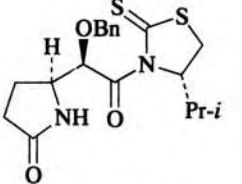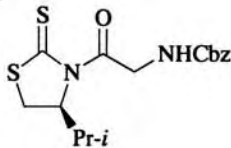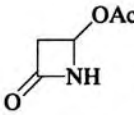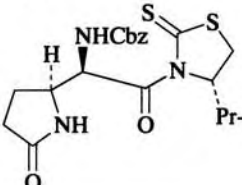
Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
C$_{14}$	Sn(OTf)$_2$, NEPIP		(46), 83/17	185
	Sn(OTf)$_2$, NEPIP		(92), >95/5	189
	Sn(OTf)$_2$, NEPIP		(57), 91/9	185
C$_{15}$	Sn(OTf)$_2$, NEPIP		(79), 97/3	187

TABLE VII. DIASTEREOSELECTIVE ALDOL ALKYLATION (*Continued*)

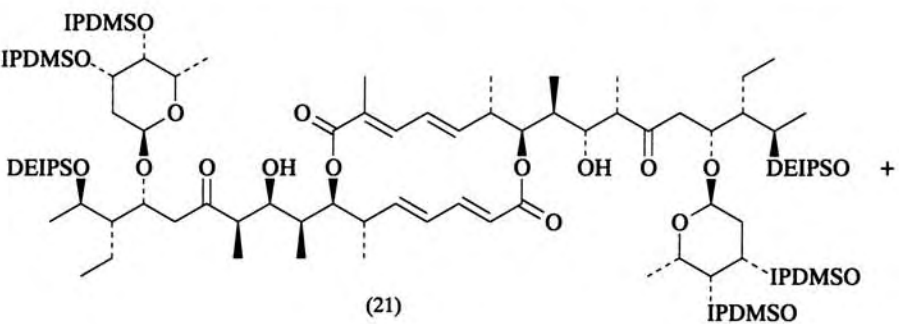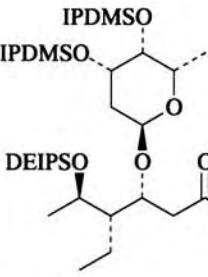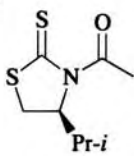| Starting Material	Enolization Reagent	Acceptor	Product(s) and Yield(s) (%), Diastereomer Ratio	Refs.
	Sn(OTf)$_2$, NEPIP		(84), 97/3	187
	Sn(OTf)$_2$, NEPIP		(57), 84/16	185
	Sn(OTf)$_2$, NEPIP		(78), >98/2	189
C$_{16}$	Sn(OTf)$_2$, NEPIP		(52), 99/1	187

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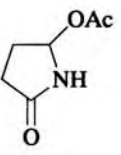13. C. H. Heathcock in *Comprehensive Organic Synthesis*, B. M. Trost, Ed., Pergamon Press, Oxford, 1991, Vol. **2**, p. 181.

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