# Lithioalkenes from Arenesulfonylhydrazones

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1. Introduction

Among the most important of all carbon–carbon bond forming methods are reactions of electrophiles with organolithium compounds. (1, 2) As part of this large group of reagents, regio- and stereoselectively prepared alkenyllithiums are valuable intermediates for the controlled construction of a wide variety of substituted alkenes. This review covers a highly selective procedure for the preparation of relatively complex alkenyllithium species from ketone arenesulfonylhydrazones. The reaction of these vinyl anions with various electrophiles affords a wide range of specifically substituted di-, tri-, and tetrasubstituted alkenes.
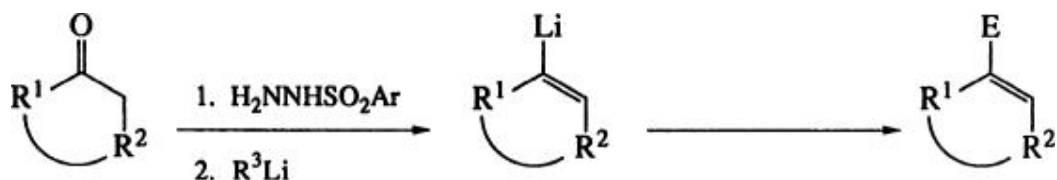
This methodology arose from early studies on the thermal decomposition of sodium salts of p-toluenesulfonylhydrazones (tosylhydrazones) and two subsequent modifications of that reaction. In the early 1950s Bamford and Stevens reported a new reaction based on the thermally induced decomposition of ketone tosylhydrazone monosodium salts, producing products derived either from carbene intermediates (aprotic conditions) or carbocations (protic conditions). The protic reaction is of marginal synthetic value because mixtures of carbocation-derived products are normally obtained; however, the aprotic reaction has found widespread use in the synthesis of multicyclic, strained hydrocarbons. Both reactions have been covered in reviews. (3)

It was later found that treating a tosylhydrazone with ethereal alkyllithium, instead of the much weaker alkoxide bases used previously, results in a very different reaction. Under these conditions an alkene derived from an alkenyllithium intermediate is the sole product. This process, commonly known as the Shapiro reaction, has been applied to the preparation of a large number of structurally diverse alkenes and is the subject of an earlier review. (3)

Unfortunately, trapping of the vinyllithium intermediate proved to be so inefficient and unpredictable under a number of different conditions that the reaction was of little utility as a method of vinyllithium generation. In 1975, however, conditions were reported (4, 5) that not only gave high yields of olefin but also nearly quantitative incorporation of electrophiles. The only remaining drawback was that efficient trapping of tosylhydrazone-derived vinyllithiums occurs only with the use of excess base (³3 equivalents of *n*-butyllithium) rather than the stoichiometric 2 equivalents required by the mechanism (Section II), even though the olefin yield was quite good. Eventually, this nagging stoichiometry problem, which necessitates the use of excess electrophile as well as excess base, was solved by the use of ketone 2,4,6-triisopropylbenzenesulfonylhydrazones (trisylhydrazones) in place of tosylhydrazones. (6) An account of some synthetically useful aspects of the Shapiro reaction and its subsequent variants has appeared. (7)

This review covers the generation of vinyllithiums from arenesulfonylhydrazones (8) under conditions that allow efficient trapping with electrophiles other than proton sources. Examples in which trapping of the intermediate vinyllithium was not demonstrated, including reactions conducted under standard "Shapiro reaction" conditions, are excluded.

2. Mechanism

The Shapiro reaction occurs when a tosylhydrazone **1** is treated with ethereal alkyllithium, resulting in the removal of the N-H proton to give **2** and then one proton from the less-substituted α position to give the dianion **3**. Elimination of lithium toluenesulfinate in the rate-limiting step gives the lithium alkenyl diazenide **4**, which suffers loss of nitrogen to afford the alkenyllithium **5**. This vinyl anion undergoes protonation under these reaction conditions to give a simple alkene as the major product, and it is logical to assume that the proton source is solvent in this situation.

However, even if this reaction is run in a very nonacidic solvent such as hexane (in which the reactants are insoluble), the lithioalkene intermediate **5** can be trapped with deuterium oxide only with very poor efficiency. Since protonation by solvent in this case is extremely unlikely, it has been suggested (9) that the proton source is actually the tosylhydrazone monoanion **2**, which is
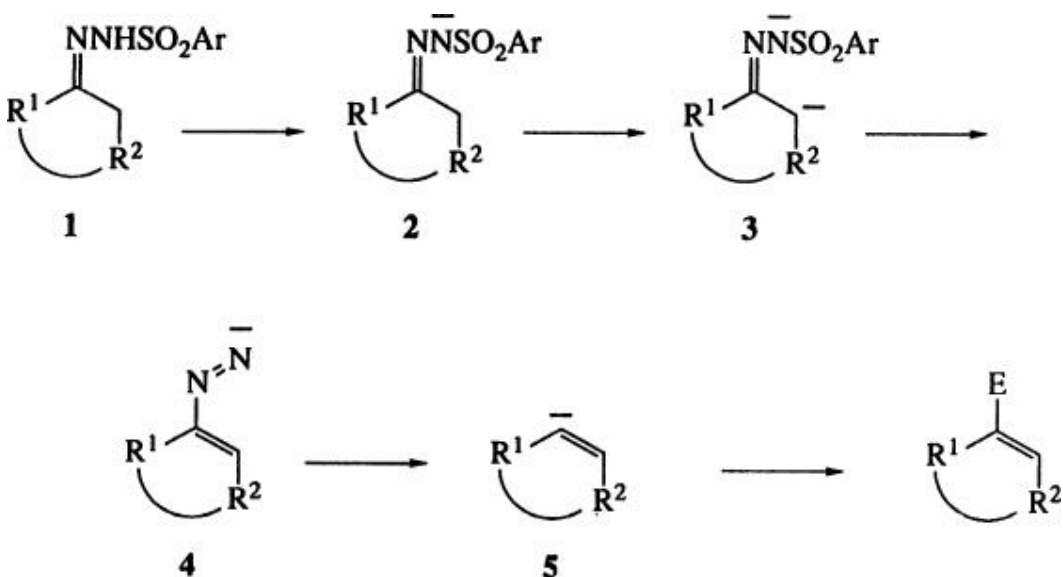
occluded in an aggregate and thus exposed to other monoanions and a surface layer of dianions, but not to alkyllithium base. As vinyl anion forms at the surface, it either diffuses away intact or first reacts with a monoanion in the adjacent layer to give a new dianion and the simple alkene. The finding (10) that 1.1 equivalents of base is sufficient to form the alkene quantitatively from tosylhydrazones (i.e., the decomposition is catalytic in external base once the monoanion has formed) supports this suggestion by illustrating that the product vinyl anion is a strong enough base to remove an α proton from unreacted tosylhydrazone monoanion.

Trapping of the vinyl anion generated from tosylhydrazones in either hexane or diethyl ether is so inefficient and unpredictable under these conditions that the reaction is of little utility as a method of vinyl anion generation. There were no examples of efficient quenching with electrophiles until two independent reports (4, 5) of successful reaction with electrophiles by the simple expedient of using *N,N,N¢,N¢*-tetramethylethylenediamine (TMEDA) as solvent. The precise reason that the use of TMEDA results in efficient vinyllithium generation without premature quenching is still unclear, although presumably it is nonacidic enough to avoid protonating the vinyl anion while providing sufficient solubility for the reactants (although it does slowly undergo metalation during the reaction (11, 12)).

One final important aspect of the tosylhydrazone dianion decomposition mechanism is the requirement for excess base ($\geq$3.0 equivalents) to obtain efficient alkenyllithium trapping. Since the benzylic position had been ruled out as the acidic site by experiments on benzenesulfonylhydrazones, (10) the aromatic protons *ortho* to the tosyl SO_2 substituent were considered, based on earlier work on the *ortho*-metalation of sulfonamides. (13) A deuterium quenching study for the reaction of 2-octanone tosylhydrazone (6) clearly shows that quantitative formation of the dianion **6** occurs at –78°, but that if the reaction mixture is allowed to warm to 0°, excess *n*-butyllithium *ortho*-metalates the ring quantitatively to give a trianion *before* the vinyl anion is formed in significant amounts. The trianion then decomposes to the vinyl anion, which is stable under these conditions and can be trapped by electrophiles. The use of only 2 equivalents of base leaves the ring unmetalated and vulnerable to attack by newly formed vinyl anion. Thus, the requirement for excess base stems from the need to "premetalate" the tosyl ring, removing the relatively acidic *ortho* hydrogen before it can protonate the alkenyllithium product.

6
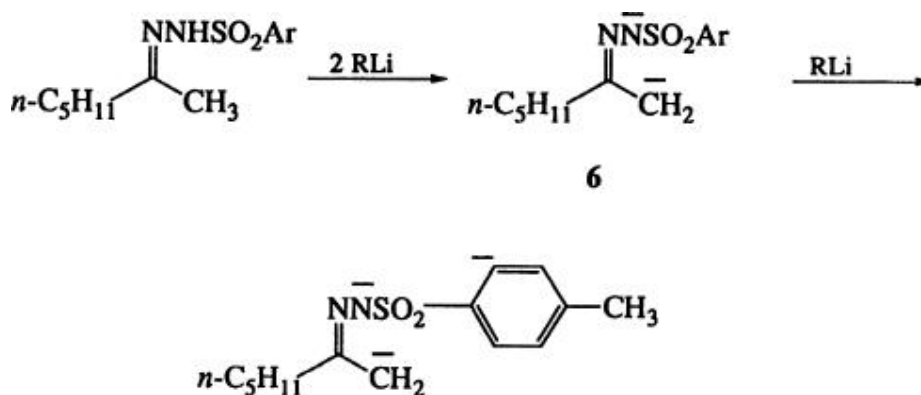
In order to solve the stoichiometry problem, a modified sulfonylhydrazone

leaving group containing no acidic *ortho* protons was required. Earlier use of 2,4,6-triisopropylbenzenesulfonyl ("trisyl") hydrazine for diazene ("diimide") generation (14) suggested employing trisylhydrazones for vinyllithium generation. Indeed, these derivatives proved to solve the stoichiometry problem, being incapable of undergoing *ortho* metalation (nor do they suffer benzylic metalation). As a result, trisylhydrazones allow the use of just 2 equivalents of strong base for dianion formation, and only a single equivalent of electrophile is needed to efficiently trap the resultant vinyllithium. Further, trisylhydrazone dianions undergo elimination much faster than do those derived from tosylhydrazones (seconds at 0° compared to hours), presumably because of the relief of steric strain in going to the transition state for trisyl elimination. This rate enhancement allows the use of even relatively acidic solvents such as tetrahydrofuran, which normally protonates vinyllithiums generated from tosylhydrazone during the relatively long time period required for tosyl dianion decomposition.

3. Scope and Limitations

3.1. Formation of Arenesulfonylhydrazones

By far the most common sulfonylhydrazone derivatives reported to undergo vinyllithium formation have been ketone tosyl- or trisylhydrazones, although there are a few reports of the use of benzenesulfonylhydrazones. In terms of availability and cost of precursors, tosylhydrazones, which are prepared from a ketone and commercially available tosylhydrazine, are preferred. Equimolar amounts of the reactants are generally dissolved in methanol, ethanol, or acetic acid—usually in the presence of an acidic catalyst such as concentrated hydrochloric acid—and allowed to react at room temperature or somewhat above, and then stored in the cold, after which the crystalline tosylhydrazone can be isolated in good yield by filtration. Even hindered ketones such as camphor react smoothly at somewhat higher temperatures. (3) Diethyl ether can also be utilized as the reaction solvent, and reportedly is superior to alcohols. (15)

Although trisylhydrazones are prepared in an analogous manner (commonly in methanol, ethanol, acetonitrile, or diethyl ether), the starting trisylhydrazine is not currently commercially available; it must be prepared from the sulfonyl chloride and hydrazine hydrate. (6) Since trisylhydrazine decomposes to diazene at a significant rate in solution at room temperature, (14) its reaction with hindered ketones (which can take many hours) should be conducted with a stoichiometric amount of acid, which protonates the basic hydrazine nitrogen and thereby retards the rate of this side reaction relative to hydrazone formation. This procedure, carried out in methanol or acetonitrile as the reaction solvent, provides trisylhydrazones of hindered ketones such as camphor and diisopropyl ketone in good yield, (6) although extraordinarily crowded ketones can be totally resistant to trisylhydrazone formation. (16)

H$_2$NNHTris → no hydrazone formed   (Ref. 16)
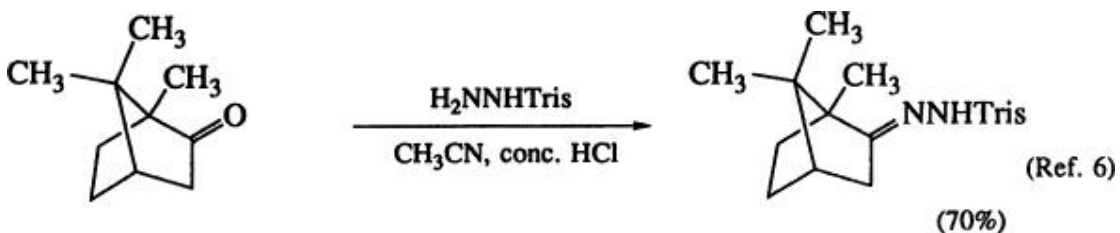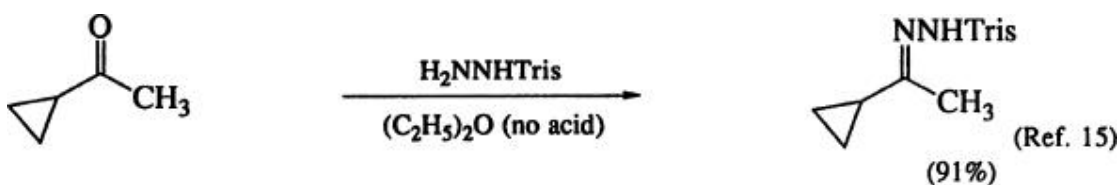
Arenesulfonylhydrazones exist as mixtures of *E* and *Z* isomers which usually cannot be physically separated at ambient temperatures (17) because the inversion barrier of the azomethine bond is too low, although spectroscopic methods can distinguish between the two isomers. (18) As expected, the *E/Z* ratio for any given hydrazone is dependent upon the sizes of the groups attached to the azomethine carbon, with the less sterically crowded *E* isomer usually predominating.

E/Z Ratio (6, 18)

85:15

>98:2

>98:2
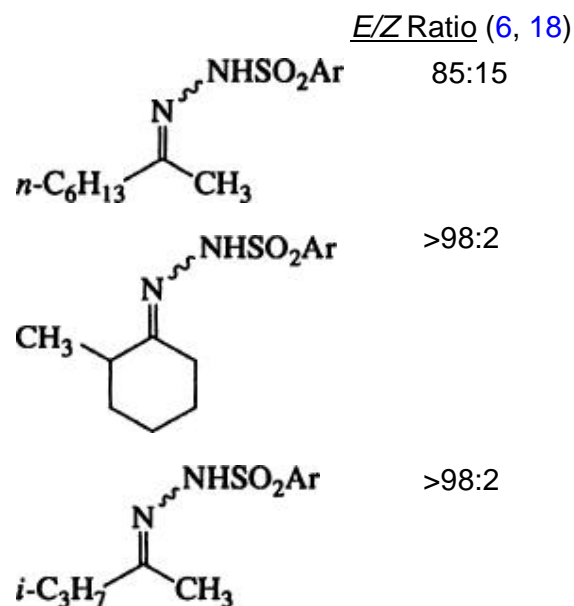
Although a number of cyclic ketones with α -stereogenic centers have been converted into arenesulfonylhydrazones, there is no unambiguous evidence on whether this process epimerizes stereochemically labile α substituents in acyclic ketones or in cyclohexanones. On the other hand, a *cis*-2,3-dialkylcyclopentanone suffers partial epimerization to the more stable

trans diastereomer during tosylhydrazone formation (and further upon standing as the crystalline solid). (19)

(ratio varies depending upon conditions)
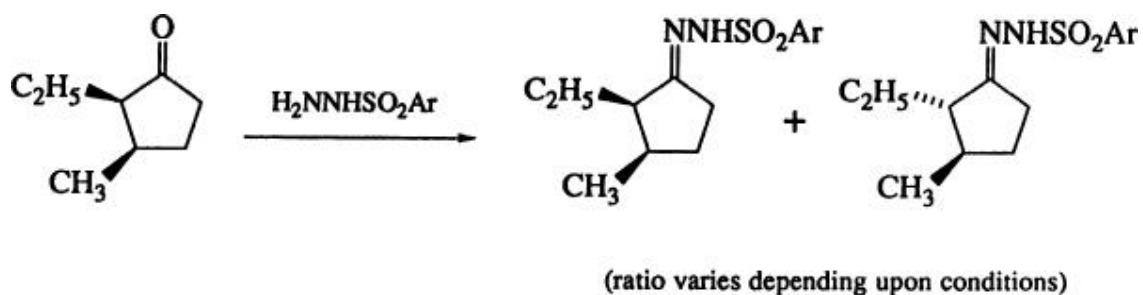
Arenesulfonylhydrazones of aldehydes are prepared by the same general method, with minor modifications. (15) The formation of β -ketoester tosylhydrazones has also been reported, (20) as has a procedure for converting orthoesters into ester tosylhydrazones. (21) Since none of these hydrazones leads to trappable vinyllithiums, however, specific details are not discussed.

Trisylhydrazones of amides ("trisylamidrazones"), which do react to give the corresponding vinyllithiums, are prepared by an indirect route that begins with acylation of trisylhydrazine. The resultant hydrazide reacts with phosphorus pentachloride and morpholine to provide the trisylamidrazone. (22)
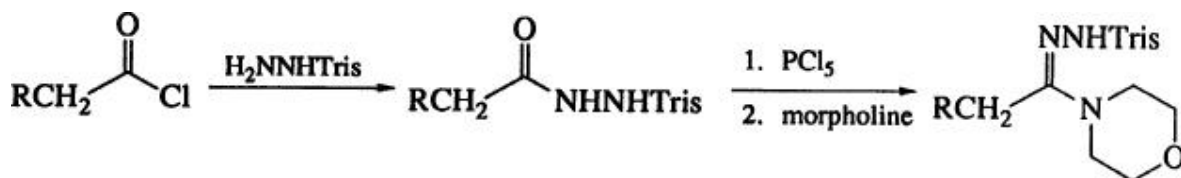
3.2. Substrates for Vinyllithium Formation

Most ketone tosyl- or trisylhydrazones with at least one α proton undergo dianion formation followed by vinyllithium formation. The range of vinyllithiums available includes those derived from saturated acyclic ketones as well as cyclic alkanones such as substituted cyclopentanones and cyclohexanones, decalones, and steroidal ketones. There are also a few examples of the reaction in medium and large rings. The generalized examples shown illustrate the structural types of vinyllithiums that have been prepared directly from tosyl- or trisylhydrazones of saturated ketones.

$$n = 1, 2, 3, 4, 8$$
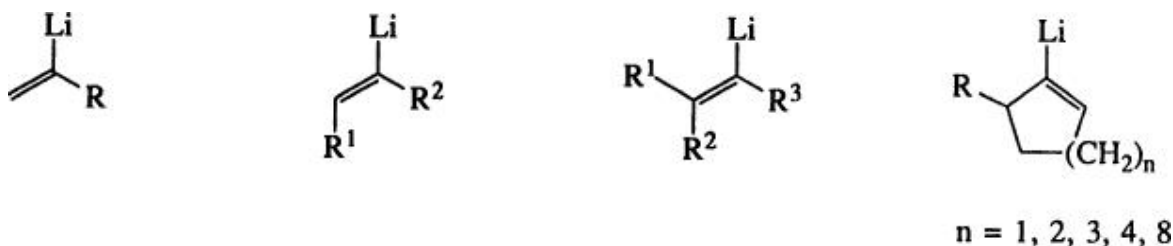
Two important substitution patterns are not shown: 1-lithioalkenes cannot be prepared by this method (for reasons to be discussed later), and more highly substituted regioisomers must be prepared by the dianion alkylation procedure described in the section "Dianion Functionalization Followed by Vinyllithium Formation."

Tosyl- or trisylhydrazones of α, β-unsaturated ketones, (5, 6, 23-29) α-keto amides, (30-32) and amides (22) also yield the expected vinyllithiums.

(Ref. 25)
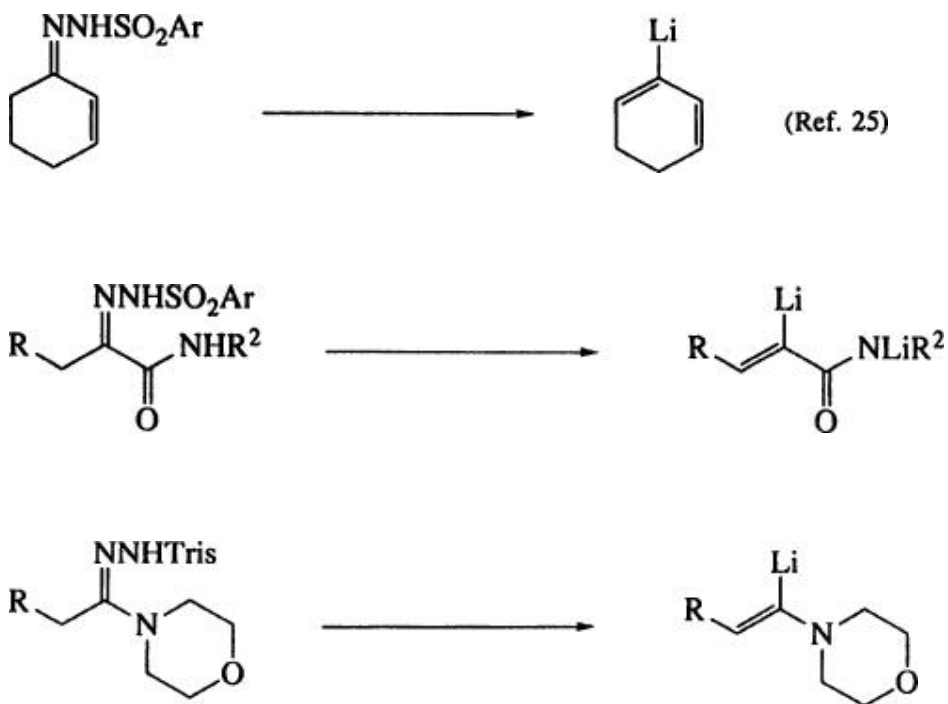
The latter example is noteworthy in that it is the only arenesulfonylhydrazone-derived vinyllithium to have been generated from a substrate other than a ketone. Since the reaction of such lithiated enamines with electrophiles gives an enamine, a very interesting double alkylation can be achieved. (22)
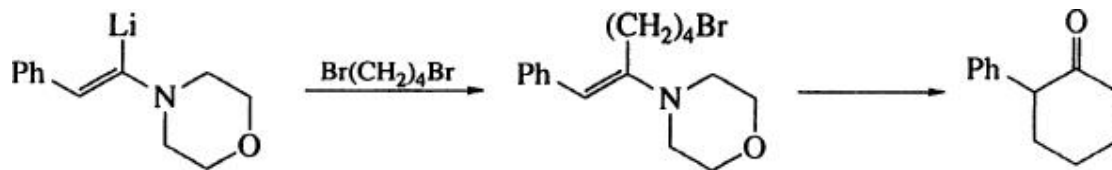
Other substrate functionality that has proven to be compatible with this method of vinyllithium formation includes alcohol groups (as alkoxides), (24, 33-36) phenyl (6, 37-40) and anisole (38, 41-43) rings, thiols, (44) polyenes, (24, 36) alkynes, (45) ketals, (46) and cyclopropanes. (38, 47)
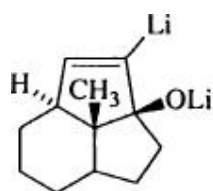
(Ref. 36)
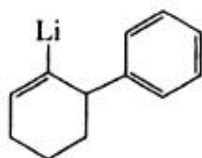
(Ref. 37)
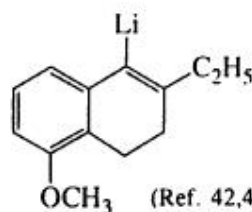
(Ref. 42,43)
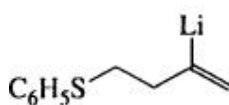
(Ref. 44)
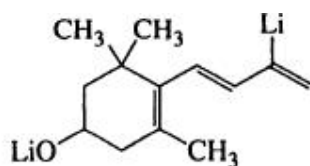
(Ref. 24)
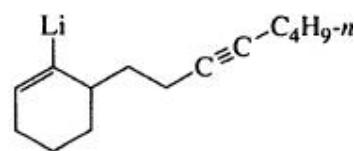
(Ref. 45)
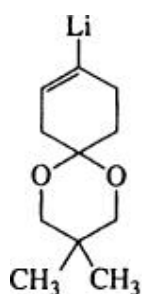
(Ref. 46)
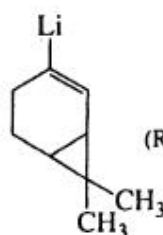
(Ref. 47)

Isolated alkenes, (48) primary chlorides, (49) and *tert*-butyldimethylsiloxy groups (50) also survive, although intramolecular trapping of these groups can occur if they are situated in an accessible position.

(Ref. 48)

major product
if R = H

major product
if R = CH₃

(Ref. 50)
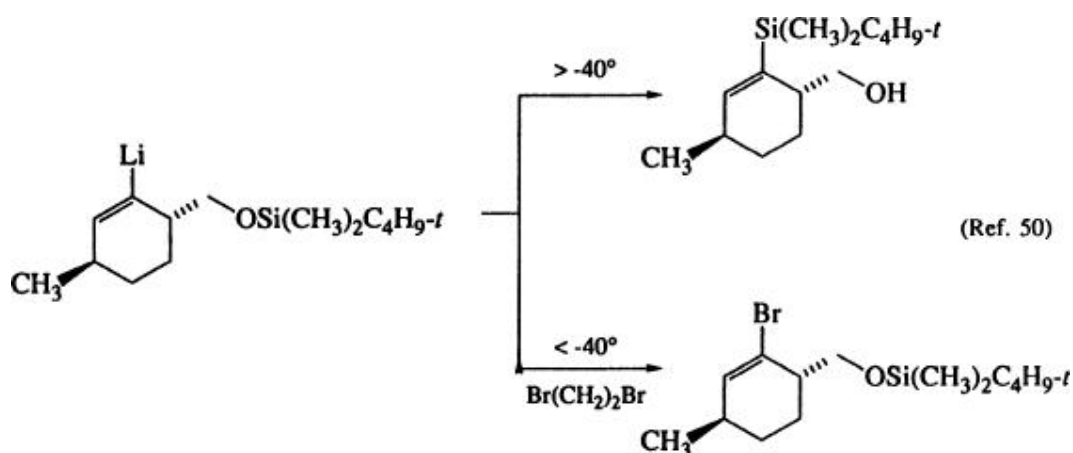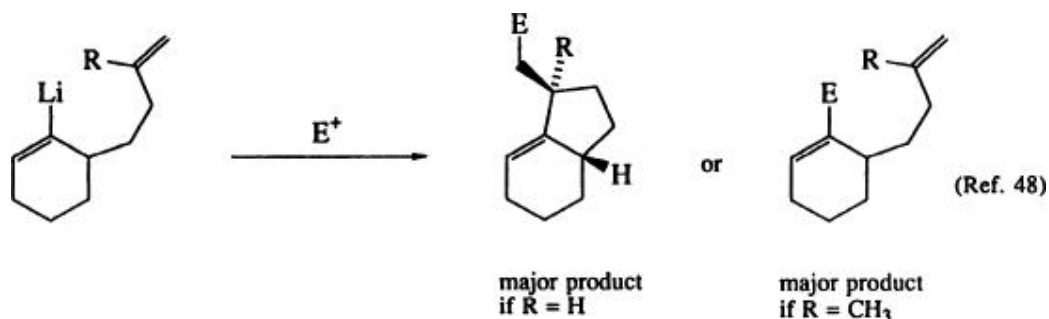
Although most ketone arenesulfonylhydrazones undergo the "normal" sequence of reactions leading to the corresponding vinyllithium, there are a few examples in which nucleophilic addition to the azomethine bond has been observed instead. (51-54) This reaction pathway is relatively rare for ketone arenesulfonylhydrazones, occurring mainly in highly α -substituted derivatives.

(Ref. 8)

(45%)   (55%)
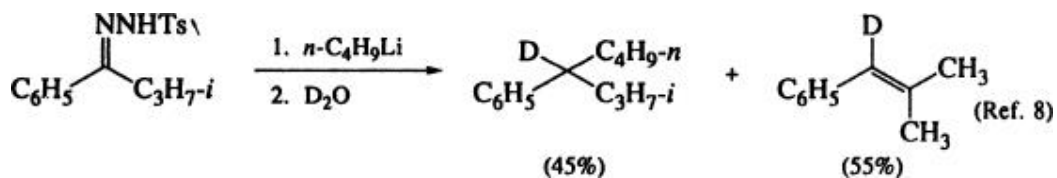
In contrast, aldehyde tosylhydrazones give exclusively products derived from addition of the alkyllithium base to the azomethine bond. (11, 55) Decomposition of the resultant adduct gives a transient alkyllithium that usually cannot be trapped with electrophiles under these reaction conditions. This characteristic reaction of the aldehyde derivatives totally precludes their use in

the formation of 1-lithioalkenes, representing a major limitation of this methodology.

$$C_6H_5(CH_2)_2CH=NNHTs \xrightarrow[\substack{THF \\ -22°}]{t\text{-}C_4H_9Li} C_6H_5(CH_2)_3C_4H_9\text{-}t \quad \left(no \quad C_6H_5CH_2\diagup\diagdown Li \right)$$
$$(61\%)$$
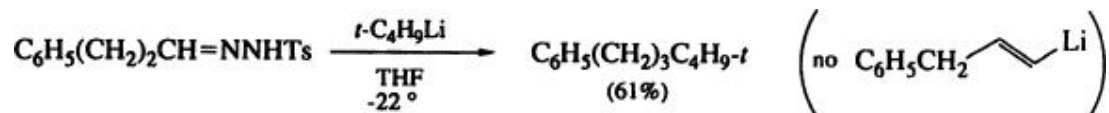
Several other specific types of related derivatives are also known not to undergo vinyllithium formation, proceeding instead through well-documented alternative pathways. For example, arenesulfonylhydrazones with a leaving group in the α position can suffer elimination at the monoanion stage, giving a tosylazoalkene as the major product. (56)
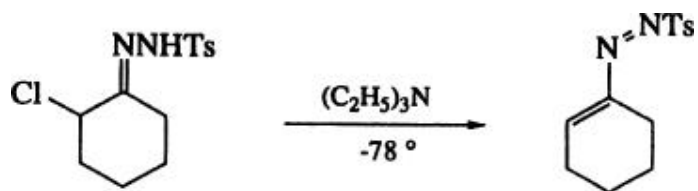
This process can serve as the first step in the preparation of lithioalkadienes (57) in an interesting alternative to the usual enone procedure illustrated previously.
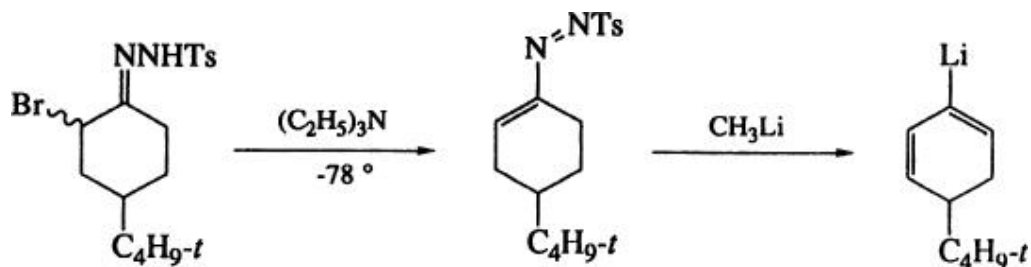
When the elimination step is the opening of an α , β -oxirane ring, this process initiates the Eschenmoser fragmentation. (58, 59)
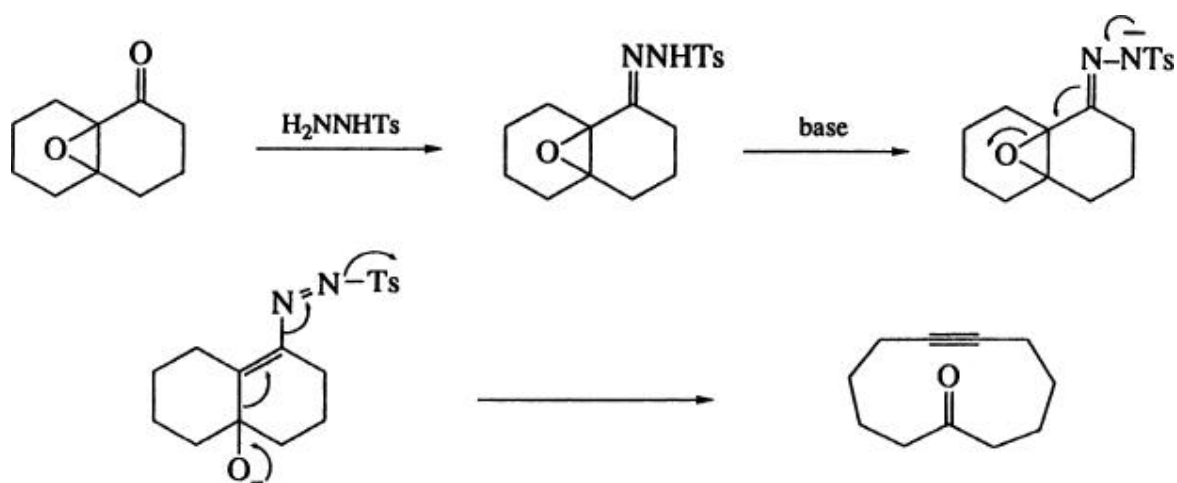
Cyclic ether derivatives give allenes via a related elimination pathway. (60)
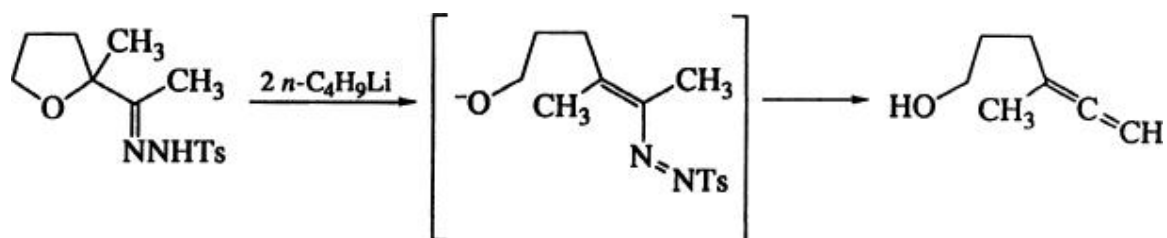
There are examples of α -methylthioketone tosylhydrazones that undergo dianion formation rather than elimination, (61) but trapping of the resultant vinyllithiums is not reported.
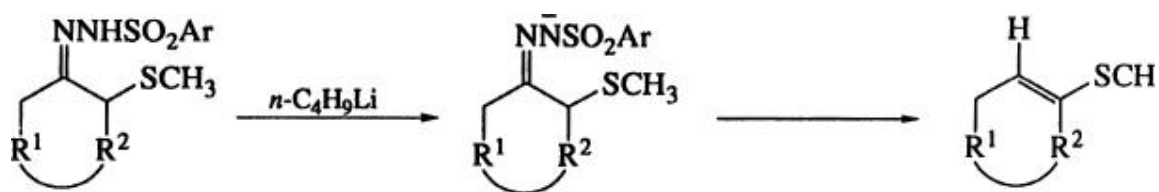
Tosylhydrazones of β -keto esters undergo the normal Shapiro reaction, but attempts at capturing the vinyllithium intermediate with electrophiles have failed. (20) Finally, although ester tosylhydrazones are easily prepared (see discussion above), there are no reports that they successfully undergo elimination to the corresponding lithiated vinyl ethers, despite the obvious potential utility of that process.

3.3. Regioselectivity
One of the most valuable attributes of arenesulfonylhydrazones as a source of vinyllithiums is that the reaction exhibits a strong preference for the formation of one of the two possible vinyllithium regioisomers. In general, one may be confident that for unsymmetrically substituted ketone tosyl- or trisylhydrazones,

deprotonation of the monoanion will occur predominantly at the less-substituted α position, i.e., $RCH_3 > R_2CH_2 > R_3CH$, to give after

$(50:1)[6]$

$(>50:1)[6]$
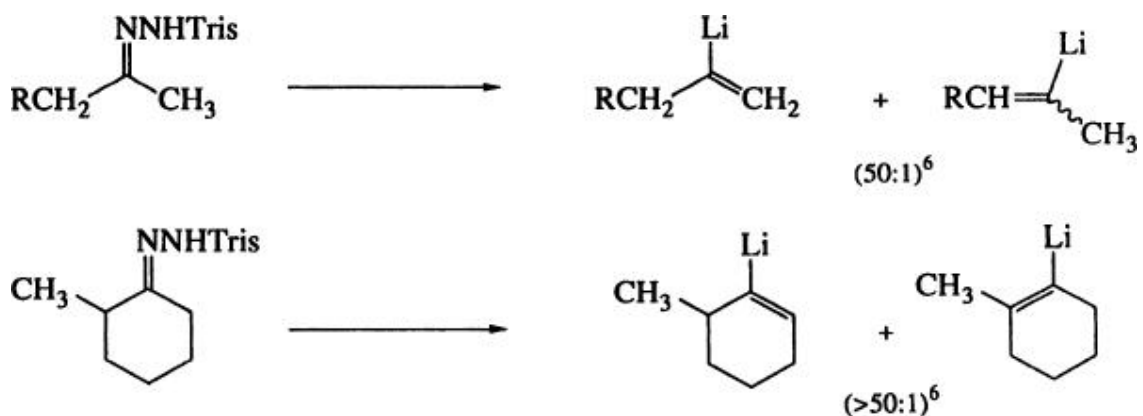
elimination the corresponding less-substituted vinyllithium product, which is generally favored over the more highly substituted regioisomer by ratios of 50:1 or more.

There are very few exceptions to this generalization. In one bicyclic derivative the bridgehead methine undergoes significant deprotonation to give the more highly substituted lithioalkene as a major byproduct. (62) Similarly, the trisylhydrazone of a β -ketoacetal undergoes deprotonation at the more highly substituted α position, which in this case results in elimination of ethoxide followed by conjugate addition–elimination of the resultant monoanion to give a 1,2-pyrazole heterocycle. (50)

(53%)   (20%)

(20%)   (45%)
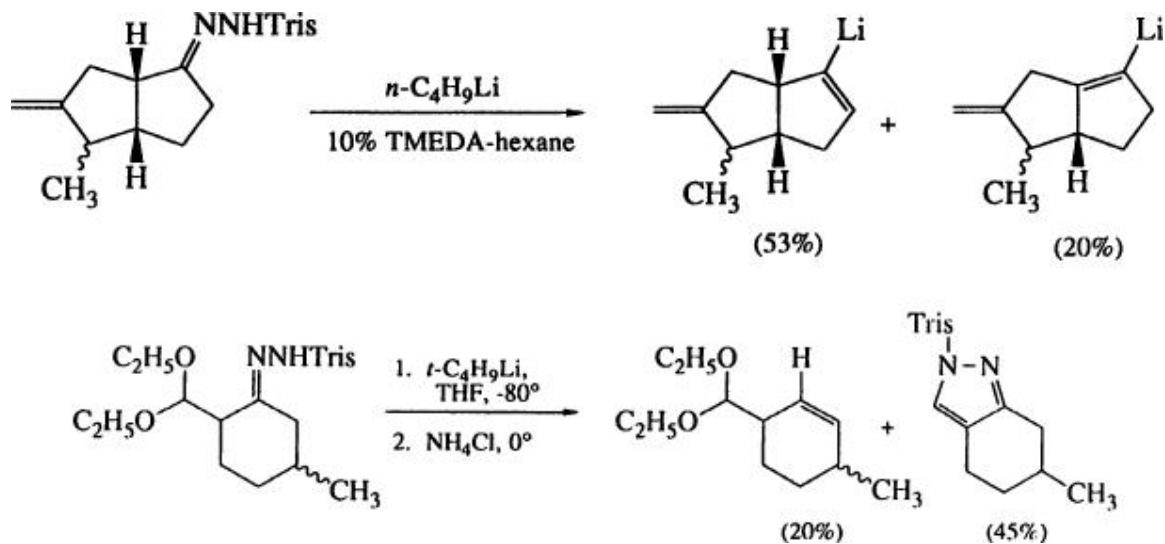
It is also possible to generate the more highly substituted vinyllithium regioisomer in some cases, but to do so requires an in situ alkylation

procedure, which is discussed in the section "Dianion Functionalization Followed by Vinyllithium Formation."

Generalizing about regioselectivity in α , β -unsaturated systems (6, 24, 25, 27-29) is much less straightforward. In these systems there can be as many as three acidic sites that could undergo deprotonation, and predicting a priori which might be preferred is treacherous. There are instances of deprotonation at the least highly substituted of several positions, and just as many counter-examples. Representative examples are shown at the top of page 14.

Vinyllithiums generated from tosyl or trisylhydrazone dianions are configurationally stable: there are no reported cases of equilibration to regio- or stereoisomers of the initially formed vinyl anion. There are, however, several examples of the formation of stabilized allyl anions from an initially formed vinyllithium. (4, 6, 63)

In contrast to the high regioselectivity observed for most saturated ketone arenesulfonylhydrazones, differential substitution adjacent to equivalently substituted α positions does not appear to afford good regiochemical control. For instance, 3-alkyl-, (6) 3,4-dialkyl-, (64) and 3,5-dialkylcyclohexanone

(Ref. 28)

(Ref. 27)

(Ref. 27)
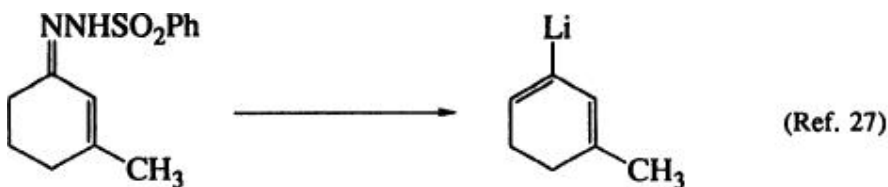
derivatives (47) exhibit virtually no regioselectivity. One 3-ketosteroid reportedly gives the $\triangle^2$ regioisomer, (41) but the yield is only 50% and no mention is made

NNHTris   1. n-C₄H₉Li
            -78°
C₆H₅ ⟍ CH₃   2. 0°, 5 min   → C₆H₅ ⟍ (Li)   —D₂O→   C₆H₅ ⟍ (D)   (74%)

(0°, 30 min)

(Ref. 6)

Li
C₆H₅ ⟍═⟍ (−) —D₂O→ C₆H₅ ⟍ (D) + C₆H₅ ⟍⟍ D

(20%)   (60%)
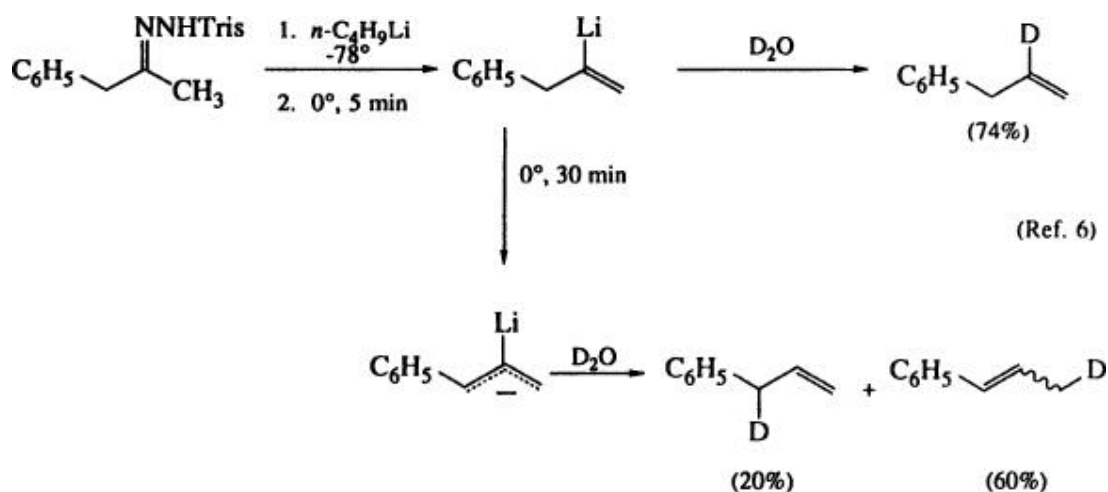
of the △³ isomer. Finally, only meager selectivity is observed in the reaction of 2-n-butyl-6-methylcyclohexanone tosylhydrazone, (65) although it is possible to obtain a single regioisomer in such systems via the dianion alkylation procedure described later.

Although the observed regiochemical preferences in dianion formation bear a strong resemblance to those of kinetic enolate formation, a few examples dramatize that the regioselectivity cannot be understood exclusively on the basis of kinetically controlled deprotonation in the less-substituted position. Specifically, the stereochemistry of the azomethine bond can come

NNHSO₂Ar
CH₃
(~1:1)⁶

CH₃ ⟍ NNHSO₂Ar
CH₃ CH₃
(3:2)⁴⁷

H
NNHSO₂Ar
H
(2:1)⁶⁴

CH₃
ArSO₂NHN ═   H
?   (Ref. 41)

CH₃
NNHSO₂Ar
C₄H₉-n
(7:3)⁶⁵
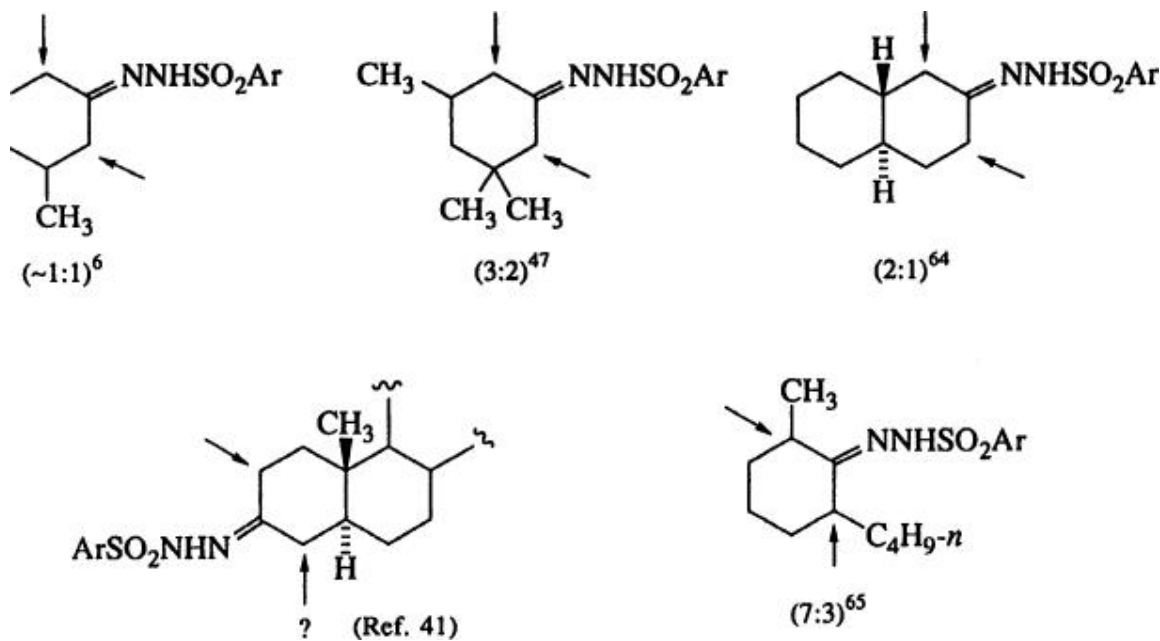
into play, i.e., a "syn directing effect" known to occur in the deprotonation of other imine derivatives. (66) Of course, these two factors themselves are not independent, since the *E* hydrazone isomer usually is present in large excess under most conditions (see examples above), so that deprotonation in the less sterically encumbered position is predicted by *either* rationale, rendering the point immaterial in most cases. However, there are circumstances under which substantial deprotonation occurs at the *more*-substituted position or, in α , β -unsaturated ketone arenesulfonylhydrazones, at a position otherwise not consistent with simple kinetically controlled deprotonation. For example, deprotonation regioselectivity for pulegone tosylhydrazone is a function of the hydrazone stereochemistry, but this effect is observed only in TMEDA and not in benzene. (17)
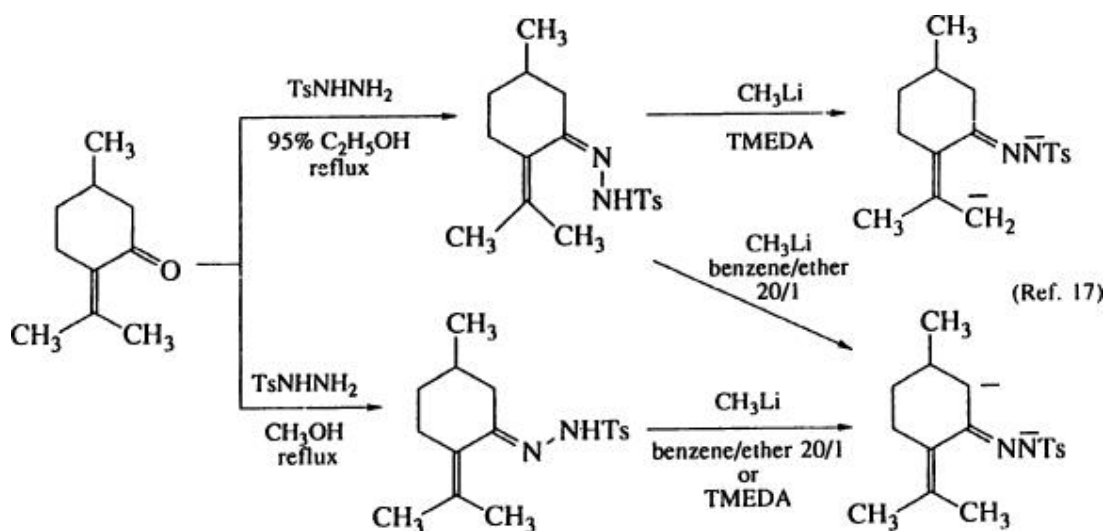
Similarly, for vinyllithiums derived from saturated methyl ketones the regioselectivity is determined by starting hydrazone *E/Z* ratios in some reaction solvents but not in others. Thus 2-octanone trisylhydrazone, which is an inseparable 85/15 mixture of *E* and *Z* isomers (determined by NMR), gives an 85/15 ratio of 1-octene/2-octene if vinyllithium formation is carried out in tetrahydrofuran, but a 98/2 ratio of the same products when 10% TMEDA–hexane is the reaction solvent. (6) The implication of this observation is that in tetrahydrofuran the regioselectivity is determined by azomethine stereochemistry (i.e., *syn* deprotonation, more evidence for which is discussed below) but that in TMEDA–hexane it is not. Note, however, that in this case a *syn*-directing effect does not occur in TMEDA, whereas in the previous example it does. Another example of such an effect in TMEDA is also reported. (62) Thus more than 10 years after it was asserted that a "detailed explanation of the observed solvent dependencies …await further studies owing to the

complexities of the reaction system. … ", (17) little headway has been made.

This solvent effect, although poorly understood, is important to keep in mind when preparing vinyllithiums from ketone arenesulfonylhydrazones that contain significant amounts of the Z isomer, such as those derived from straight-chain 2-alkanones. In those cases, one should not use tetrahydrofuran because mixtures of regioisomeric alkene products are likely (recall, of course, that tetrahydrofuran generally cannot be used for tosylhydrazone reactions anyway because it protonates the vinyllithium product during the relatively long time required for tosylhydrazone dianion elimination). Fortunately, for a large number of ketone substitution patterns there is very little of the Z hydrazone formed, so that tetrahydrofuran can be used for many trisylhydrazone reactions without sacrificing regioselectivity.

3.4. Stereoselectivity

The issue of stereoselectivity of vinyllithium generation from acyclic tosyl- or trisylhydrazones has been addressed in only a few cases. For symmetrical straight-chain ketone derivatives, the E vinyllithium is the exclusive product. (6, 25, 37, 38, 44, 67, 68) Unfortunately, hydrocarbon branching in the α ' position degrades the stereoselectivity considerably. (6)
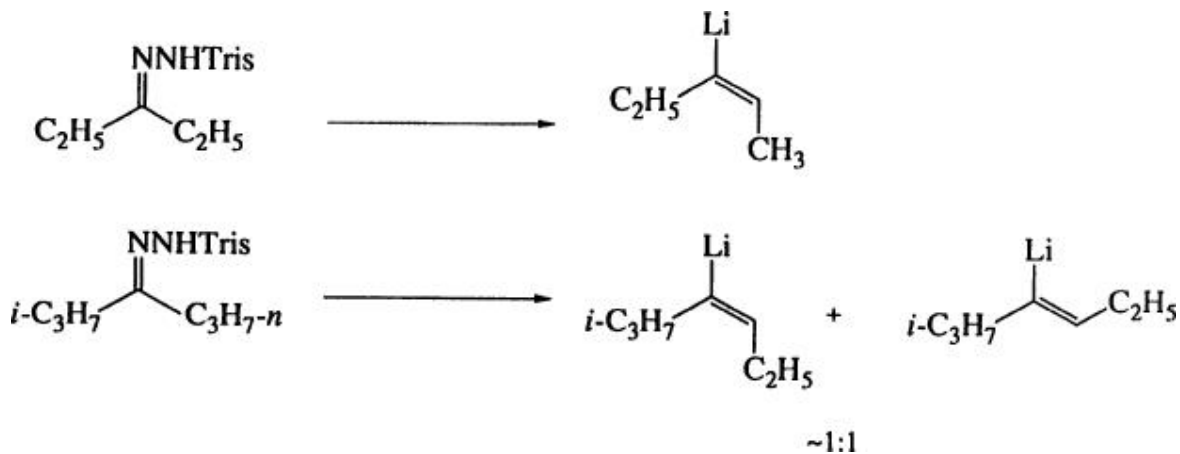
These results are consistent with *syn* deprotonation of the hydrazone monoanion conformer that positions the α -alkyl group *anti* to the (in-plane) hydrazone moiety during dianion formation. (69)

Favored

Disfavored
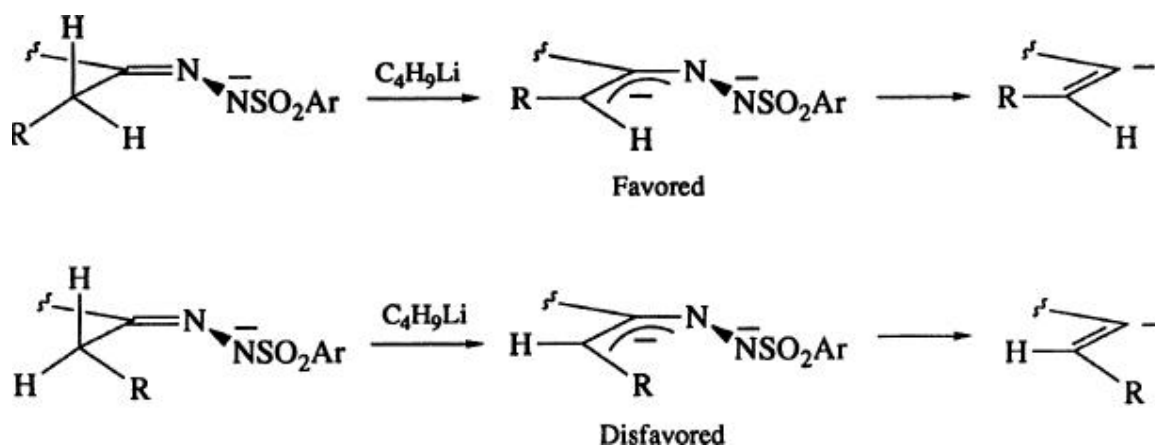
Related unsymmetrical derivatives substituted farther from the azomethine bond are not useful because they would give mixtures of regioisomers; however, this problem can be overcome by use of the dianion alkylation procedure described in the following section.

α -Ketoamide trisylhydrazones give predominantly (Z)-vinyllithium isomers, the reversal presumably being due to the intermediacy of the allenyl dianion, which is not subject to the same type of allylic strain in the deprotonation transition state. (31, 32)
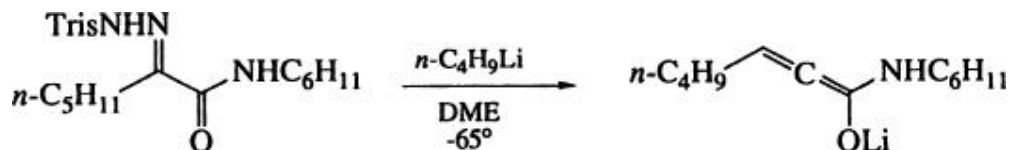
Stereochemistry is also an issue in the formation of vinyllithiums from medium (70) and large ring ketones, (37, 38, 64, 68) for which there is also a preference for the E isomer.

(Ref. 70)

(Ref. 37)
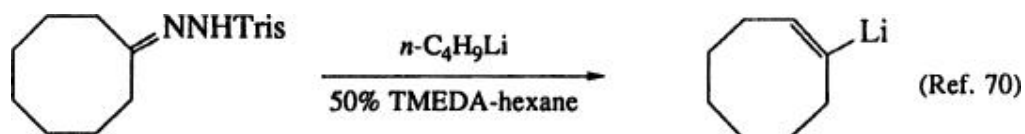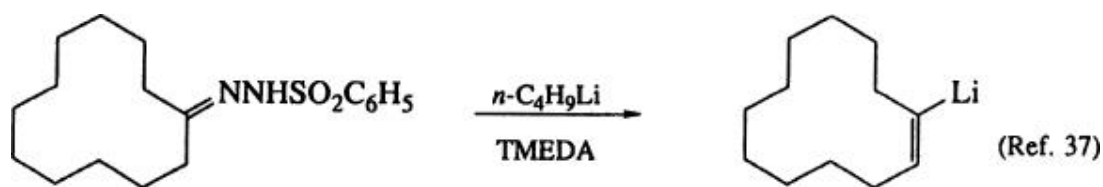
3.5. Dianion Functionalization Followed by Vinyllithium Formation

The *syn* deprotonation of trisylhydrazones that occurs in ethereal solvents makes it possible in some cases to completely reverse the normal preference for formation of the less-substituted vinyllithium. By employing a one-flask dianion alkylation procedure it is possible to obtain predictable regiochemical control in the formation of nearly symmetrical acyclic vinyllithiums that would be impossible to prepare selectively by the direct reaction. For example, acetone trisylhydrazone in tetrahydrofuran can be converted into the corresponding dianion, followed by alkylation at –78° with a primary alkyl iodide. This monoanion is regiochemically stable at that temperature, and upon the addition of another equivalent of alkyllithium base it undergoes exclusive *syn* deprotonation at the more highly substituted α position to give a dianion that decomposes to (*Z*)-2-lithio-2-octene. (69) Less than 2% of the less-substituted regioisomer is produced.
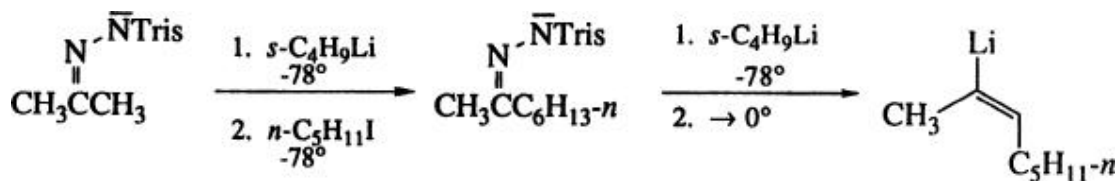
Note that this procedure completely reverses the regioselectivity observed for the direct reaction of 2-octanone trisylhydrazone. Furthermore, the reaction is very stereoselective as well, giving no detectable amount of the (*E*)-vinyllithiums. Although this reaction sequence has yet to be employed extensively, it has proven useful in syntheses of (±)-ovalicin, (71) aklavinone, (42) the defense substance of *L. longipes*, (72) and a number of α-alkylidenelactones. (34, 35) In general, trisylhydrazones are preferred because tetrahydrofuran can be used as the reaction solvent, and the initial alkylation usually proceeds more smoothly in that solvent than in TMEDA, especially for reactive electrophiles such as methyl iodide.

Adding to the versatility of the dianion alkylation procedure is the observation that it is possible to obtain either vinyllithium regioisomer from the same

alkylated monoanion. For example, the normal in situ alkylation–deprotonation sequence shown (34) gives the more highly substituted (Z)-lithioalkene; however, if the monoanion is quenched with acetic acid and isolated, the hydrazone group equilibrates from Z to E, and the less-substituted vinyllithium is formed upon treatment with butyllithium under the usual conditions.

The dianion alkylation sequence has also been investigated in cyclic systems. The substituted cyclohexanone trisylhydrazone dianions tested undergo elimination too rapidly (even at –78°) to be alkylated efficiently, (65) but tosylhydrazones can be utilized effectively even in tetrahydrofuran. Interestingly, although the alkylation and subsequent vinyllithium formation proceed smoothly, *the regioselectivity of the process reverses if there is a competition between anti CH$_2$ and syn CH deprotonation.* Under those circumstances, *anti*
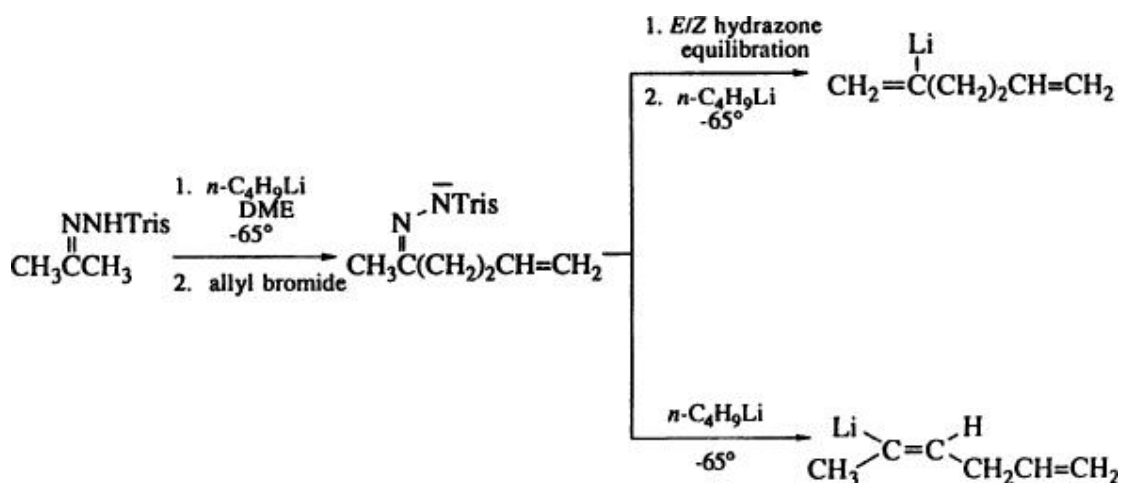
deprotonation is favored, and the less-substituted vinyllithium is formed. (65) This is also true in acyclic systems. (65)
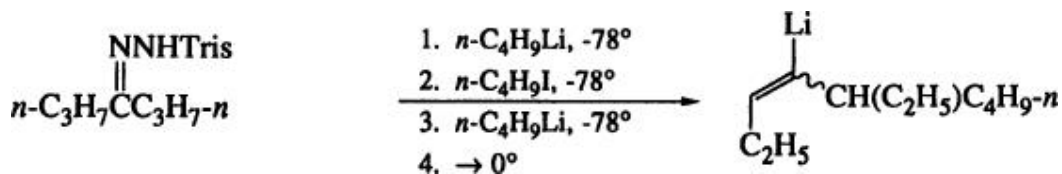
In ring systems in which there is no *anti* CH$_2$ in the initially formed alkylation product, however, it is possible to remove the tertiary α proton to give highly substituted vinyllithiums. (65)
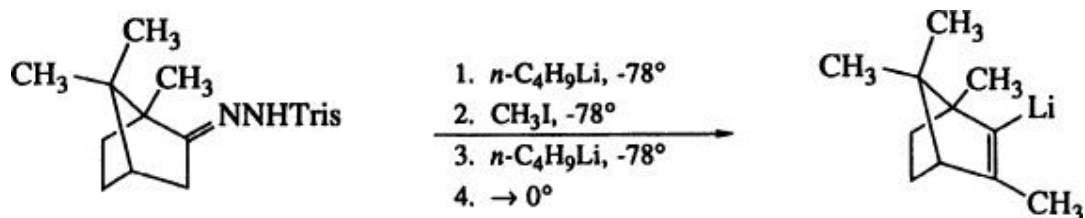
When a ketone, rather than an alkyl halide, is the initial electrophile, subsequent deprotonation occurs in the less-substituted (*anti*) position even when the *syn* group is CH_2. (33-35) This regioselectivity is thought to be controlled by the β -alkoxide group, which strongly disfavors deprotonation in the adjacent *syn*- α position for all substitution patterns tested.
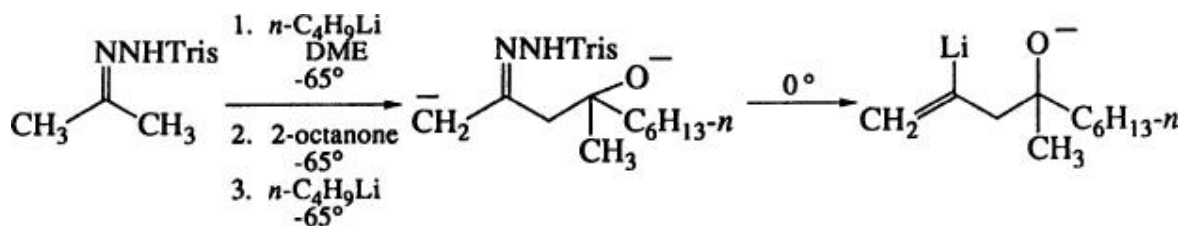
Finally, the dianion alkylation procedure allows for remarkable regiochemical control in the preparation of 1-lithio-2,6-dialkylcyclohexenes, which are produced nonselectively in the direct reaction of the dialkylcyclohexanone tosylhydrazones themselves. Specifically, alkylation of the dianion of 2-methylcyclohexanone tosylhydrazone at –78° is followed by deprotonation (presumably *anti*) exclusively adjacent to the α -methyl group, and finally elimination to a *single* vinyllithium regioisomer. (65) If instead the (alkylated) monoanion azomethine *Z* stereoisomer is allowed to equilibrate (by aqueous workup and isolation) prior to dianion formation and decomposition, a 7:3 mixture of vinyllithium regioisomers is formed.

only isomer
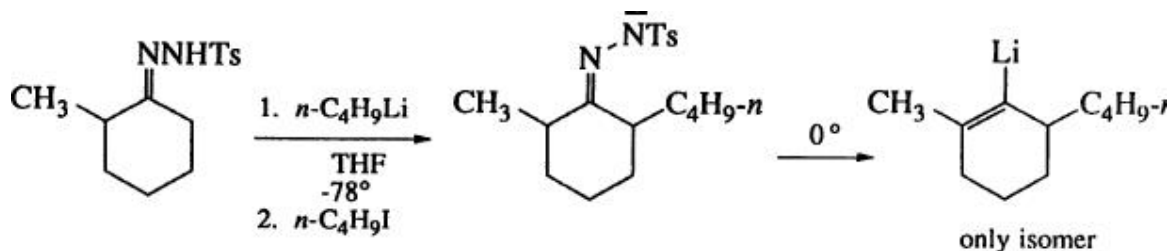
This result is explained by axial alkylation of the initial (methyl equatorial) dianion to give a monoanion conformer that does not equilibrate at –78°. Removal of the only remaining axial αproton, as shown, gives the dianion regioisomer leading to the observed product. It probably is not necessary to invoke "freezing out" of the butyl–axial conformer, since that one would most likely be preferred because of allylic strain in the corresponding equatorial conformer with a *syn* azomethine group. Either way, this reaction
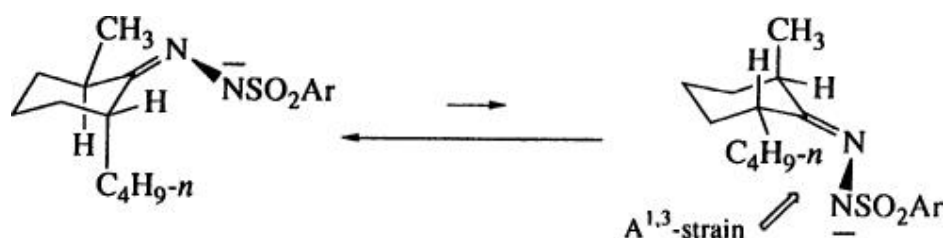
confers superb regiochemical control in the formation of vinyllithiums that would be isomerically very impure if prepared directly from the parent 2,6-dialkyl ketone. Furthermore, the other regioisomer could almost certainly be prepared by methylation of 2-*n*-butylcyclohexanone tosylhydrazone monoanion, thus providing in principle complete control of regiochemistry in these systems.

3.6. Reaction with Electrophiles
The lithioalkenes prepared by this methodology exhibit the chemical behavior that one would expect of them, i.e., that of reactive organolithium species which undergo deuteration, substitution, and addition reactions with a wide range of electrophiles. It should be remembered that the use of tosylhydrazones demands that the reaction mixture be quenched with a minimum of 2.0 equivalents of the electrophile. This requirement may be unacceptable if the electrophile is a valuable one, and if so can be avoided by employing the corresponding trisylhydrazone instead.

3.6.1.1. Deuteration
The reaction has been utilized extensively for the preparation of monodeuterated alkenes. (4-6, 32, 36, 40, 45, 55, 57, 73-76) Its particular value in this regard lies in the high regioselectivity of vinyllithium formation combined with the obvious positional predictability of deuterium incorporation.

(Ref. 6)

(Ref. 55)

(Ref. 5)
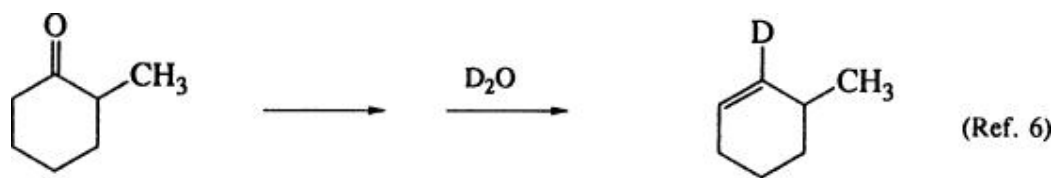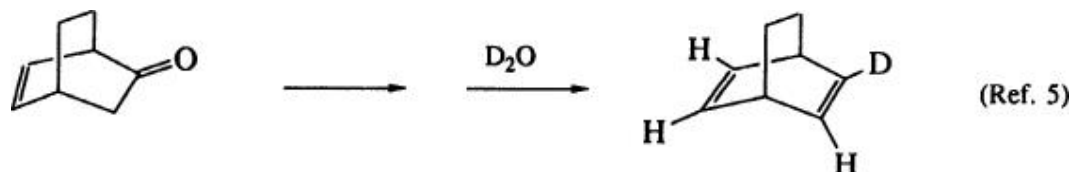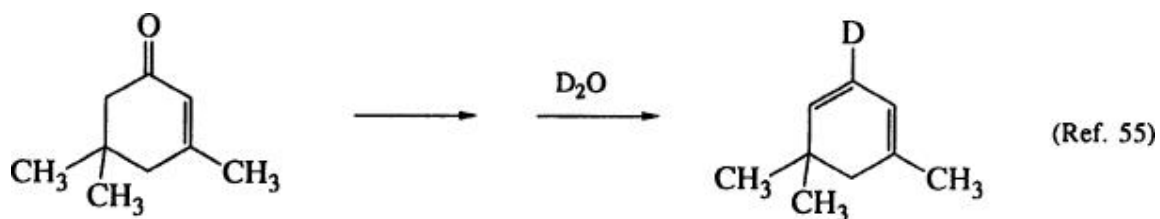
It is also possible to prepare specifically polydeuterated alkenes by generating vinyllithiums from α -deuterated ketones, and then quenching with deuterium oxide. (76, 77)

(Ref. 76)

(Ref. 77)
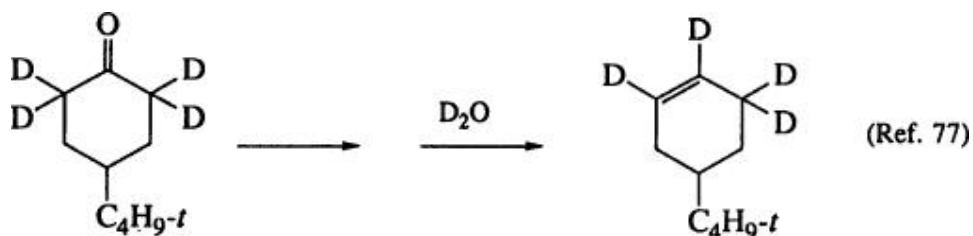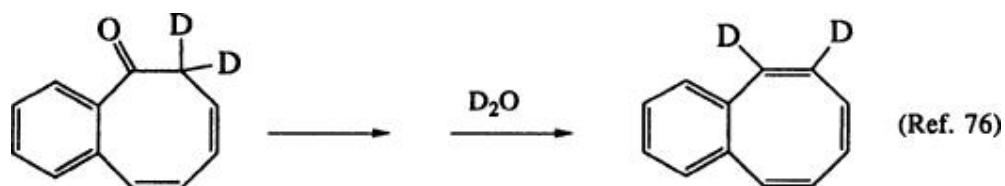
3.6.1.2. Formation of C — C Bonds

Direct S_N2 alkylation of the vinyllithiums generated from arenesulfonylhydrazones proceeds efficiently only with methyl iodide (4, 22, 29, 39, 55, 78) and primary alkyl bromides or iodides. (6, 25, 37, 65, 79) Fortunately, an indirect procedure has been developed that provides excellent yields of alkylated products that are completely inaccessible via the direct route. (80, 81) the vinyllithium is quenched with a trialkylborane to give the

corresponding "ate" complex, which undergoes oxidative coupling in the presence of iodine.
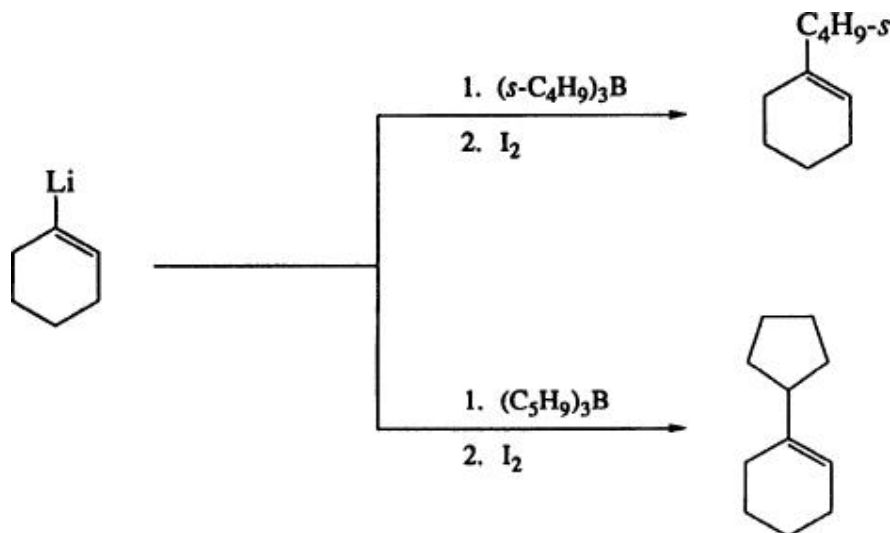
Although substitution reactions of allylic halides or tosylates have not been reported for vinyllithiums generated from arenesulfonylhydrazones, a conjugated allene can be formed in fair yield by S_N2' displacement of a propargylic tosylate with a mixed cuprate. (50)
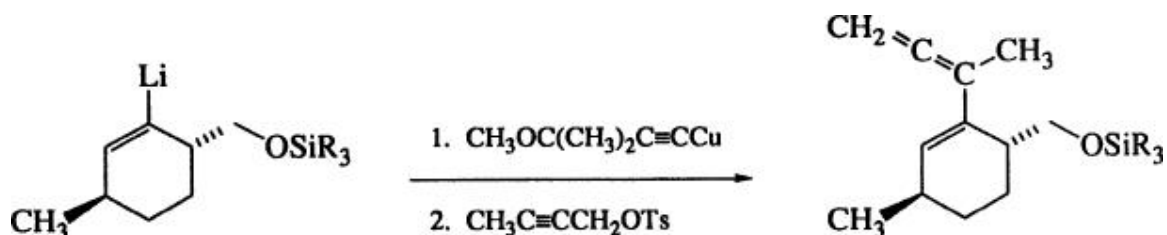
Reactions with carbonyl electrophiles provide a wide variety of substituted alkenes. For example, α , β -unsaturated aldehydes can be prepared in good yield by treating the vinyllithium with dimethylformamide (DMF) followed by simple aqueous workup. (6, 11, 28, 41, 47, 65, 69, 82-84)

(Ref. 6,83)
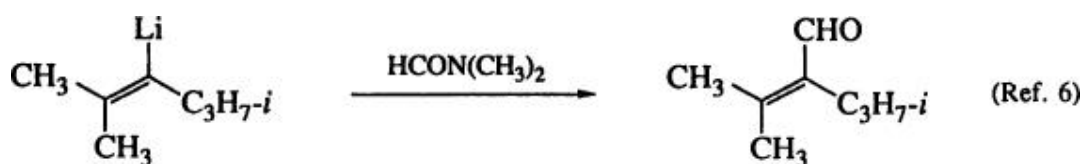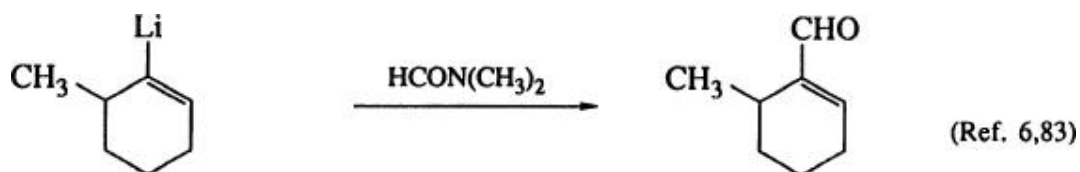
Reaction with carbon dioxide provides a convenient means of preparing α , β -unsaturated acids, (6, 29, 62) and when carboxylation is combined with the dianion alkylation procedure described above, an interesting α -methylene lactone synthesis is possible. (33-35)
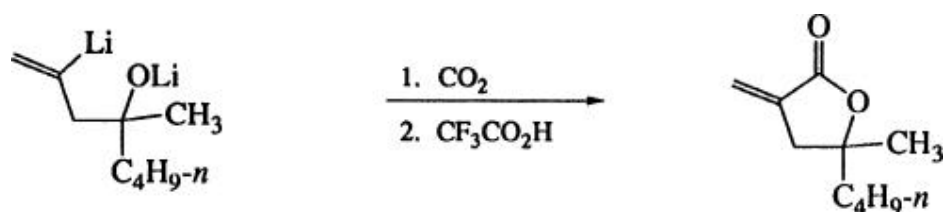
α , β -Unsaturated esters can be prepared by carboxylation followed by treatment with diazomethane, (62) and in the case of a hindered vinyllithium via direct reaction with ethyl chloroformate. (65)

Primary allylic alcohols are formed in fair yield when vinyllithiums are treated with gaseous formaldehyde. (30-32, 42-44, 69) Alternatively, the lithioalkene can be treated sequentially with dimethylformamide and sodium borohydride to give the same product somewhat more conveniently and often in better yield. (42, 43, 85)

(Ref. 42,43)
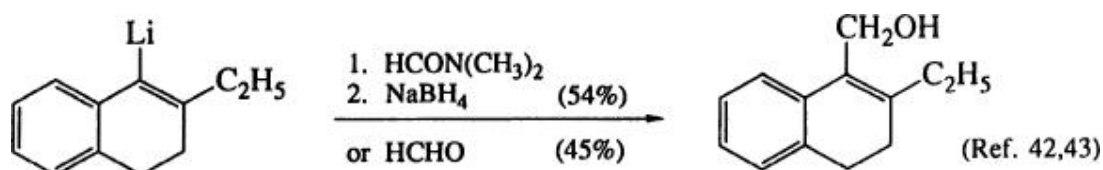
Secondary allylic alcohols are produced by reaction of vinyllithiums with aldehydes, (6, 23, 29-32) and α , β -unsaturated aldehydes react in a 1,2 fashion to give bis-allylic alcohols. (23, 24, 31, 32)

(Ref. 23)

(Ref. 24)
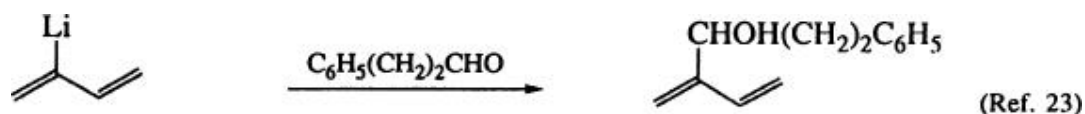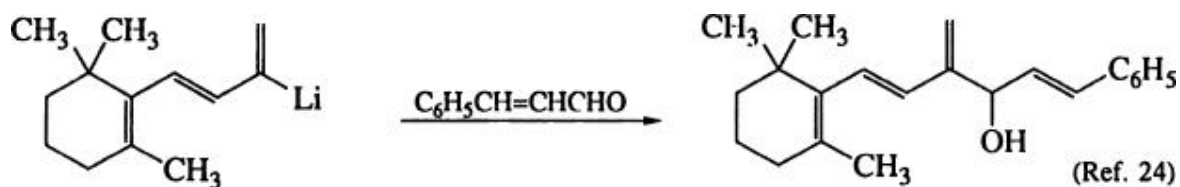
This reaction has been used to advantage in the preparation of precursors for silyl-directed Nazarov cyclizations. (64)
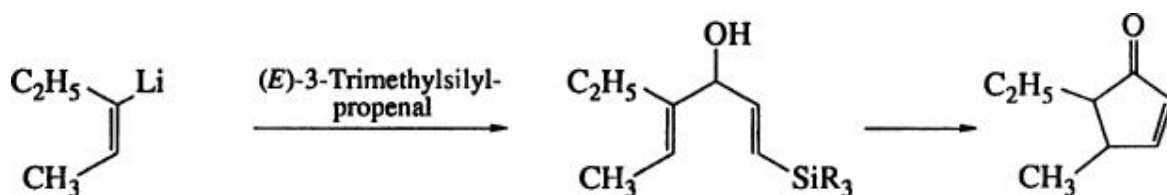
Reactions of vinyllithiums with saturated acyclic (31, 32) and cyclic (29, 30) ketones proceed smoothly to give tertiary allylic alcohols that usually can be isolated without significant dehydration. (86) α , β -Unsaturated ketones undergo 1,2 addition under these conditions, (29) although conjugate addition is readily accomplished by forming the phenylthio mixed cuprate prior to addition of the electrophile. (67)

(Ref. 29)

1. C_6H_5SCu

2.

(Ref. 67)
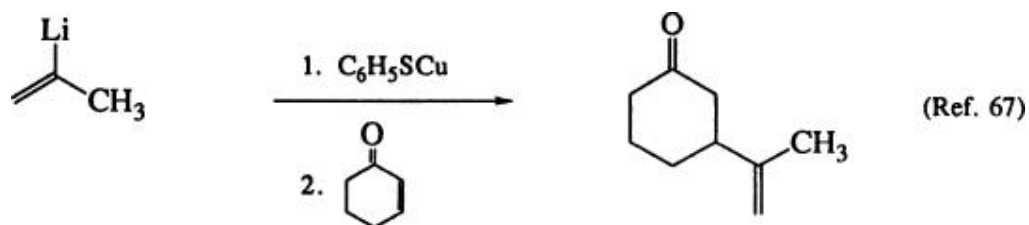
Finally, chromium hexacarbonyl undergoes addition to one of the CO ligands, giving the vinylcarbene complex. (46)
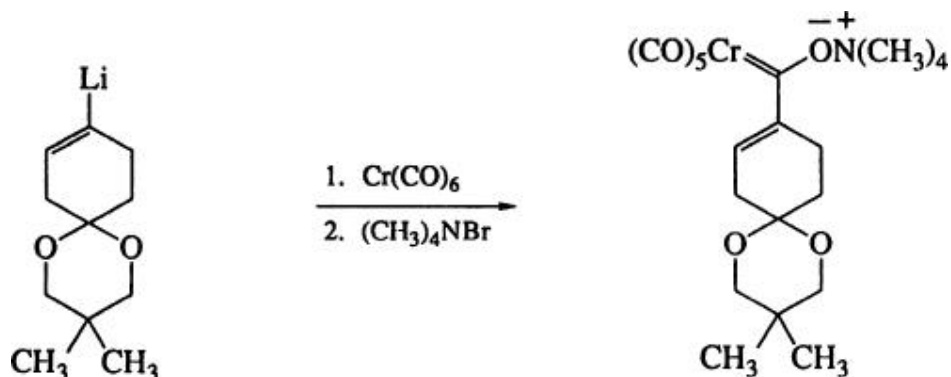
3.6.1.3. Formation of C-Heteroatom Bonds

Vinyl halides can be prepared by quenching vinyllithiums with the appropriate electrophilic halogen species. The procedure affords vinyl bromides (from 1,2-dibromoethane) (6, 45, 48, 50, 65) and vinyl iodides (from iodine) (11) with good control of regiochemistry.
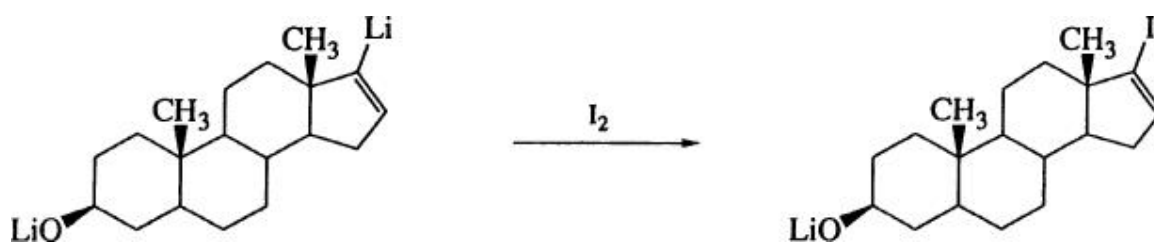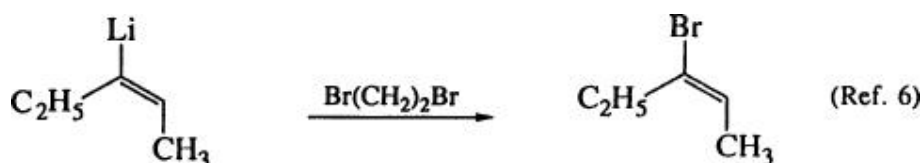
Enephosphinylation of a large number of vinyllithiums can be accomplished by reaction with chlorodialkylphosphines to give the corresponding vinylphosphine, and subsequent oxidation with hydrogen peroxide provides the vinylphosphine oxide in good yield. (38)

$$\overset{\text{Li}}{\triangle}\text{=}\quad\xrightarrow{(C_6H_5)_2PCl}\quad\overset{P(C_6H_5)_2}{\triangle}\text{=}\quad\xrightarrow{30\%\ H_2O_2}\quad\overset{PO(C_6H_5)_2}{\triangle}\text{=}$$
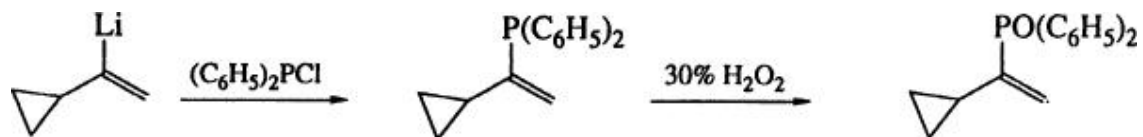
3.6.1.4. Formation of C-Metalloid Bonds

Vinyllithiums derived from arenesulfonylhydrazones have been utilized extensively for the regioselective preparation of vinylsilanes. (6, 19, 25-27, 37, 38, 41, 63, 68, 70, 87-91) This procedure is particularly valuable for the preparation of certain cyclic vinylsilanes and acylic regioisomers that cannot be prepared using conventional methods such as hydrosilylation of alkynes.

$$\overset{\text{Li}}{\underset{C_6H_{13}\text{-}n}{\diagup}}\quad\xrightarrow{(CH_3)_3SiCl}\quad\overset{Si(CH_3)_3}{\underset{C_6H_{13}\text{-}n}{\diagup}}\qquad\text{(Ref. 6)}$$

$$\overset{\text{Li}}{\bigcirc}\quad\xrightarrow[\underset{CH_3}{}]{1\text{-}C_{10}H_7\cdots\overset{C_6H_5}{\overset{|}{Si}}\text{--}Cl}\quad\overset{C_6H_5\cdots\overset{C_{10}H_7\text{-}1}{Si}\cdots CH_3}{\bigcirc}\qquad\text{(Ref. 70)}$$

$$\overset{\text{Li}}{\underset{CH_3}{\bigcirc}}\quad\xrightarrow{(CH_3)_3SiCl}\quad\overset{Si(CH_3)_3}{\underset{CH_3}{\bigcirc}}\qquad\text{(Ref. 25)}$$
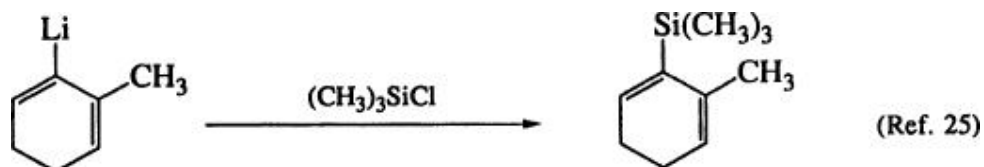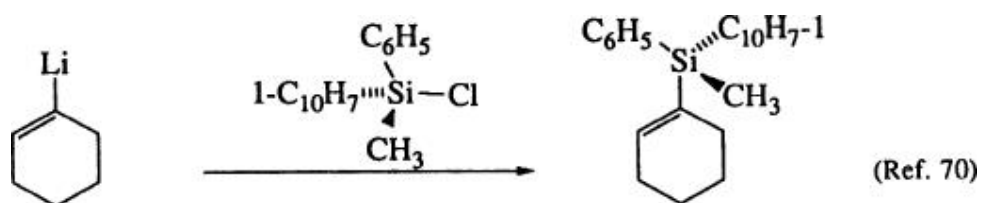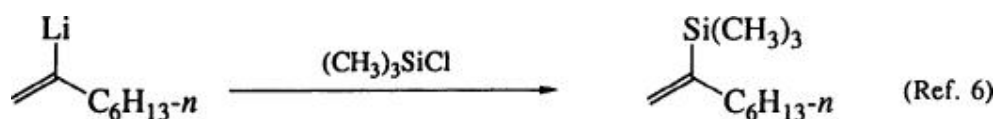
Vinylstannanes (19, 25, 71, 72, 92) and vinylgermanes (25) are available by the analogous procedure, a process that also serves as an indirect method for the formation of nitroalkenes, since the vinylstannanes produced from trisylhydrazones can be efficiently nitrated. (92)

$$\overset{CH_3}{\underset{CH_3}{\bigcirc}}\text{Li}\quad\xrightarrow{(CH_3)_3SnCl}\quad\overset{CH_3}{\underset{CH_3}{\bigcirc}}Sn(CH_3)_3\quad\xrightarrow[\text{DMSO}]{C(NO_2)_4}\quad\overset{CH_3}{\underset{CH_3}{\bigcirc}}NO_2$$
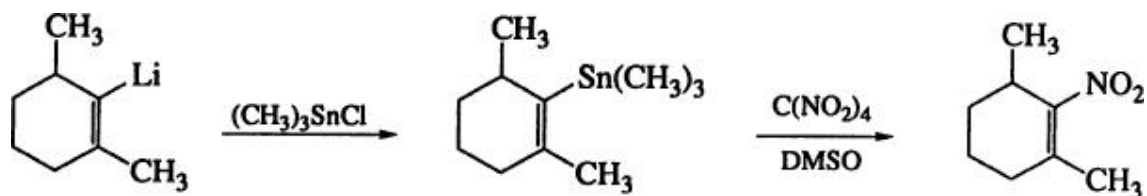
3.6.1.5. Internal Electrophiles

Vinyllithiums can be generated in the presence of suitably placed internal electrophiles, and cyclization to 5–7-membered carbocycles ensues. For instance, deprotonation and subsequent elimination of trisylhydrazones occurs under sufficiently mild conditions that primary alkyl halides survive and undergo intramolecular displacement. (49)
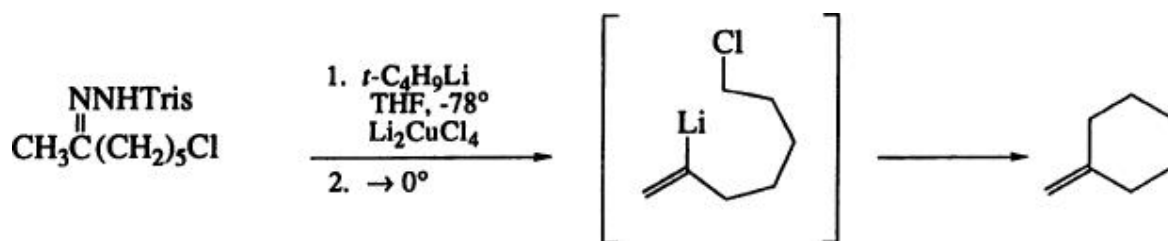
Monosubstituted alkenes also serve as internal electrophiles, although in this case the reaction is limited to the formation of cyclopentanes. (48) Remarkably high diastereoselectivities have been noted for some of the substrates tested, and the resultant alkyllithiums can be trapped with electrophiles.

trans/cis = 10/1

only diastereomer detected
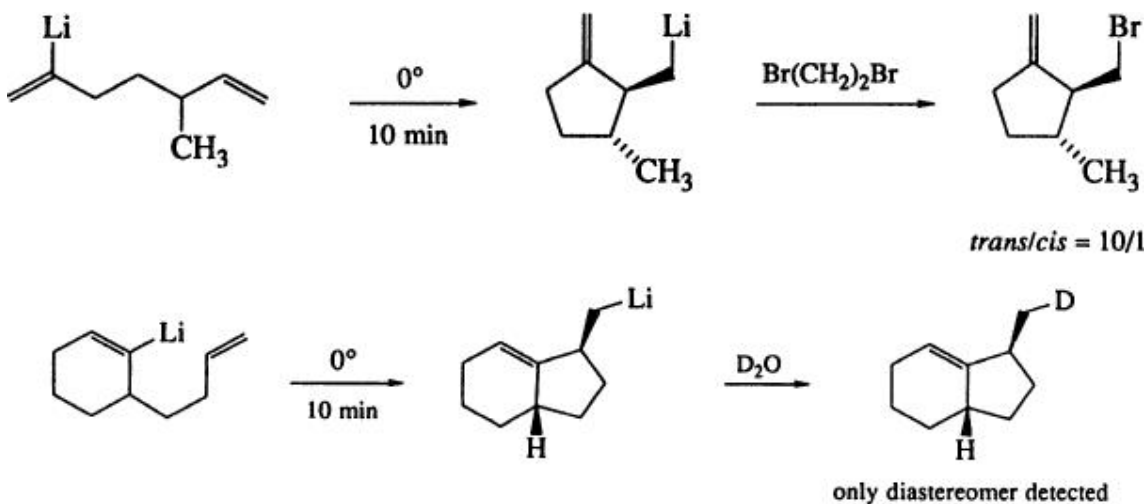
Furthermore, this selectivity can act in concert with the regio- and stereo-selective features of dianion alkylation and vinyllithium generation (described above) to afford a unique route to substituted alkylidenecyclopentanes. (48)

1. $t\text{-}C_4H_9Li$
   10% TMEDA-hexane
   $-78°$
2. CH_3I, $-78°$
3. $t\text{-}C_4H_9Li$, $-78°$
4. $\rightarrow 0°$

E^+

$cis/trans = 50/1$,
$E/Z > 50/1$
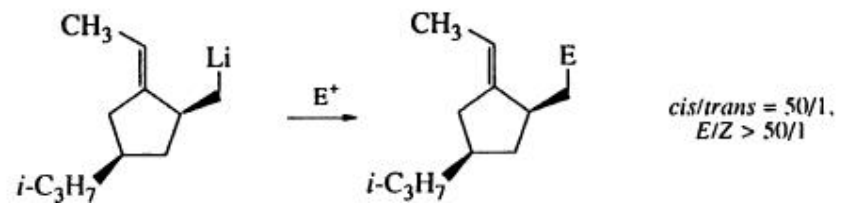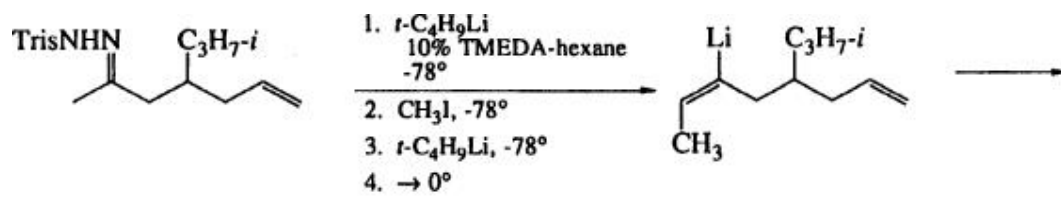
4. Comparison with Other Methods

There are several alternative methods of carrying out the overall transformation of a ketone into an alkene, with or without the intermediacy of vinyl organometallic species. The simplest of these, addition of nucleophiles to ketones followed by dehydration, suffers from a lack of regio- and stereochemical control in the elimination step but should be considered in simple cases. Recent innovations such as organometallic coupling of vinyl halides (93, 94) or vinyl triflates (95) often overcome this problem, and triflates are especially useful because they are formed from ketones under either kinetic or thermodynamic conditions, allowing good overall control of regiochemistry. Since the emphasis of this review is on the preparation of vinyllithiums, however, this section will focus on alternative methods of forming these particular intermediates, especially those that allow the formation of vinyllithiums that cannot be (or as yet have not been) prepared from arenesulfonylhydrazones.

Organolithium reagents generally are prepared by one of four standard metalation procedures: (1, 2) (a) halide lithiation, (b) lithium–halide exchange, (c) lithium–metalloid exchange, and (d) deprotonation. Specific vinyllithiums can be prepared by all of these methods, but each is subject to limitations. Most importantly, routes a and b are restricted by a limited range of isomerically pure haloalkene precursors, particularly for nonterminal derivatives. A number of methods for the formation of vinyl halides have been developed, including bromination–dehydrobromination of alkenes, (96-98) electrophilic substitution of vinylsilanes, (99, 100) hydroboration–bromination of alkynes, (101) hydroalanation–bromination of alkynes, (102) hydrozirconation–bromination of alkynes, (103) catalytic hydrogenation of iodoalkynes, (104) bromoselenation–oxidation–elimination of alkenes, (105) nucleophilic opening–elimination of epoxy silanes, (106) S_N2 substitution with 2,3-dichloropropene, (107) phosphorus pentahalide reaction with ketones, (108-110) iodine reaction with hydrazones, (111) iodine reaction with alkenylboronates, (112) organocopper addition to alkynes/iodine, (113) organozinc addition to alkynes/*N*-bromosuccinimide, (114) lithium aluminum hydride reduction of propargylic alcohols/iodine, (115) and dihalocarbene addition–ring expansion of cyclic alkenes. (116, 117) Many of these procedures, however, are applicable only to the preparation of acyclic 1- and 2-haloalkenes with limited numbers of alkyl substitutents or to specific cyclic derivatives. Especially problematic is the synthesis of *internal* acyclic or cylic haloalkenes, which is plagued by a general lack of regiochemical control and by competitive *gem*-dihalide formation.

Despite several relatively recent reports addressing both of these problems, at

least in some specific instances, (118-120) the shortage of general procedures for the regioselective formation of vinyl halides is a major shortcoming of methods a and b. In fact, one can reasonably argue that arenesulfonylhydrazone chemistry is the best method of preparing many vinyl halides, which obviously eliminates the need to prepare them to begin with if the vinyllithium intermediate is the desired target. 1-Halo-1-alkenes cannot, however, be prepared by the arenesulfonylhydrazone route (recall that aldehyde arenesulfonylhydrazones undergo addition of alkyllithiums rather than deprotonation).

Given the availability of a particular vinyl halide, however, methods a and b are relatively general, (121, 122) and can afford a number of vinyllithiums that cannot be prepared from arenesulfonylhydrazones, (123-135) representative examples of which are shown.

By Direct Halide Lithiation   By Halogen-Metal Exchange
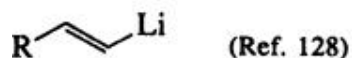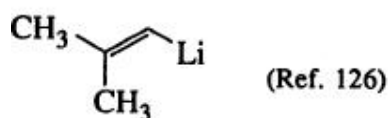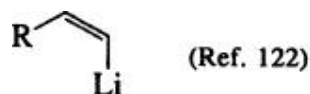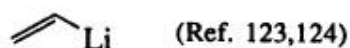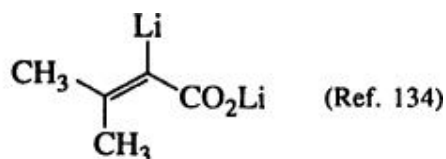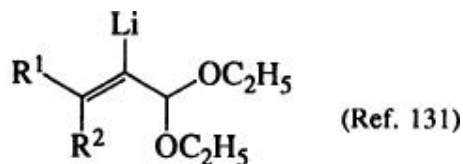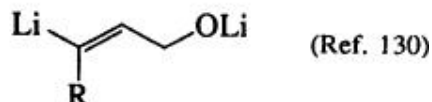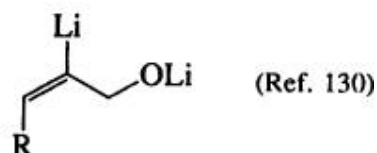
Method c, perhaps the most familiar example of which is the generation of vinyllithium from tetravinyltin, (125) also provides access to nucleophilic 1-metallo-1-alkenes via a large number of alkyne hydrometalation reaction sequences (101-103, 113, 136-140) that again exhibit regiochemistry complementary to the arenesulfonylhydrazone methodology.

$$R_3Sn\diagup\hspace{-0.3em}\diagdown\hspace{-0.3em}OTHP \longrightarrow Li\diagup\hspace{-0.3em}\diagdown\hspace{-0.3em}OTHP \qquad \text{(Ref. 137)}$$

There is one indirect hydrostannylation process that results in the opposite regioisomer, (141) and thus provides access (via lithium–tin exchange) to the same types of 2-lithio-1-alkenes that can be prepared from arenesulfonylhydrazones. Since terminal alkynes (rather than ketones) serve as starting materials for this procedure, it can be a very useful alternative depending on the relative availabilities of the two appropriate precursors.

$$R-C\equiv CH \xrightarrow{(CH_3)_3SnCuBr\cdot S(CH_3)_2} \underset{R}{\overset{Sn(CH_3)_3}{\diagup}} \xrightarrow{CH_3Li} \underset{R}{\overset{Li}{\diagup}}$$

ratio of regioisomers $\cong$ 10/1
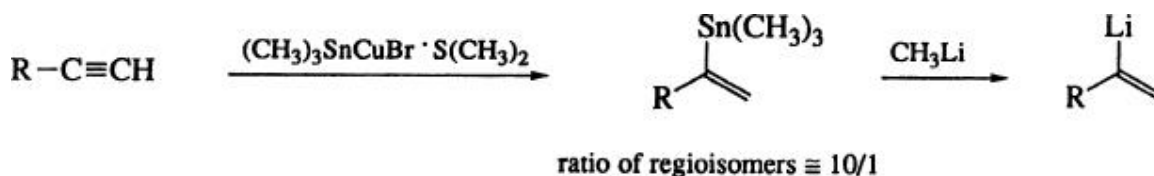
It is also possible to prepare vinylstannanes regioselectively from ketones, via vinyl triflates derived from the corresponding enolates. (140) Thus when combined with stannane lithiation this method achieves the same net transformation as does arenesulfonylhydrazone chemistry. Although the overall procedure is more roundabout, and subject to some limitations, it is a useful alternative to arenesulfonylhydrazone chemistry because the regioselectivity is determined simply by kinetic versus thermodynamic enolate formation. In particular, this is an effective method for the preparation of the more highly substituted vinyllithium regioisomer.
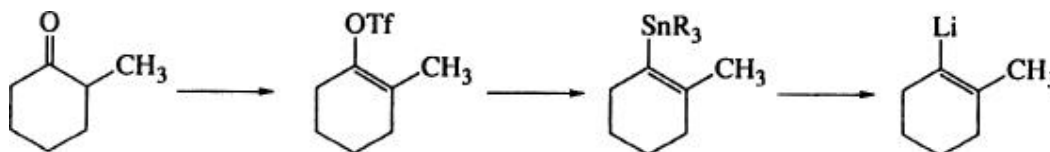
Direct deprotonation of alkenes to form alkenyllithiums (method d) is not general because of competitive formation of the corresponding allyllithium. There are, however, numerous useful applications that afford heteroatomsubstituted vinyllithiums that cannot be prepared from arenesulfonylhydrazones. (142-148)

(Ref. 142)

(Ref. 146)

(Ref. 143)

(Ref. 147)

(Ref. 144)

(Ref. 148)
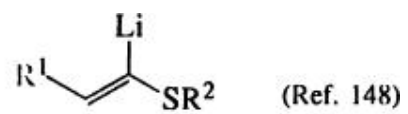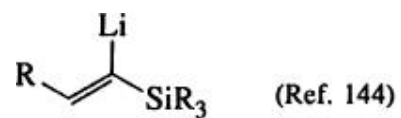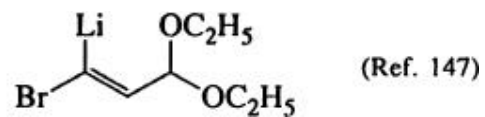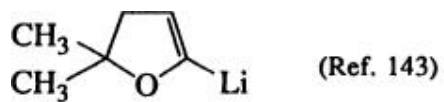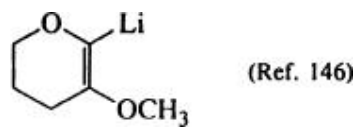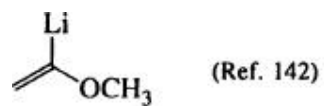
5. Experimental Conditions

For tosylhydrazones the choice of reaction solvent is usually limited to TMEDA or TMEDA–hydrocarbon mixtures if the vinyllithium is to be trapped efficiently. Generally, at least 3 equivalents of *n*-butyllithium is added to the tosylhydrazone in solution between –50° and 0° (TMEDA freezes at –55°), followed by stirring at ambient temperature for several hours before quenching with an excess of the desired electrophile. In many cases, particularly on a small scale, the progress of vinyllithium formation cannot be followed reliably by monitoring nitrogen evolution because the rate is too low. Most tosylhydrazones with 2 or 3 α protons yield vinyllithiums. However, if removal of an α -methine proton is required, acceptable yields of vinyllithiums are not obtained; (149) trisylhydrazones must be used in these cases. (6)

The range of solvents in which vinyllithiums can be generated from trisylhydrazones is somewhat greater than it is for tosylhydrazones. Because of their greater solubility in nonpolar solvents, trisylhydrazone dianions can be generated in hydrocarbons containing relatively small amounts (typically 10% by volume) of TMEDA. Further, ethereal solvents such as tetrahydrofuran (THF), diethyl ether, and dimethoxyethane (glyme, DME), in which tosylhydrazones are inefficient as vinyllithium precursors, can also be used.

In contrast to the tosylhydrazone reaction, careful attention must be paid to the conditions under which trisylhydrazones are deprotonated. *The importance of adhering to the following specific deprotonation requirements for trisylhydrazones cannot be overly stressed, since incomplete deprotonation before warming invariably results in a reduced yield of the vinyllithium*. For trisylhydrazones derived from methyl ketones, 2 equivalents of *n*-butyllithium is added to the hydrazone solution at –78°, followed after 15 minutes by warming to 0° until nitrogen evolution ceases, which is usually within 1 minute (CAUTION: Gas evolution can be quite vigorous, especially on a large scale.) It is important to note that significant protonation of the newly formed vinyllithium by tetrahydrofuran can often be detected within 10 minutes at 0°, so that prompt addition of the electrophile is necessary.

If the α position of the trisylhydrazone to be deprotonated is monosubstituted (i.e., — CH_2R rather than — CH_3), it is necessary to use a stronger base and longer deprotonation time; for example, *sec*- or *tert*-butyllithium for 2 hours at –78°. (6) Although there are some examples of deprotonation being conducted at slightly higher temperatures, (34, 38) to do so can risk a reduced yield of the vinyllithium because under these conditions some trisylhydrazone dianions (especially those of "locked" cyclohexanones) undergo significant elimination to the vinyllithium, which is protonated by unreacted monoanion. (65)

For still more highly substituted derivatives, in which an α -methine proton must be removed, ambient temperature is required for the deprotonation step. (6) Since this

process takes more than an hour at 20° for diisopropyl ketone trisylhydrazone, hexane–TMEDA is used as the reaction solvent (tetrahydrofuran would most likely protonate the vinyllithium competitively during this extended period).

6. Experimental Procedures

6.1.1.1. Cyclohexanone Trisylhydrazone [General Procedure for Preparing Trisylhydrazones of Unhindered Ketones in Methanol] (6)

To a stirred suspension of 29.8 g (0.10 mol) of finely ground trisylhydrazine in 100 mL of methanol was added 9.82 g (0.10 mol) of freshly distilled cyclohexanone. The addition of 1 mL of concentrated hydrochloric acid caused the mixture to clear rapidly, after which a fine granular product began to crystallize. The reaction mixture was chilled at –10° overnight and filtered. The product was washed with cold methanol and dried at room temperature at 0.5 torr to yield 30.8 g (81%) of white crystals, mp 123–124° dec; IR (CHCl$_3$) 3240, 2945, 2880, 1640, 1168, 1155, 1010, 650 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.25 (d, J = 7 Hz, 18H), 1.57 (br s, 6H), 2.30 (br s, 4H), 2.90 (septet, J = 7 Hz, 1H), 4.26 (septet, J = 7 Hz, 2H), 7.18 (2 overlapping s; 3H (aryl and NH)). Anal. Calcd for C$_{21}$H$_{34}$N$_2$O$_2$S : C, 66.64; H, 9.05. Found: C, 66.85; H, 8.89.

6.1.1.2. Camphor Trisylhydrazone [General Procedure for Preparing Trisylhydrazones of Hindered Ketones in Acetonitrile] (6)

To a solution of 33.0 g (0.11 mol) of trisylhydrazine in 100 mL of acetonitrile was added 15.2 g (0.10 mol) of camphor and 10 mL (0.12 mol) of concentrated hydrochloric acid. The solution was stirred overnight at room temperature and cooled at 0° for 4 hours, and the resulting white solid was collected. The crude product was taken up in a minimum amount of chloroform, filtered, concentrated in vacuo, and dried at 0.5 torr to give 30.3 g (70%) of a white solid, mp 197–199° (dec); ^{1}H NMR (CDCl$_3$) δ 0.60 (s, 3H), 0.80 (s, 6H), 1.25 (2 overlapping d, J = 7 Hz, 18H), 1.4–2.4 (m, 7H), 2.88 (septet, J = 7 Hz, 1H), 4.23 (septet, J = 7 Hz, 2H), 7.15 (s, 2H), 7.45 (br s, 1H). Anal. Calcd for C$_{25}$H$_{40}$N$_2$O$_2$S : C, 69.40; H, 9.32. Found: C, 69.28; H, 9.30.

6.1.1.3. Cyclohexyl Methyl Ketone Trisylhydrazone [General Procedure for Preparing Trisylhydrazones in Diethyl Ether] (15)

Cyclohexyl methyl ketone (2.52 g, 0.02 mol) was added to 5.97 g (0.02 mol) of trisylhydrazine suspended in 70 mL of diethyl ether in a 100-mL recovery flask sealed with a rubber septum. The reaction mixture became homogeneous, and TLC on silica gel developed with 65:30:5 hexane–ethyl acetate–methanol showed trisylhydrazine at R_f 0.50 and product at R_f 0.67. After the mixture had been stirred magnetically for 18 hours, TLC indicated that the reaction was complete. The ether was evaporated with a stream of nitrogen until crystallization commenced, whereupon the mixture was placed in the freezer (–20°) for 1 hour. The white solid was isolated by suction filtration on a sintered-glass frit and washed with a little cold ether. It was dried under a nitrogen cone and then under vacuum to yield 7.08 g (87%) of product, mp 142–143°. Two further crops, totaling 4%, could be gleaned from the mother liquors by repeating the cycle of reducing the volume and cooling. ^{1}H NMR

(CDCl$_3$) δ 0.87–1.87 (m, 10 *H*), 1.27 (d, *J* = 7 Hz, 18*H*), 1.75 (s, 3*H*), 2.13 (m, 1*H*), 2.93 (septet, *J* = 7 Hz, 1*H*), 4.28 (septet, *J* = 7 Hz, 2*H*), 7.18 (s, 2*H*), 7.2 (br s, 1*H*).

6.1.1.4. Cyclododecanone Benzenesulfonylhydrazone [General Procedure for Preparing Tosylhydrazones and Benzenesulfonylhydrazones in Ethanol] (37)

The ketone (1 equivalent) was dissolved in absolute ethanol along with the benzenesulfonyl- or tosylhydrazine (1 equivalent) and a catalytic amount of *p*-toluenesulfonic acid. The mixture was heated to reflux under nitrogen for 0.4–5 hours and cooled. The crystals so obtained were filtered and recrystallized from ether–hexane. If crystals did not precipitate from solution, the reaction mixture was concentrated, and the oily residue was taken up in ether and precipitated by the addition of hexane: 93%; mp 163–168°; ^{1}H NMR (CDCl$_3$) δ 8.0–7.8 (m, 2*H*), 7.6–7.4 (m, 3*H*), 2.2 (br t, *J* = 6 Hz, 4*H*), 2.0–1.8 (br m, 20*H*).

6.1.1.5. 2-Lithio-1-octene [Terminal Lithioalkene Formation from a Methyl Ketone Trisylhydrazone] (6)

2-Octanone trisylhydrazone was placed in a flame-dried flask flushed with nitrogen. A solution (10 mL/g of trisylhydrazone) of 10% TMEDA in hexane was added, stirring was begun, and the flask was cooled in a dry ice–acetone bath to –78°. *n*-Butyllithium in hexane (2 M, 2.0–2.2 equivalents) was then added dropwise, either from a dropping funnel or through a septum via syringe, causing the solution to turn dark orange-red. After stirring at –78° for 15 minutes, the solution was allowed to warm to ~0°, during which time it turned light yellow. The reaction flask was then cooled in an ice bath until nitrogen evolution ceased (~10 minutes), followed by addition of electrophile as described below.

6.1.1.6. 2-n-Hexyl-1-phenyl-2-propenol [Lithioalkene Reaction with an Aldehyde] (6)

A solution of 2-lithio-1-octene was prepared as described above from 10.0 g (0.0245 mol) of the trisylhydrazone and 25.7 mL (0.0514 mol) of 2.0 M *n*-butyllithium. The solution was treated with stirring at 0° with 3.12 g (0.0294 mol) of freshly distilled benzaldehyde. The reaction was stirred for 1 hour at room temperature and then worked up by pouring into water, extracting several times with ether, washing the combined organic layers with water several times to remove traces of TMEDA, and drying over magnesium sulfate. A GLC analysis (6% SE-30 on Chromosorb W column at 200°) of the crude product showed a single peak in 84% yield, using purified product as standard. Short-path distillation afforded 3.31 g (62%) of the product as a colorless liquid, bp 135–138° (1.0 torr); ^{1}H NMR (CDCl$_3$) δ 0.83 (t, *J* = 6 Hz, 3*H*), 1.0–1.5 (m, 8*H*), 1.85 (m, 2*H*), 2.57 (s, 1*H*), 4.90 (s, 1*H*), 5.03 (s, 1*H*), 5.18 (s, 1*H*), and 7.28 (s, 5*H*); MS *m/e* 133 (base) and 218 (parent). Anal. Calcd for C$_{15}$H$_{22}$O : C, 82.52; H, 10.16. Found: C, 82.57; H, 10.18.

6.1.1.7. 2-n-Butyl-1-octene [Lithioalkene Reaction with a Primary Bromide] (*6*)
A solution of 2-lithio-1-octene was prepared as described above and treated with 4.03 g (0.0294 mol) of *n*-butyl bromide. After stirring at room temperature for 4 hours the reaction was worked up as described above (GLC yield 72%). Distillation through a 10-cm Vigreux column afforded 2.39 g (58%) of a clear liquid, bp 87–89° (28 torr); ^{1}H NMR (CDCl$_3$) δ 0.88 (t, *J* = 6 Hz, 6*H*), 1.0–1.7 (m, 12*H*), 2.00 (t, *J* = 6 Hz, 4*H*), and 4.70 (s, 2*H*); MS *m/e* 168 (parent) and 56 (base).

6.1.1.8. 2-Trimethylsilyl-1-octene [Lithioalkene Reaction with Trimethylsilyl chloride] (*6*)
A solution of 2-lithio-1-octene was prepared as described above and treated at 0° with 3.18 g (0.0294 mol) of chlorotrimethylsilane. After stirring for 1 hour at room temperature the reaction mixture was worked up as described above. A GLC analysis showed 1-octene (5%) and the vinylsilane (71%). The crude material was subjected to short-path distillation, affording 2.50 g (55%) of clear liquid, bp 78–80° (14 torr); ^{1}H NMR (CDCl$_3$) δ 0.00 (s, 9*H*), 0.80 (t, *J* = 6 Hz, 3*H*), 1.0–1.7 (m, 8*H*), 2.05 (m, 2*H*), 5.25 (m, 1*H*), 5.45 (m, 1*H*); MS *m/e* 184 (parent) and 73 (base). Careful GLC–mass spectral analysis showed ~1% of an isomeric product. Anal. Calcd. for C$_{11}$H$_{24}$Si : C, 71.65; H, 13.12. Found: C, 71.62; H, 12.97.

6.1.1.9. 2-Bromo-1-octene [Lithioalkene Reaction with Dibromoethane] (*6*)
A solution of 2-lithio-1-octene was prepared as described above from 4.1 g of the trisylhydrazone (0.010 mol) and 10.0 mL (0.020 mol) of 2.0 M *n*-butyllithium in hexane. The solution was treated at 0° with 2.00 g (0.0106 mol) of 1,2-dibromoethane and stirred until gas evolution ceased. Standard workup followed by short-path distillation afforded 0.83 g (43%) of the vinyl bromide, bp 70–72° (18 torr); ^{1}H NMR (CDCl$_3$) δ 0.88 (t, *J* = 6 Hz, 3*H*), 1.29 (m, 8*H*), 2.41 (br t, *J* = 7 Hz, 2*H*), 5.37 (d, *J* = 1.3 Hz, 1*H*), and 5.52 (q, *J* = 1.3 Hz, 1*H*).

6.1.1.10. 3-Methylcyclohexene-2-carboxaldehyde [Regioselective Lithioalkene Formation from an α -Substituted Ketone Trisylhydrazone] (*6*)
A solution of 2-lithio-3-methylcyclohexene was prepared by treating 10.0 g (0.255 mol) of 2-methylcyclohexanone trisylhydrazone in 10% TMEDA–hexane with 48.7 mL (0.0536 mol) of 1.1 M *sec*-butyllithium in hexane. After the resultant reddish solution was stirred for 2 hours at –78° it was warmed to 0°. When nitrogen evolution had ceased (5 minutes), 2.05 g (0.0280 mol) of *N,N*-dimethylformamide was added. After stirring for 1 hour at room temperature the reaction was worked up as described above. Short-path distillation afforded 1.99 g (63%) of colorless liquid, bp 88–90° (26 torr); IR 2840, 2735, 1698, 1650 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.07 (d, *J* = 7 Hz, 3*H*), 1.6 (m, 4*H*), 2.3 (m, 2*H*), 2.67 (m, 1*H*), 6.74 (t of d, *J* = 4, 0.7 Hz, 1*H*), and 9.37 (s, 1*H*).

6.1.1.11. 3-Methyl-2-isopropyl-2-butenal [Lithioalkene Formation from an α , α -Disubstituted Ketone Trisylhydrazone] (6)

To a stirred solution of 10.0 g (0.0254 mol) of diisopropyl ketone trisylhydrazone in 100 mL of 50% TMEDA–hexane at –78° was added 70 mL (0.077 mol) of 1.1 M *sec*-butyllithium in cyclohexane. The reaction mixture was immersed in a room temperature bath and stirring was continued for 1.5 hours, at which time 3.70 g (0.051 mol) of *N,N*-dimethylformamide was added. After stirring for 1 hour the reaction mixture was worked up as described above to give the product in a GC yield of 74%. Short-path distillation afforded 1.71 g (53%) of a clear liquid, bp 70–73° (25 torr); IR 2810, 2780, 1680, and 1625 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.15 (d, *J* = 7 Hz, 6*H*), 1.97 (s, 3*H*), 2.15 (s, 3*H*), 2.9 (septet of d, *J* = 7, 1.5 Hz, 1*H*), and 10.11 (d, *J* = 1.5 Hz, 1*H*). Anal. Calcd for C$_8$H$_{14}$O : C, 76.14; H, 11.18. Found: C, 76.25; H, 11.27.

6.1.1.12. (E)-4-(Trimethylsilyl)-3-heptene [General Procedure for the Preparation of Vinylsilanes from Tosyl- or Benzenesulfonylhydrazones; Stereoselective Formation of an (E)-Vinyllithium] (37)

A dry, three-necked flask equipped with a stirring bar, a nitrogen inlet, a rubber septum, and an Erlenmeyer flask containing the *p*-toluene- or benzenesulfonylhydrazone (ca. 5 g) connected by a short piece of Gooch tubing was charged with dry TMEDA. The solvent was cooled to –45°, and *n*-butyllithium (4 equivalents) in hexane was introduced via syringe. To this cold solution was slowly added in portions the arenesulfonylhydrazone. A dark red color developed immediately. Upon completion of the addition (10–20 minutes), the solution was stirred for an additional 30–60 minutes before it was allowed to warm to room temperature for 1–2 hours. During this time, nitrogen was evolved. When nitrogen evolution had ceased, the red solution was cooled to 0°, and chlorotrimethylsilane (4 equivalents) was slowly injected from a syringe. The solution generally lightened to a yellow color and then slowly turned black. After being stirred at 0° for 30 minutes, the reaction mixture was allowed to warm to room temperature where it was kept for several hours prior to being poured into water (200 mL) and pentane (100 mL). The organic layer was separated and subsequently extracted with water (2 × 200 mL), saturated copper sulfate solution (2 × 200 mL), and brine (100 mL). The dried solution was concentrated, applied to neutral alumina, and eluted with pentane through a short (5-cm) plug of neutral alumina to remove the colored material. The eluant was concentrated and used as obtained or was distilled. For 4-heptanone benzenesulfonylhydrazone as starting material, (*E*)-4-(trimethylsilyl)-3-heptene was obtained in a yield of 97%: bp 43° (32 torr); ^{1}H NMR (CDCl$_3$) δ 5.76 (t, *J* = 7 Hz, 1*H*), 2.4–1.9 (m, 4*H*), 1.74–1.24 (m, 2*H*), 1.2–0.7 (m, 6*H*), 0.15 (s, 9*H*). Anal. Calcd for C$_{10}$H$_{22}$Si : C, 70.49; H, 13.02. Found: C, 70.64; H, 13.03.

6.1.1.13. 3-Methyl-2-bornenecarboxaldehyde [In Situ Dianion Alkylation–Lithioalkene Formation in Tetrahydrofuran] (65)

The dianion of camphor trisylhydrazone was prepared as follows. A dry 100-mL round-bottomed flask fitted with a rubber septum was charged with 25 mL of dry THF and 4.50 g (0.010 mol) of camphor trisylhydrazone, and the mixture was stirred magnetically until all solid had dissolved. The temperature was lowered to –78° with a dry ice–acetone bath, and 20 mL (0.028 mol) of *sec*-butyllithium was added dropwise from a syringe over a 10-minute period. The resultant dianion was treated with 2.56 g (0.018 mol) of freshly distilled methyl iodide. After the mixture was stirred for 2 hours at –78°, 24 mL (0.034 mol) of *sec*-butyllithium was added, and the stirred solution allowed to warm toward room temperature until vigorous nitrogen evolution ceased, at which time 4 mL of DMF was added and the solution stirred for 5 minutes. The reaction mixture was poured into water and extracted with several portions of ether. The combined organic layers were washed with water, dried over MgSO$_4$, and concentrated. Short-path distillation afforded 0.82 g (46%) of product as a light yellow liquid, bp 69–70° (0.05 mm); IR 2980, 2745, 1675, 1612, 1345, and 760 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.80 (s, 6*H*), 0.90–2.3 (m, 5*H*), 1.26 (s, 3*H*), 2.12 (s, 3*H*), 9.87 (s, 1*H*). Anal. Calcd for C$_{12}$H$_{18}$O : C, 80.85; H, 10.18. Found: C, 80.92; H, 10.27.

6.1.1.14. rel-(1R,3aS)-2,3,3a,4,5,6-Hexahydro-1-(deuteriomethyl)indene [Lithioalkene Cyclization] (48)

A solution of 0.432 g (1.00 mmol) of 2-(4-butenyl)-cyclohexanone trisylhydrazone in 5 mL of THF was cooled to –78° under argon, and 1.5 mL (2.10 mmol) of a 1.4-M solution of *sec*-butyllithium in cyclohexane was added dropwise. After 30 minutes the resultant red-orange solution was warmed to 0° with an ice bath, resulting in the vigorous evolution of nitrogen (vented through a bubbler) and a change of color to pale yellow. The reaction was quenched after 10 minutes by the dropwise addition of D$_2$O followed by a standard aqueous workup. Bulb-to-bulb distillation gave 0.119 g (87%) of the cyclized product; ^{1}H NMR (250 MHz, CDCl$_3$) δ 1.02 (m, *J* = 7 Hz, 2*H*), 1.45 (m, 2*H*), 1.91 (m, 6*H*), 2.21 (m, 1*H*), 2.45 (m, 1*H*), 5.38 (br s, 1*H*); GC–MS, *m/e* 137 (12), 136 (20), 121 (100), 108 (12), 107 (17), 95 (36), 93 (37), 91 (21), 81 (12), 80 (14), 79 (60), 77 (19), 67 (19); HRMS, *m/e* calcd for C$_{10}$H$_{15}$D , (M$^+$) 137.1315. Found: 137.1302. GC–MS showed no detectable minor isomer.

7. Tabular Survey

The examples in the tables were obtained by searches of *Chemical Abstracts* and *Science Citation Index* through mid-1987. The survey is divided into six tables, according to the type of vinyllithium that has been generated. Individual examples within each Table are listed in order of increasing carbon number of the starting ketone.

The specific hydrazone type, conditions for vinyllithium formation, electrophile, and product(s) are listed. Yields are in parentheses and refer to the conversion of the arenesulfonylhydrazone into the final product (not into the vinyllithium itself). For reactions in which more than one product was reported, yields for each are listed whether or not each was isolated separately. A dash indicates that no yield was given. For Tables III–VI, the first electrophile listed is that which reacts with the dianion, usually at –78°, and the second quenches the vinyllithium. In the few cases for which three reagents are listed in the "electrophile" column, explanatory notes are given.

Relative stereochemistry for reactants, electrophiles, and products is indicated by the usual wedge-dash conventions. In compounds with multiple stereogenic centers, simple lines are used to represent bonds to atoms for which relative stereochemistry is unknown or not given in the original work, i.e., the compound may or may not be a mixture of more than one diastereomer. Likewise, if alkene stereochemistry is not shown explicitly, it was not given in the original paper. Wavy lines connote definite but unquantified mixtures of diastereomers at the indicated stereogenic center(s).

The following abbreviations are used in the tables:

BSH   benzenesulfonylhydrazone

DME   1,2-dimethoxyethane
THF   tetrahydrofuran
TMEDA *N,N,N′,N′*-tetramethylethylenediamine
Tosyl   *p*-toluenesulfonyl
Trisyl   2,4,6-triisopropylbenzenesulfonyl
Ts   *p*-toluenesulfonyl

Table I. Acyclic Vinyllithium Reagents

View PDF

Table II. Cyclic Vinyllithium Reagents

View PDF

Table III. Dianion Alkylation Followed by Acyclic Vinyllithium Formation

View PDF

Table IV. Dianion Alkylation Followed by Cyclic Vinyllithium Formation

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Table V. Acyclic Vinyllithium Formation and Cyclization with an Internal Electrophile

[View PDF](#)

Table VI. Cyclic Vinyllithium Formation and Cyclization with an Internal Electrophile

[View PDF](#)

TABLE I. ACYCLIC VINYLLITHIUM REAGENTS
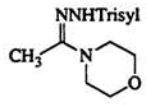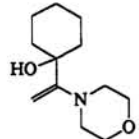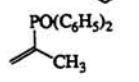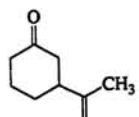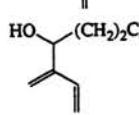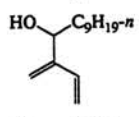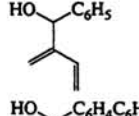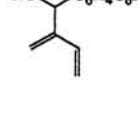
Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
C₂ Acetyl Chloride	NNHTrisyl, CH₃—C=N—(morpholine)	t-C₄H₉Li, THF	Cyclohexanone	(≥60)[a]	22
C₃ Acetone	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	1. (C₆H₅)₂PCl 2. 30% H₂O₂	(63)	38
	"	t-C₄H₉Li, THF, C₆H₅SCu	2-Cyclohexenone	(51)	67
C₄ CH₃COCH=CH₂	"	CH₃Li, DME	C₆H₅(CH₂)₂CHO	HO—(CH₂)₂C₆H₅ (55)	23
	"	"	n-C₉H₁₉CHO	HO—C₉H₁₉-n (49)	23
	"	"	C₆H₅CHO	HO—C₆H₅ (46)	23
	"	"	2-C₆H₅C₆H₄CHO	HO—C₆H₄C₆H₅-2 (50)	23

TABLE I. Acyclic Vinyllithium Reagents (*Continued*)
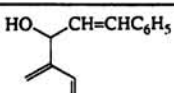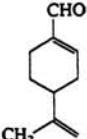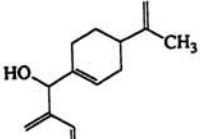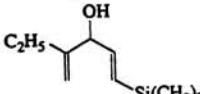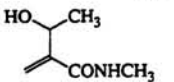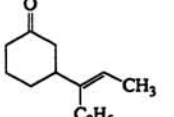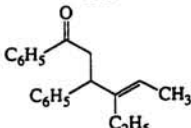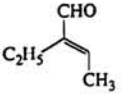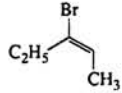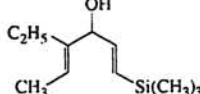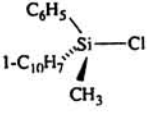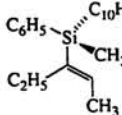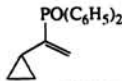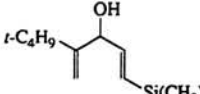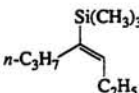
Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
"	"	"	C₆H₅CH=CHCHO	HO–CH=CHC₆H₅ structure (32)	23
	"	"	CHO-substituted cyclohexene (4-isopropenyl)	HO– structure (40)	23
2-Butanone	"	s-C₄H₉Li, 50% TMEDA, hexane	(E)-3-Trimethylsilyl-propenal	OH structure, C₂H₅ ... Si(CH₃)₃ (90)	64
CH₃COCONHCH₃	"	n-C₄H₉Li, DME	CH₃CHO	HO–CH₃ structure, CONHCH₃ (45)	30
C₅ 3-Pentanone	"	t-C₄H₉Li, THF, C₆H₅SCu	2-Cyclohexenone	cyclohexanone structure, CH₃ / C₂H₅ (43)	67
	"	"	Chalcone	C₆H₅ structure, C₆H₅ / C₂H₅ / CH₃ (40)	67
	"	n-C₄H₉Li, 10% TMEDA, hexane	HCON(CH₃)₂	CHO structure, C₂H₅ / CH₃ (70)	6
	"	"	Br(CH₂)₂Br	Br structure, C₂H₅ / CH₃ (69)	6
	"	s-C₄H₉Li, 50% TMEDA, hexane	(E)-3-Trimethylsilyl-propenal	OH structure, C₂H₅ / CH₃ ... Si(CH₃)₃ (73)	64
	"	n-C₄H₉Li, 50% TMEDA, hexane	C₆H₅(CH₃)(1-C₁₀H₇)Si–Cl	C₆H₅Si(C₁₀H₇-1)(CH₃) structure, C₂H₅ / CH₃ (34)	70
i-C₃H₇COCH₃	"	n-C₄H₉Li, TMEDA	1. (C₅H₉)₃B 2. I₂	2-Cyclopentyl-3-methylbutene (78)	80
	"	n-C₄H₉Li, 10% TMEDA, hexane	1. (n-C₆H₁₃)₃B 2. I₂	CH₂=C(C₆H₁₃-n)C₃H₇-i (79)	80
	"	n-C₄H₉Li, THF	n-C₅H₁₁Br	CH₂=C(C₅H₁₁-n)C₃H₇-i (45)	79
Acetylcyclopropane	"	n-C₄H₉Li, 10% TMEDA, hexane	1. (C₆H₅)₂PCl 2. 30% H₂O₂	PO(C₆H₅)₂ structure on cyclopropane (72)	38
C₆ t-C₄H₉COCH₃	Tosyl	n-C₄H₉Li, TMEDA	n-C₄H₉Br	CH₂=C(C₄H₉-n)C₄H₉-t (66)	4
	Trisyl	n-C₄H₉Li, THF	"	" (47)	79
	"	n-C₄H₉Li, 50% TMEDA, hexane	(E)-3-Trimethylsilyl-propenal	OH structure, t-C₄H₉ ... Si(CH₃)₃ (72)	64
C₇ 2-Heptanone	Tosyl	n-C₄H₉Li, TMEDA	"	CH₂=C[Si(CH₃)₃]C₅H₁₁-n (84) / (26)	37 / 25
4-Heptanone	BSH	n-C₄H₉Li, TMEDA	(CH₃)₃SiCl	Si(CH₃)₃ structure, n-C₃H₇ / C₂H₅ (97)	37

TABLE I.   ACYCLIC VINYLLITHIUM REAGENTS (*Continued*)
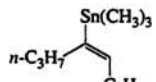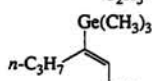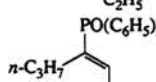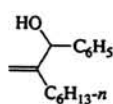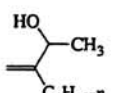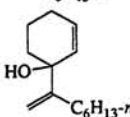
Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	Tosyl	"	"	" (38)	25
	Trisyl	n-C$_4$H$_9$Li, 10% TMEDA, hexane	"	" (96)	87
	BSH	n-C$_4$H$_9$Li, THF	"	" (18)	68
	"	n-C$_4$H$_9$Li, TMEDA, THF	"	" (40)	68
	"	n-C$_4$H$_9$Li, TMEDA	"	" (63)	68
	Tosyl	"	(CH$_3$)$_3$SnCl	(43)	25
	"	"	(CH$_3$)$_3$GeCl	(47)	25
	Trisyl	n-C$_4$H$_9$Li, 10% TMEDA, hexane	1. (C$_6$H$_5$)$_2$PCl 2. 30% H$_2$O$_2$	(68)	38
	"	"	CO$_2$	(E)-C$_2$H$_5$CH=C(CO$_2$H)C$_3$H$_7$-n (—)	6
(i-C$_3$H$_7$)$_2$CO	"	n-C$_4$H$_9$Li, 10% TMEDA, hexane	HCON(CH$_3$)$_2$	(CH$_3$)$_2$C=C(CHO)C$_3$H$_7$-i (74)	6
	"	"	n-C$_4$H$_9$Br	(CH$_3$)$_2$C=C(C$_4$H$_9$-n)C$_3$H$_7$-i (42)	6
C$_8$ 2-Octanone	Tosyl	n-C$_4$H$_9$Li, TMEDA	CO$_2$	CH$_2$=C(CO$_2$H)C$_6$H$_{13}$-n (52)	29
	"	"	n-C$_4$H$_9$Br	CH$_2$=C(C$_4$H$_9$-n)C$_6$H$_{13}$-n (65)	29
	Trisyl	n-C$_4$H$_9$Li, 10% TMEDA, hexane	"	" (72)	6
	"	"	CH$_3$I	CH$_2$=C(CH$_3$)C$_6$H$_{13}$-n (71)	29
	"	"	Br(CH$_2$)$_2$Br	CH$_2$=CBrC$_6$H$_{13}$-n (43)	6
	"	"	(CH$_3$)$_3$SiCl	CH$_2$=C[Si(CH$_3$)$_3$]C$_6$H$_{13}$-n (71)	6
	Tosyl	n-C$_4$H$_9$Li, TMEDA	D$_2$O	CH$_2$=CDC$_6$H$_{13}$-n (91)	5
	"	"	"	" (97)	6
	"	n-C$_4$H$_9$Li, 50% TMEDA, hexane	"	" (—)	74
	Trisyl	n-C$_4$H$_9$Li, 10% TMEDA, hexane	C$_6$H$_5$CHO	(84)	6
	Tosyl	n-C$_4$H$_9$Li, TMEDA	"	" (78)	29
	"	"	CH$_3$CHO	(75)	29
	"	"	2-Cyclohexenone	(67)	29

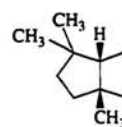TABLE I. Acyclic Vinyllithium Reagents (*Continued*)
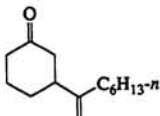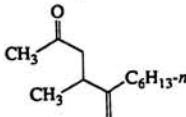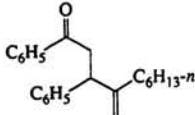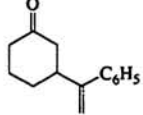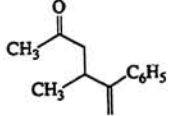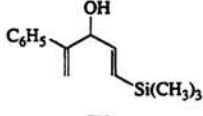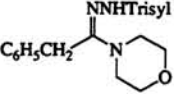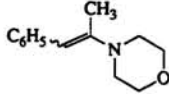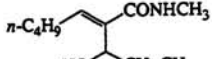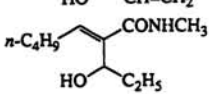
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43

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	Trisyl	t-C$_4$H$_9$Li, THF, C$_6$H$_5$SCu	2-Cyclohexenone	(structure, C$_6$H$_{13}$-n) (36)	67
	"	"	3-Pentene-2-one	(structure, CH$_3$, CH$_3$, C$_6$H$_{13}$-n) (82)	67
	"	"	Chalcone	(structure, C$_6$H$_5$, C$_6$H$_5$, C$_6$H$_{13}$-n) (31)	67
	"	n-C$_4$H$_9$Li, 20% TMEDA, hexane	1. (n-C$_3$H$_7$)$_3$B 2. I$_2$	CH$_2$=C(C$_3$H$_7$-n)C$_6$H$_{13}$-n (69)	80
	"	"	1. (n-C$_4$H$_9$)$_3$B 2. I$_2$	CH$_2$=C(C$_4$H$_9$-n)C$_6$H$_{13}$-n (77)	80
	"	"	1. (i-C$_4$H$_9$)$_3$B 2. I$_2$	CH$_2$=C(C$_4$H$_9$-i)C$_6$H$_{13}$-n (94)	80
	"	"	1. (s-C$_4$H$_9$)$_3$B 2. I$_2$	CH$_2$=C(C$_4$H$_9$-s)C$_6$H$_{13}$-n (73)	80
	"	"	1. (C$_5$H$_9$)$_3$B 2. I$_2$	CH$_2$=C(C$_5$H$_9$)C$_6$H$_{13}$-n (95)	80
Acetophenone	"	"	1. (n-C$_6$H$_{13}$)$_3$B 2. I$_2$	CH$_2$=C(C$_6$H$_{13}$-n)C$_6$H$_5$ (63)	80
	"	"	1. (n-C$_3$H$_7$)$_3$B 2. I$_2$	CH$_2$=C(C$_3$H$_7$-n)C$_6$H$_5$ (84)	80
	"	"	1. (n-C$_4$H$_9$)$_3$B 2. I$_2$	CH$_2$=C(C$_4$H$_9$-n)C$_6$H$_5$ (93)	80
	"	"	1. (i-C$_4$H$_9$)$_3$B 2. I$_2$	CH$_2$=C(C$_4$H$_9$-i)C$_6$H$_5$ (97)	80
	"	"	1. (s-C$_4$H$_9$)$_3$B 2. I$_2$	CH$_2$=C(C$_4$H$_9$-s)C$_6$H$_5$ (82)	80
	"	"	1. (C$_5$H$_9$)$_3$B 2. I$_2$	CH$_2$=C(C$_5$H$_9$)C$_6$H$_5$ (83)	80
	Tosyl	n-C$_4$H$_9$Li, TMEDA	C$_2$H$_5$Br	1-Phenyl-1-butene (50)	4
	"	"	CO$_2$	2-Phenylpropenoic acid (61)	29
	"	"	D$_2$O	C$_6$H$_5$CD=CH$_2$ (94)	5
	Trisyl	t-C$_4$H$_9$Li, THF, C$_6$H$_5$SCu	2-Cyclohexenone	(structure, C$_6$H$_5$) (83)	67
	"	"	3-Penten-2-one	(structure, CH$_3$, CH$_3$, C$_6$H$_5$) (78)	67
	"	s-C$_4$H$_9$Li, 50% TMEDA, hexane	(E)-3-Trimethylsilyl-propenal	(structure, C$_6$H$_5$, OH, Si(CH$_3$)$_3$) (70)	64
C$_6$H$_5$CH$_2$COCl	C$_6$H$_5$CH$_2$-C(=NNHTrisyl)-N(morpholine)	t-C$_4$H$_9$Li, THF	CH$_3$I	(structure, C$_6$H$_5$, CH$_3$, N-morpholine) (≥80)[b]	22
n-C$_5$H$_{11}$COCONHCH$_3$	Trisyl	n-C$_4$H$_9$Li, DME	CH$_2$=CHCHO	(structure, n-C$_4$H$_9$, CONHCH$_3$, HO, CH=CH$_2$) (50)	31
	"	"	C$_2$H$_5$CHO	(structure, n-C$_4$H$_9$, CONHCH$_3$, HO, C$_2$H$_5$) (64)	31
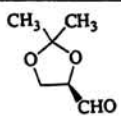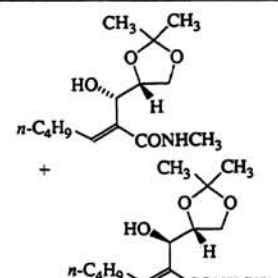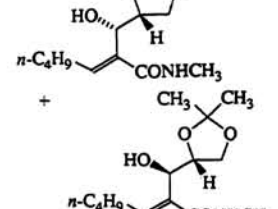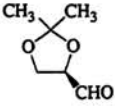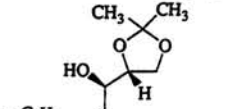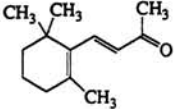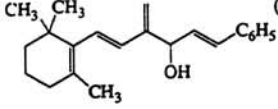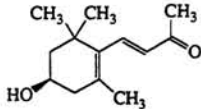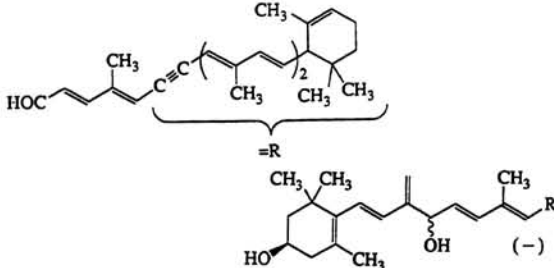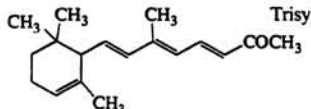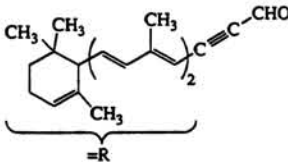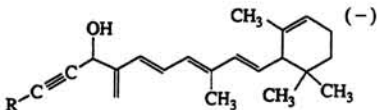
TABLE I. ACYCLIC VINYLLITHIUM REAGENTS (*Continued*)

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	"	"			31
C$_9$ CH$_3$CO(CH$_2$)$_7$Cl	Trisyl	n-C$_4$H$_9$Li, 10% TMEDA, hexane	D$_2$O	CH$_2$=CD(CH$_2$)$_7$Cl (95)	45
C$_6$H$_5$COC$_2$H$_5$	BSH	n-C$_4$H$_9$Li, TMEDA	(CH$_3$)$_3$SiCl	I (−)	37
	"	n-C$_4$H$_9$Li, TMEDA 2 h, 50°	"	I (13) 	63
	"	n-C$_4$H$_9$Li, TMEDA 3 h, 60°	"	I (58)	63
	"	n-C$_4$H$_9$Li, TMEDA	"	I (−)	37
	Tosyl	"	CH$_3$I	C$_6$H$_5$C(CH$_3$)=CHCH$_3$ (95) *cis:trans*, 1:1	4
C$_6$H$_5$CH$_2$COCH$_3$	Trisyl	1. n-C$_4$H$_9$Li, 10% TMEDA, hexane, −78° 2. →0°, 5 min	D$_2$O		6
			"	I(") (−)	40
			(CH$_3$)$_3$SiCl	I[E = Si(CH$_3$)$_3$] (51) + II(") (5) + III(") (2)	6
			C$_6$H$_5$CHO	I(E = C$_6$H$_5$CHOH) (60) + II(") (<5) + III(") (<5)	6
		1. n-C$_4$H$_9$Li, 10% TMEDA, hexane, −78° 2. →0°, 30 min^c	D$_2$O		6
			(CH$_3$)$_3$SiCl	I(E = Si(CH$_3$)$_3$) (10) + II(") (54) + III(") (5)	6
			n-C$_4$H$_9$Br	I(E = n-C$_4$H$_9$) (60) + II(") (<5) + III(") (<5)	6
	Tosyl	n-C$_4$H$_9$Li, TMEDA	CH$_3$I	C$_6$H$_5$C(CH$_3$)=CH$_2$ (55) + C$_6$H$_5$CH=CHC$_2$H$_5$ (45) *cis:trans*, 19:26	4
CH$_3$COCONHC$_6$H$_{11}$	"	n-C$_4$H$_9$Li, DME	CH$_2$=CHCHO	(81)	31, 32

TABLE I. ACYCLIC VINYLLITHIUM REAGENTS (*Continued*)

46

47

C₁₂

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	"	"	C₂H₅CHO	HO, C₂H₅ / CONHC₆H₁₁ (81)	31, 30
	"	"	CH₃CHO	HO, CH₃ / CONHC₆H₁₁ (74)	30
	"	"	Cyclohexanone	HO / CONHC₆H₁₁ (70)	30
	"	"	D₂O	CH₂=CDCONHC₆H₁₁ (54)	32
	"	"	HCHO	CH₂OH / CONHC₆H₁₁ (59)	32, 30, 31
	"	"	n-C₃H₇CHO	HO, C₃H₇-n / CONHC₆H₁₁ (80)	32, 30
	"	"	CH₃ CH₃ dioxolane CHO	HO... H / CONHC₆H₁₁ (46) + HO H / CONHC₆H₁₁ (14)	32
	"	"	Acetone	COH(CH₃)₂ / CONHC₆H₁₁ (59)	32, 31
C₆H₅(CH₂)₂COCl	NNHTrisyl C₆H₅(CH₂)₂ N-morpholine	t-C₄H₉Li, THF	CH₃I	CH₃ C₆H₅CH₂ N-morpholine (≥25%)ᵈ	22
C₁₀ CH₃CO(CH₂)₂C₆H₅	Tosyl	n-C₄H₉Li, TMEDA	CH₃I	C₆H₅(CH₂)₂C(CH₃)=CH₂ (55)	4
C₆H₅S(CH₂)₂COCH₃	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	HCHO	C₆H₅S(CH₂)₂C(CH₂OH)=CH₂ (53)	44
CH₃COCONHCH₂C₆H₅	"	n-C₄H₉Li, DME	CH₃CHO	HO, CH₃ / CONHCH₂C₆H₅ (57)	30
	"	"	C₂H₅CHO	HO, C₂H₅ / CONHCH₂C₆H₅ (58)	30
C₆H₅COC₃H₇-i	Tosyl	n-C₄H₉Li, TMEDA	CH₃I	C₆H₅C(CH₃)=C(CH₃)₂ (63)	4
	"	"	D₂O	C₆H₅CD=C(CH₃)₂ (55)	4
CH₃ O / CH₃ CH₃ CH₃ (structure)	"	"	HCON(CH₃)₂	CH₃ CHO (structure) (60)	47
C₁₃ n-C₅H₁₁COCONHC₆H₁₁	Trisyl	n-C₄H₉Li, DME	D₂O	n-C₄H₉ D / CONHC₆H₁₁ (62)	32
	"	"	Acetone	n-C₄H₉ COH(CH₃)₂ / CONHC₆H₁₁ (21)	32, 31

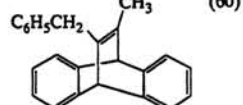TABLE I. ACYCLIC VINYLLITHIUM REAGENTS (*Continued*)

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	"	"	CD₃COCD₃	(38)	32, 31
	"	"	CH₂=CHCHO	(51)	32, 31
	"	"	C₂H₅CHO	(64)	32
	"	"		(13) + (21)	32
	"	s-C₄H₉Li, 50% TMEDA, hexane	C₆H₅CH=CHCHO	(65)	24
	"	"		(−)	24
C₁₄ C₆H₅COCH₂C₆H₅	Tosyl	s-C₄H₉Li, TMEDA	CH₃I	1,3-Diphenylpropene (85) *cis:trans*, 4:13	4
C₁₈	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane		(−)	24

[a] The yield reported for ketone produced by hydrolysis of the enamine was 60%.
[b] The yield reported for ketone produced by hydrolysis of the enamine was 80%.
[c] These are conditions of equilibration for the initially formed vinyllithium with corresponding allyllithium.
[d] The yield reported for ketone produced by hydrolysis of the enamine was 25%.
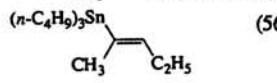
TABLE II. CYCLIC VINYLLITHIUM REAGENTS
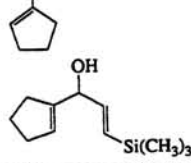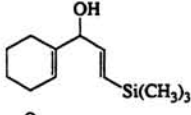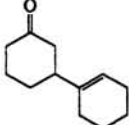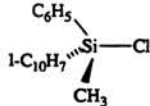
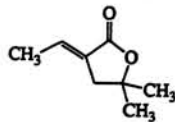|	Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
C₅	Cyclopentanone	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	1. (n-C₄H₉)₃B 2. I₂	1-(n-Butyl)cyclopentene (95)	81
		"	"	1. (s-C₄H₉)₃B 2. I₂	1-(2-Butyl)cyclopentene (93)	81
		"	"	1. (i-C₄H₉)₃B 2. I₂	1-(2-Methylpropyl)cyclopentene (90)	81
		"	"	1. (C₅H₉)₃B 2. I₂	1-(Cyclopentyl)cyclopentene (98)	81
		"	"	1. (n-C₆H₁₃)₃B 2. I₂	1-(n-Hexyl)cyclopentene (96)	81
		"	"	1. (C₆H₅)₂PCl 2. 30% H₂O₂	PO(C₆H₅)₂ (75) [cyclopentene-1-yl]	38
		"	s-C₄H₉Li, 50% TMEDA/hexane	(E)-3-Trimethylsilyl-propenal	[1-(1-hydroxy-3-trimethylsilyl-2-propenyl)cyclopentene] OH ... Si(CH₃)₃ (22)	64
		Tosyl	n-C₄H₉Li, TMEDA	(CH₃)₃SiCl	1-(Trimethylsilyl)cyclopentene (50)	37, 88, 25
C₆	Cyclohexanone	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	1. (n-C₄H₉)₃B 2. I₂	1-(n-Butyl)cyclohexene (77)	81
		"	"	1. (s-C₄H₉)₃B 2. I₂	1-(2-Butyl)cyclohexene (96)	81
		"	"	1. (i-C₄H₉)₃B 2. I₂	1-(2-Methylpropyl)cyclohexene (67)	81
		"	"	1. (C₅H₉)₃B 2. I₂	1-(Cyclopentyl)cyclohexene (79)	81
		"	"	1. (n-C₃H₇)₃B 2. I₂	1-(n-Propyl)cyclohexene (82)	81
		"	"	1. (C₆H₅)₂PCl 2. 30% H₂O₂	PO(C₆H₅)₂ (73) [cyclohexene-1-yl]	38
		"	n-C₄H₉Li, 50% TMEDA, hexane	(E)-3-Trimethylsilyl-propenal	[1-(1-hydroxy-3-trimethylsilyl-2-propenyl)cyclohexene] OH ... Si(CH₃)₃ (69)	64
		"	t-C₄H₉Li, THF, C₆H₅SCu	2-Cyclohexenone	[3-(cyclohexen-1-yl)cyclohexanone] (52)	67
		Tosyl	n-C₄H₉Li, TMEDA	C₂H₅Br	1-(Ethyl)cyclohexene (76)	4
		"	"	n-C₃H₇Br	1-(n-Propyl)cyclohexene (67)	4
		"	"	HCON(CH₃)₂	1-Cyclohexenecarboxaldehyde (54)	47
		"	"	(CH₃)₃SnCl	1-(Trimethylstannyl)cyclohexene (47)	25
		BSH	"	(CH₃)₃SiCl	1-(Trimethylsilyl)cyclohexene (87)	37
		"	n-C₄H₉Li, THF	"	" (33)	68
		"	n-C₄H₉Li, TMEDA, THF	"	" (43)	68
		"	n-C₄H₉Li, TMEDA	"	" (48)	68
		Tosyl	"	"	" (68, 87)	25, 87, 88
		Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	"	" (83)	6
		"	n-C₄H₉Li, 50% TMEDA, hexane	C₆H₅ ... 1-C₁₀H₇ Si Cl CH₃	C₆H₅ ... C₁₀H₇-1 Si CH₃ [cyclohexen-1-yl] (69)	70

TABLE II. CYCLIC VINYLLITHIUM REAGENTS (*Continued*)
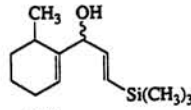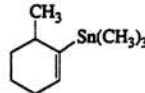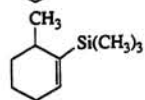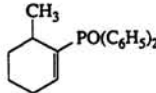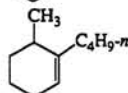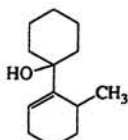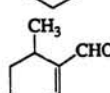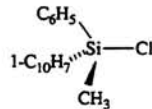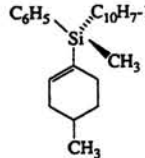
Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
2-Cyclohexenone	Tosyl	n-C$_4$H$_9$Li, 50% TMEDA, hexane	(CH$_3$)$_3$SiCl	2-(Trimethylsilyl)-1,3-cyclohexadiene (40)	25
	"	CH$_3$Li, TMEDA, ether	"	" (23)	26
	BSH	n-C$_4$H$_9$Li, 50% TMEDA, hexane	"	" (26)	27
C$_7$ 2-Methylcyclohexanone	Trisyl	n-C$_4$H$_9$Li, 10% TMEDA, hexane	1. (n-C$_3$H$_7$)$_3$B 2. I$_2$	3-Methyl-2-n-propylcyclohexene (93)	81
	"	"	1. (n-C$_4$H$_9$)$_3$B 2. I$_2$	3-Methyl-2-n-butylcyclohexene (92)	81
	"	"	1. (s-C$_4$H$_9$)$_3$B 2. I$_2$	3-Methyl-2-(2-butyl)cyclohexene (94)	81
	"	"	1. (C$_5$H$_9$)$_3$B 2. I$_2$	3-Methyl-2-cyclopentylcyclohexene (87)	81
	"	"	1. (i-C$_4$H$_9$)$_3$B 2. I$_2$	3-Methyl-2-(2-methylpropyl)-cyclohexene (96)	81
	"	"	1. (n-C$_6$H$_{13}$)$_3$B 2. I$_2$	3-Methyl-2-n-hexylcyclohexene (92)	81
	"	n-C$_4$H$_9$Li, 50% TMEDA, hexane	(E)-3-Trimethylsilyl-propenal	(73)	64
	"	n-C$_4$H$_9$Li, 10% TMEDA, hexane	(CH$_3$)$_3$SnCl	(91)	92
	BSH	n-C$_4$H$_9$Li, TMEDA	(CH$_3$)$_3$SiCl	(91)	37
	Tosyl	"	"	" (68)	25, 89, 88, 41, 87
	Trisyl	n-C$_4$H$_9$Li, 10% TMEDA, hexane	D$_2$O	(88)	6
	Tosyl	n-C$_4$H$_9$Li, TMEDA	"	" (80)	5
	Trisyl	"	1. (C$_6$H$_5$)$_2$PCl 2. 30% H$_2$O$_2$	(77)	38
	"	s-C$_4$H$_9$Li, 50% TMEDA, hexane	n-C$_4$H$_9$Br	(59)	6
	Tosyl	n-C$_4$H$_9$Li, TMEDA	"	" (86)	29
	"	"	Cyclohexanone	(48)	29
	"	"	HCON(CH$_3$)$_2$	(60)	83
	Trisyl	s-C$_4$H$_9$Li, 50% TMEDA, hexane	"	" (63)	6
	"	n-C$_4$H$_9$Li, 50% TMEDA, hexane		(53)	70

TABLE II.   CYCLIC VINYLLITHIUM REAGENTS (*Continued*)
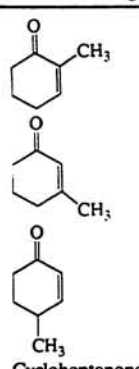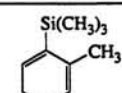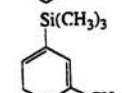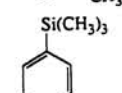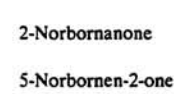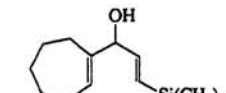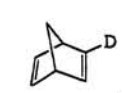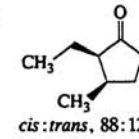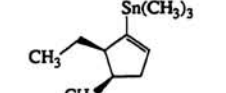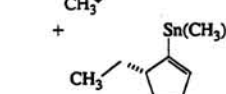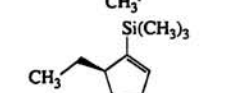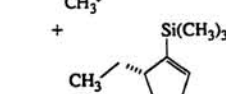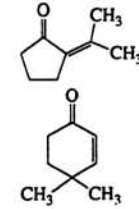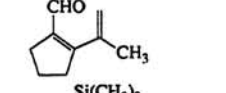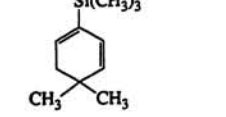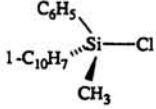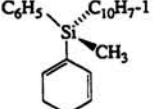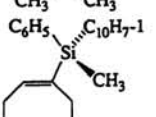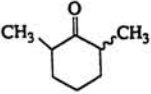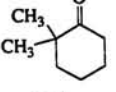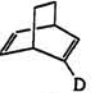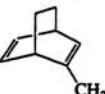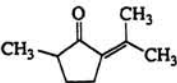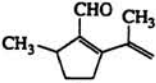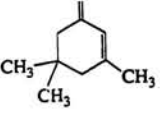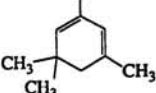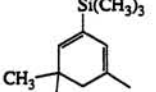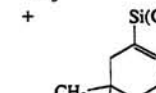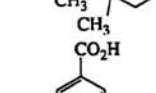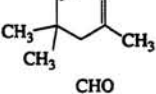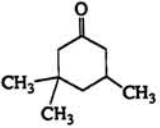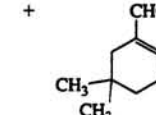
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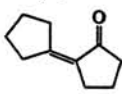| Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)		Refs.
[2-methylcyclohex-2-enone]	Tosyl	n-C₄H₉Li, TMEDA	(CH₃)₃SiCl	[Si(CH₃)₃ / CH₃ cyclohexene]	(44)	25
[3-methylcyclohex-3-enone derivative]	BSH	n-C₄H₉Li, 50% TMEDA, hexane	"	[Si(CH₃)₃ / CH₃]	(62)	27
[4-methylcyclohex-2-enone]	"	"	"	[Si(CH₃)₃ / CH₃]	(58)	27
Cycloheptanone	"	n-C₄H₉Li, TMEDA	"	1-(Trimethylsilyl)cycloheptene	(94)	37
	"	n-C₄H₉Li, THF	"	"	(19)	68
	"	n-C₄H₉Li, TMEDA, THF	"	"	(30)	68
	Tosyl	n-C₄H₉Li, TMEDA	"	"	(62)	25, 88
	"	"	(CH₃)₃SnCl	1-(Trimethylstannyl)cycloheptene	(56)	25
	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	"	"	(84)	92
	BSH	n-C₄H₉Li, TMEDA	(CH₃)₃GeCl	1-(Trimethylgermanyl)cycloheptene	(64)	25
	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	HCON(CH₃)₂	1-Cycloheptenecarboxaldehyde	(—)	84
	·"	s-C₄H₉Li, 50% TMEDA, hexane	(E)-3-Trimethylsilyl-propenal	[cycloheptenyl–CH(OH)–CH=CH–Si(CH₃)₃]	(66)	64
2-Norbornanone	Tosyl	n-C₄H₉Li, TMEDA	D₂O	2-(Deuterio)norbornene	(11)	75
5-Norbornen-2-one	"	"	"	[norbornadiene–D]	(25)	55
C₈ [2-ethyl-3-methylcyclopentanone] *cis:trans*, 88:12	"	n-C₄H₉Li, TMEDA	(CH₃)₃SnCl	[Sn(CH₃)₃ / CH₃ / CH₃ cyclopentene]	(49)	19
				+ [Sn(CH₃)₃ / CH₃ / CH₃]	(12)	
	"	"	(CH₃)₃SiCl	[Si(CH₃)₃ / CH₃ / CH₃ cyclopentene]	(50)	19
				+ [Si(CH₃)₃ / CH₃ / CH₃]	(18)	
[2-(isopropylidene)cyclopentanone]	Trisyl	s-C₄H₉Li, THF	HCON(CH₃)₂	[CHO / cyclopentene–C(CH₃)=CH₂]	(37)	28
[4,4-dimethylcyclohex-2-enone]	BSH	n-C₄H₉Li, 50% TMEDA, hexane	(CH₃)₃SiCl	[Si(CH₃)₃ / CH₃ CH₃]	(67)	27

TABLE II. CYCLIC VINYLLITHIUM REAGENTS (Continued)

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	Trisyl	"	C_6H_5, 1-$C_{10}H_7$, CH_3 Si—Cl	(57)	70
Cyclooctanone	"	"	"	(46)	70
	BSH	n-C_4H_9Li, THF	$(CH_3)_3SiCl$	1-(Trimethylsilyl)cyclooctene (16)	68
	"	n-C_4H_9Li, TMEDA, THF	"	" (23)	68
(2,6-dimethylcyclohexanone)	Trisyl	s-C_4H_9Li, TMEDA	$(CH_3)_3SnCl$	2,6-Dimethyl-2-(trimethylstannyl)-cyclohexene (66)	92
(2,2-dimethylcyclohexanone)	BSH	n-C_4H_9Li, TMEDA	$(CH_3)_3SiCl$	3,3-Dimethyl-2-(trimethylsilyl)-cyclohexene (—)	37
(bicyclo[2.2.2]octenone)	"	CH_3Li, TMEDA	D_2O	(67)	55
	"	"	CH_3I	(63)	55
(C₉ cyclopentanone with isopropylidene)	Trisyl	s-C_4H_9Li, THF	$HCON(CH_3)_2$	CHO (37)	28
(3,5,5-trimethylcyclohex-2-enone)	Tosyl	n-C_4H_9Li, TMEDA	D_2O	(93)	5
	"	n-C_4H_9Li, TMEDA	$(CH_3)_3SiCl$	$Si(CH_3)_3$ (45) + $Si(CH_3)_3$ (5)	6
	"	"	CO_2	CO_2H (45)	29
(3,3,5-trimethylcyclohexanone)	"	"	$HCON(CH_3)_2$	CHO (26) + CHO (39)	47

TABLE II. CYCLIC VINYLLITHIUM REAGENTS (*Continued*)

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	BSH	*n*-C₄H₉Li, TMEDA	D₂O	(40)	150
C₁₀ (CH₂)₂C(CH₃)=CH₂	Trisyl	*n*-C₄H₉Li, 10% TMEDA, ether	D₂O	(CH₂)₂C(CH₃)=CH₂ (95)	45
(CH₂)₂CH=CH₂	"	*t*-C₄H₉Li, DME	Br(CH₂)₂Br	(CH₂)₂CH=CH₂ (83)	48
C₄H₉-*n*	"	*t*-C₄H₉Li, THF	D₂O	C₄H₉-*n* (87)	45
	"	*n*-C₄H₉Li, 10% TMEDA, hexane	1. (C₆H₅)₂PCl 2. 30% H₂O₂	PO(C₆H₅)₂ (73)	38
	"	*s*-C₄H₉Li, 50% TMEDA, hexane	(*E*)-3-Trimethylsilyl propenal	CHOHCH=CHSi(CH₃)₃ (86)	64
	BSH	*n*-C₄H₉Li, TMEDA	(CH₃)₃SiCl	Si(CH₃)₃ (67)	37, 41
Camphor	Tosyl	"	D₂O	(95)	5
	"	"	*n*-C₄H₉Br	C₄H₉-*n* (50)	29
	Trisyl	*s*-C₄H₉Li, 50% TMEDA, hexane	"	" (53)	151
	"	*s*-C₄H₉Li, 50% TMEDA, hexane	"	" (70)	6
	"	"	HCON(CH₃)₂	Sn(CH₃)₃ (79)	6
	Tosyl	*n*-C₄H₉Li, TMEDA	"	" (10)	47
	"	"	(CH₃)₃SiCl	Si(CH₃)₃ C₄H₉-*t* (15)	25
	BSH	*n*-C₄H₉Li, 50% TMEDA, hexane	"	Si(CH₃)₃ (76)	27
	Tosyl	*n*-C₄H₉Li, TMEDA	"	Si(CH₃)₃ (66)	89

TABLE II. CYCLIC VINYLLITHIUM REAGENTS (*Continued*)
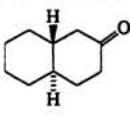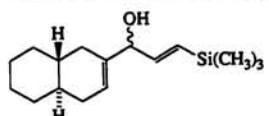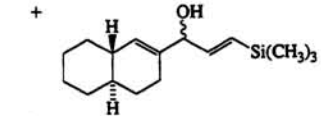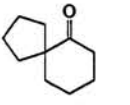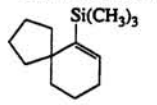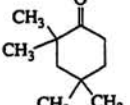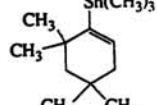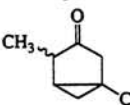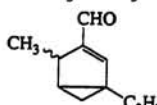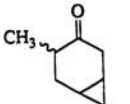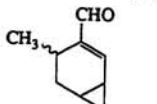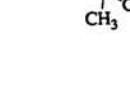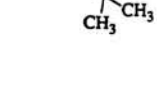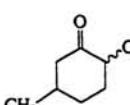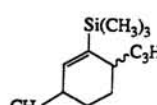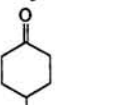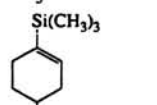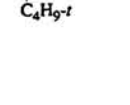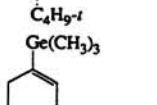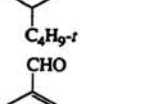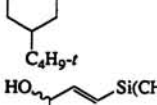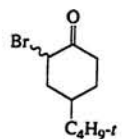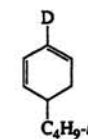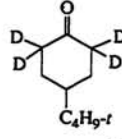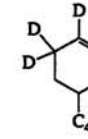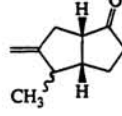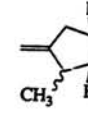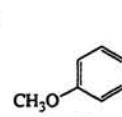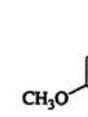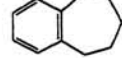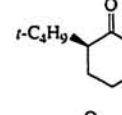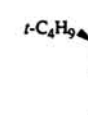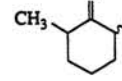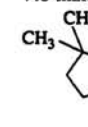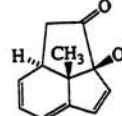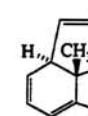
Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	Trisyl	n-C₄H₉Li, 50% TMEDA, hexane	(E)-3-Trimethylsilyl-propenal	(53) + 2:1 mixture of diastereomers[e]	64
	BSH	n-C₄H₉Li, TMEDA	(CH₃)₃SiCl	(67)	41
	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	(CH₃)₃SnCl	(94)	92
	Tosyl	n-C₄H₉Li, TMEDA	HCON(CH₃)₂	(60)	47
	"	"	"	(55)	47
	"	"	(CH₃)₃SiCl	(85)	37, 41
	"	"	"	(97) (71)	37 25, 87
	"	"	(CH₃)₃GeCl	(58)	25
	"	"	HCON(CH₃)₂	(57)	47
	Trisyl	s-C₄H₉Li, 50% TMEDA, hexane	(E)-3-Trimethylsilyl-propenal	(78)	64
	"	n-C₄H₉Li, 10% TMEDA, hexane	(CH₃)₃SnCl	(79)	92

TABLE II. Cyclic Vinyllithium Reagents (*Continued*)

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
(Br, O, C₄H₉-*t* cyclohexanone)	Tosyl	1. (C₂H₅)₃N 2. CH₃Li, TMEDA	D₂O	(D, C₄H₉-*t*) (39)	57
(D,D,D,D, O, C₄H₉-*t* cyclohexanone)	"	*n*-C₄H₉Li, TMEDA	"	(D,D,D) (41)	77
(bicyclic, H, O, =CH₂, CH₃, H)	Trisyl	*n*-C₄H₉Li, 10% TMEDA, hexane	1. CO₂ 2. CH₂N₂	H, CO₂CH₃ I (53)	62
				+ CO₂CH₃ II (20)	
	"	*t*-C₄H₉Li, 10% TMEDA, hexane	"	I (16)	62
				+ II (20)	
	"	*n*-C₄H₉Li, DME	"	I (52)	62
				+ II (20)	
	"	*s*-C₄H₉Li, DME	"	I (44)	62
				+ II (5)	
	"	*n*-C₄H₉Li, DME	"	I (30)	62
				+ II (0)	
C₁₁ (CH₃O, O, tetralone tricyclic)	BSH	*n*-C₄H₉Li, TMEDA	(CH₃)₃SiCl	Si(CH₃)₃, CH₃O (67)	41
(benzosuberone, O)	"	"	"	Si(CH₃)₃ (88)	37
(*t*-C₄H₉, O, CH₃ cyclohexanone)	Tosyl	*n*-C₄H₉Li, 10% TMEDA, hexane	D₂O	*t*-C₄H₉, D, CH₃ (60)	62
(CH₃, O, C₄H₉-*n* cyclohexanone)	"	*s*-C₄H₉Li, THF	HCON(CH₃)₂	CH₃, CHO, C₄H₉-*n* (—)	65
				+ CH₃, CHO, C₄H₉-*n* (—) 7:3 mixture of isomers	
(CH₃, CH₃, H, O, CH₃ bicyclic)	Trisyl	*n*-C₄H₉Li, 10% TMEDA, hexane	(CH₃)₃SiCl	CH₃, CH₃, H, Si(CH₃)₃, CH₃ (58)	90, 91
(H, O, CH₃, OH tricyclic)	"	CH₃Li, benzene, ether	D₂O	H, D, CH₃, OH (63)	92

TABLE II. CYCLIC VINYLLITHIUM REAGENTS (*Continued*)

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
(structure)	"	n-C$_4$H$_9$Li, THF	1. Cr(CO)$_6$ 2. (CH$_3$)$_4$NBr	(CO)$_5$Cr O$^-$N$^+$(CH$_3$)$_4$ (41) (structure)	46
C$_{12}$ (structure)	"	n-C$_4$H$_9$Li, 10% TMEDA, hexane	C$_4$H$_9$Br	C$_4$H$_9$-n (45) (structure)	152
(structure)	"	n-C$_4$H$_9$Li, 10% TMEDA, hexane	1. (C$_6$H$_5$)$_2$PCl 2. 30% H$_2$O$_2$	PO(C$_6$H$_5$)$_2$ (73) (structure)	38
	BSH	n-C$_4$H$_9$Li, TMEDA	(CH$_3$)$_3$SiCl	Si(CH$_3$)$_3$ (95) (structure)	37, 87
	Trisyl	s-C$_4$H$_9$Li, 50% TMEDA, hexane	(*E*)-3-Trimethylsilyl-propenal	HO Si(CH$_3$)$_3$ (72) (structure)	64
CH$_3$ (CH$_2$)$_2$CH=CH$_2$ (structure)	"	"	1. HCON(CH$_3$)$_2$ 2. NaBH$_4$	CH$_3$ (CH$_2$)$_2$CH=CH$_2$ (structure) CH$_2$OH (65)	85
C$_6$H$_5$ (structure)	BSH	n-C$_4$H$_9$Li, TMEDA, 60°, 3 h	(CH$_3$)$_3$SiCl	C$_6$H$_5$ Si(CH$_3$)$_3$ (73)[b] (structure)	63
	"	n-C$_4$H$_9$Li, TMEDA	"	Si(CH$_3$)$_3$ C$_6$H$_5$ (48) (structure)	37
D D (structure)	Tosyl	CH$_3$Li, ether	D$_2$O	D D (55) (structure)	76
C$_{13}$ CH$_3$ CH$_3$ (CH$_2$)$_2$COCH$_3$ (structure)	"	s-C$_4$H$_9$Li, TMEDA, hexane	HCON(CH$_3$)$_2$	CH$_3$ CH$_3$ (CH$_2$)$_2$C(CHO)=CH$_2$ (50) (structure)	82
C$_2$H$_5$ OCH$_3$ (structure)	Trisyl	n-C$_4$H$_9$Li, THF	1. HCON(CH$_3$)$_2$ 2. NaBH$_4$	CH$_2$OH C$_2$H$_5$ OCH$_3$ (54) (structure)	43, 42
	"	"	HCHO	" (45)	43, 42
CH$_3$ (structure) CH$_3$ CH$_3$ H	"	n-C$_4$H$_9$Li, 10% TMEDA, hexane	HCON(CH$_3$)$_2$	CH$_3$ CHO (structure) CH$_3$ CH$_3$ H (78)	11

64

65

TABLE II. CYCLIC VINYLLITHIUM REAGENTS (*Continued*)
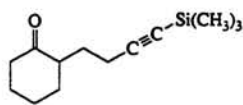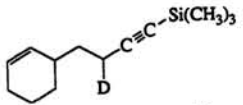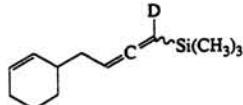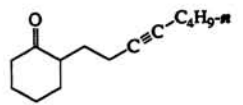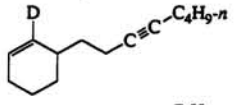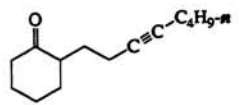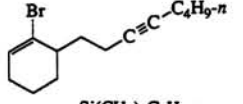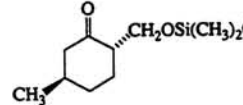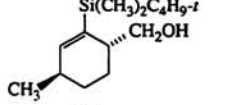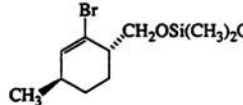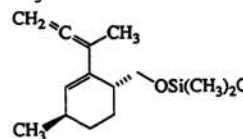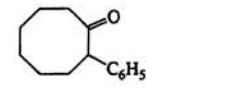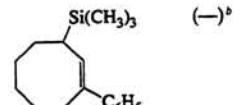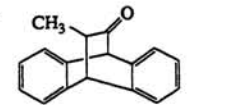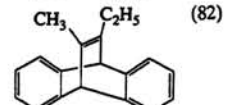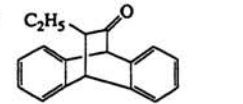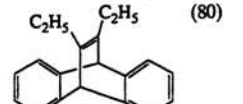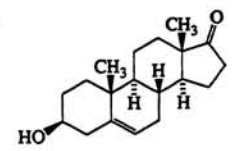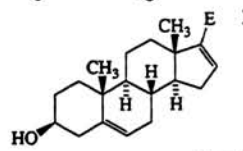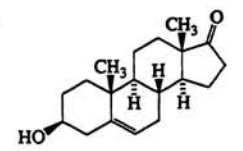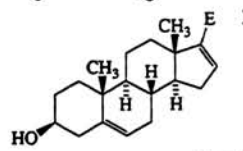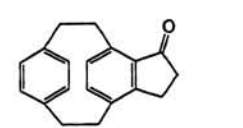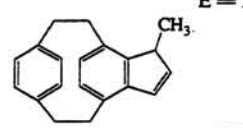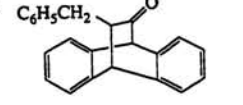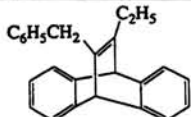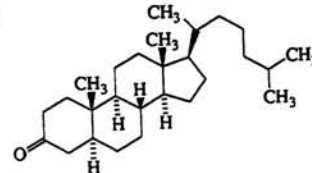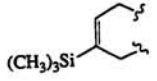
Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	"	s-C₄H₉Li, 10% TMEDA, hexane	D₂O	(15) (30)	45
C₁₄	"	s-C₄H₉Li, 10% TMEDA, hexane	D₂O	(59)	45
	"	"	Br(CH₂)₂Br	(48)	45
	"	s-C₄H₉Li, DME, > −40°	—	(92)	50
	"	s-C₄H₉Li, DME, < −40°	Br(CH₂)₂Br	(70)	50
	"	"	CH₃OC(CH₃)₂C≡CCu, CH₃C≡CCH₂OTs	(55)	50
	BSH	n-C₄H₉Li, TMEDA, 60°, 3 h	(CH₃)₃SiCl	(—)[b]	63
C₁₇	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	C₂H₅I	(82)	39
C₁₈	"	"	"	(80)	39
C₁₉	"	"	HCON(CH₃)₂	E = CHO (50)	11
	"	"	I₂	E = I (33)	153
	Tosyl	n-C₄H₉Li, 10% TMEDA, benzene	CH₃I	(68)[b]	
C₂₃ C₆H₅CH₂	Trisyl	n-C₄H₉Li, 10% TMEDA, hexane	CH₃I	(60)	39

66

67

TABLE II. CYCLIC VINYLLITHIUM REAGENTS (*Continued*)

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	"	"	C₂H₅I	(72)	39
C₂₇	BSH	*n*-C₄H₉Li, TMEDA	(CH₃)₃SiCl	(50)	37, 41

89

a The major regioisomer was not specified.
b This product is formed by rearrangement of the initially formed vinyllithium to the allyllithium, followed by trapping with the electrophile.

TABLE III. DIANION ALKYLATION FOLLOWED BY ACYCLIC VINYLLITHIUM FORMATION
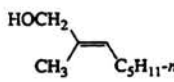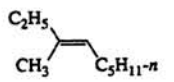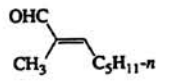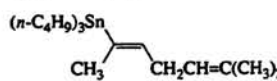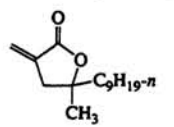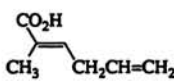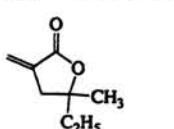
Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
C_3 Acetone	Trisyl	s-C_4H_9Li, THF	1. n-$C_5H_{11}I$ 2. H_2O	(Z)-CH_3CH=CHC_5H_{11}-n (77)	69
	"	"	1. n-$C_5H_{11}I$ 2. HCHO	HOCH$_2$ (52) CH_3 C_5H_{11}-n	69
	"	"	1. n-$C_5H_{11}I$ 2. C_2H_5I	C_2H_5 (47) CH_3 C_5H_{11}-n	69
	"	"	1. n-$C_5H_{11}I$ 2. $HCON(CH_3)_2$	OHC (56) CH_3 C_5H_{11}-n	69
	"	"	1. $(CH_3)_2C$=$CHCH_2Br$ 2. $(n$-$C_4H_9)_3SnCl$	$(n$-$C_4H_9)_3Sn$ (90) CH_3 CH_2CH=$C(CH_3)_2$	71
	"	"	1. C_2H_5I 2. $(n$-$C_4H_9)_3SnCl$	$(n$-$C_4H_9)_3Sn$ (56) CH_3 C_2H_5	72
	"	n-C_4H_9Li, DME	1. n-$C_9H_{19}COCH_3$ 2. CO_2 3. $CF_3CO_2H^a$	(61) C_9H_{19}-n CH_3	33
	"	"	1. CH_2=$CHCH_2Br$ 2. CO_2	CO_2H (26) CH_3 CH_2CH=CH_2	34
	"	"	1. $C_2H_5COCH_3$ 2. CO_2 3. $CF_3CO_2H^a$	CH_3 C_2H_5	33
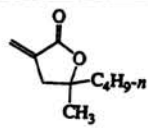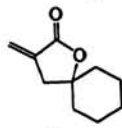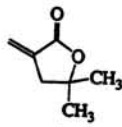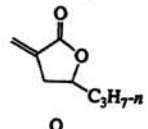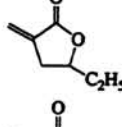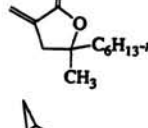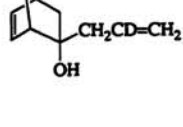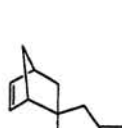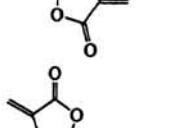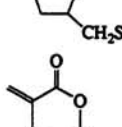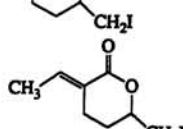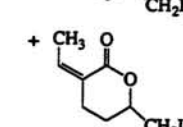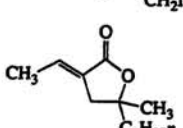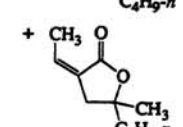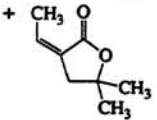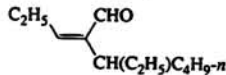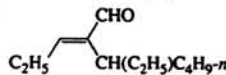
Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	"	"	1. $n\text{-}C_4H_9COCH_3$ 2. CO_2 3. $CF_3CO_2H^a$	(66)	33, 34
	"	"	1. Cyclohexanone 2. CO_2 3. $CF_3CO_2H^a$	(40)	33, 34
	"	"	1. Acetone 2. CO_2 3. $CF_3CO_2H^a$	(57)	33, 34
	"	"	1. $n\text{-}C_3H_7CHO$ 2. CO_2 3. $CF_3CO_2H^a$	(61)	33
	"	"	1. $n\text{-}C_2H_5CHO$ 2. CO_2 3. $CF_3CO_2H^a$	(45)	33, 34
	"	"	1. $n\text{-}C_6H_{13}COCH_3$ 2. CO_2 3. $CF_3CO_2H^a$	(61)	33
	"	"	1. 5-Norbornen-2-one 2. D_2O	(70)	35
	"	"	1. 5-Norbornen-2-one 2. CO_2 3. $CF_3CO_2H^a$	(61)	35
	"	"	1. $C_2H_5SeCH_2CHO$ 2. CO_2 3. $CF_3CO_2H^a$	(2)	35
	"	"	1. $CH_2=CHCH_2Br$ 2. CO_2 3. I_2^b	(50)	35
C_4 2-Butanone	"	"	"	(39) + (6)	35, 34
	"	"	1. $n\text{-}C_4H_9COCH_3$ 2. CO_2 3. $CF_3CO_2H^a$	(12) + (5)	34

70

71

TABLE III.   Dianion Alkylation Followed by Acyclic Vinyllithium Formation (*Continued*)

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	"	"	1. CH₃COCH₃ 2. CO₂ 3. CF₃CO₂H[a]	(35) + (2)	34
C₇ 4-Heptanone	Trisyl	"	1. *n*-C₄H₉I 2. HCON(CH₃)₂	(69) + (17)	65

[a] This reagent induces lactonization of the hydroxy acid.
[b] This reagent induces iodolactonization.

TABLE IV. DIANION ALKYLATION FOLLOWED BY CYCLIC VINYLLITHIUM FORMATION
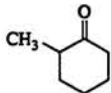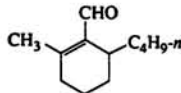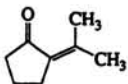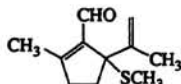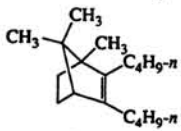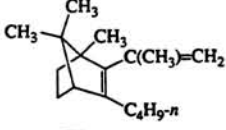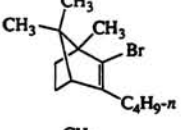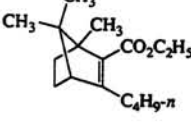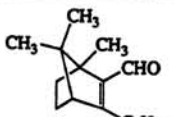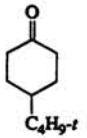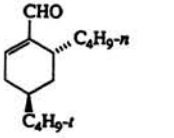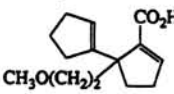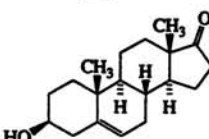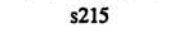
Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
C_7	Tosyl	"	1. $n\text{-}C_4H_9I$ 2. $HCON(CH_3)_2$	(47)[a]	65
C_8	Trisyl	"	1. $CH_3S_2CH_3$[b] 2. CH_3I 3. $HCON(CH_3)_2$	(38)	28
C_{10} Camphor	"	$n\text{-}C_4H_9Li$, THF	1. $n\text{-}C_4H_9I$ 2. $n\text{-}C_4H_9I$	(62)	65
	"	"	1. $n\text{-}C_4H_9I$ 2. CH_3COCH_3	(33)[c]	65
	"	"	1. $n\text{-}C_4H_9I$ 2. BrC_2H_4Br	(72)	65
	"	"	1. $n\text{-}C_4H_9I$ 2. $ClCO_2C_2H_5$	(54)	65

TABLE IV. DIANION ALKYLATION FOLLOWED BY CYCLIC VINYLLITHIUM FORMATION (*Continued*)

Starting Carbonyl Compound	Hydrazone	Conditions	Electrophile	Product and Yield (%)	Refs.
	"	"	1. n-C_4H_9I 2. $HCON(CH_3)_2$	(46)	65
	Tosyl	s-C_4H_9Li, THF	1. n-C_4H_9I 2. $HCON(CH_3)_2$	(43)	65
	"	n-C_4H_9Li, THF, hexane	1. $CH_3O(CH_2)_2I$ 2. CO_2	(50)	154
C_{19}	Trisyl	s-C_4H_9Li, THF	1. n-C_4H_9I 2. $HCON(CH_3)_2$	s215 (72)	65

[a] Less than 5% of regioisomer is formed.

[b] More *sec*-butyllithium is added after this sulfonylation.

[c] The initially formed tertiary allylic alcohol undergoes dehydration during workup and purification during workup and purification.

TABLE V. ACYCLIC VINYLLITHIUM FORMATION AND CYCLIZATION WITH AN INTERNAL ELECTROPHILE
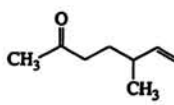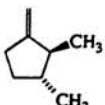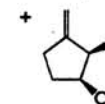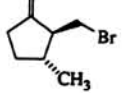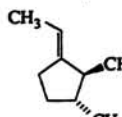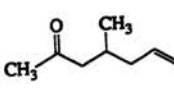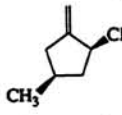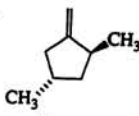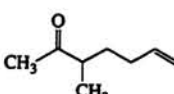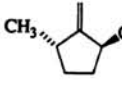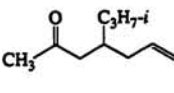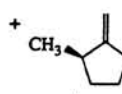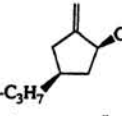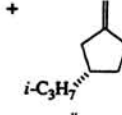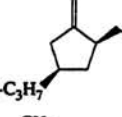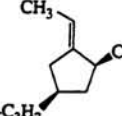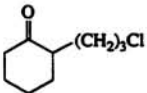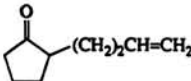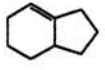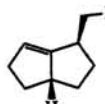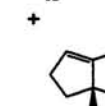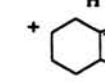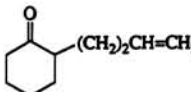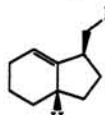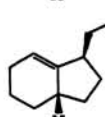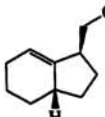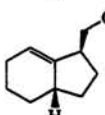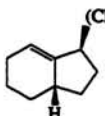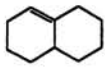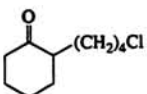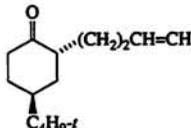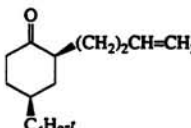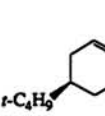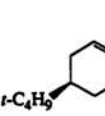
Starting Ketone with Internal Electrophile	Hydrazone	Conditions	Added Electrophile	Product and Yield (%)		Refs.
C_6 $CH_3CO(CH_2)_4Cl$	Trisyl	s-C_4H_9Li, 10% TMEDA, hexane	—	Methylenecyclopentane	(40) (85)	49 48
C_7 $CH_3CO(CH_2)_5Cl$	"	"	—	Methylenecyclohexane	(59)	49
	"	t-C_4H_9Li, THF, Li_2CuCl_4, 0°		"	(66)	49
	"	t-C_4H_9Li, THF	n-C_3H_7I	n-C_3H_7 (94)		48
C_8 $CH_3CO(CH_2)_6Cl$	"	"	—	Methylenecycloheptane	(30)	49
		t-C_4H_9Li, THF, Li_2CuCl_4			(72)	49
	"	t-C_4H_9Li, 10% TMEDA, hexane	—	(70) + (7)		48

TABLE V. Acyclic Vinyllithium Formation and Cyclization with an Internal Electrophile (*Continued*)

Starting Ketone with Internal Electrophile	Hydrazone	Conditions	Added Electrophile	Product and Yield (%)	Refs.
	"	"	Br(CH₂)₂Br	(61)	48
	"	t-C₄H₉Li, TMEDA, DME	CH₃I[*]	(73)	48
	"	t-C₄H₉Li, 10% TMEDA, hexane	—	(64) + (6)	48
	"	t-C₄H₉Li, 10% TMEDA, hexane	—	(70) + (15)	48
C₁₀	"	t-C₄H₉Li, 10% TMEDA, hexane	—	(89) + (4)	48
	"	"	Br(CH₂)₂Br	(80)	48
	"	"	CH₃I[*]	(85)	48

[*] The initially formed dianion is alkylated at −78° with the indicated electrophiles before the added electrophiles before the addition of more *tert*-butyllithium and warming to form the vinyllithium.

TABLE VI. CYCLIC VINYLLITHIUM FORMATION AND CYCLIZATION WITH AN INTERNAL ELECTROPHILE

Starting Ketone with Internal Electrophile	Hydrazone	Conditions	Added Electrophile	Product and Yield (%)	Refs.
C₉ O / (CH₂)₃Cl	Trisyl	s-C₄H₉Li, 10% TMEDA, hexane		(82)	49
O / (CH₂)₂CH=CH₂	"	t-C₄H₉Li, 10% TMEDA, ether	D₂O	(65) + (4) + (6)	48
C₁₀ O / (CH₂)₂CH=CH₂	"	t-C₄H₉Li, THF	D₂O	(87)	48
	"	"	Br(CH₂)₂Br	(61)	48
	"	t-C₄H₉Li, 10% TMEDA, hexane	"	" (81)	48
	"	t-C₄H₉Li, THF	HCON(CH₃)₂	CHO (61)	48
	"	"	CO₂	CO₂H (50)	48
	"	"	Ethylene oxide	(CH₂)₃OH (49)	48
O / (CH₂)₄Cl	"	n-C₄H₉Li, 10% TMEDA, hexane		(65)	49
C₁₄ O / (CH₂)₂CH=CH₂ / C₄H₉-t	"	t-C₄H₉Li, THF	D₂O	D (80) t-C₄H₉	48
O / (CH₂)₂CH=CH₂ / C₄H₉-t	"	"	"	D (90) t-C₄H₉	48

8. Acknowledgment

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Oxidation of Alcohols to Carbonyl Compounds via Alkoxysulfonium Ylides: The Moffatt, Swern, and Related Oxidations

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1. Introduction

The use of dimethyl sulfoxide as an oxidizing agent began with the discoveries by Kornblum and co-workers (1) that certain α -bromo ketones were converted into glyoxals under mild conditions by treatment with dimethyl sulfoxide (Eq. 1), and that primary tosylates such as *n*-octyl tosylate were converted into the corresponding aldehydes using dimethyl sulfoxide and sodium bicarbonate at 150° for 3 minutes. (2) The initial step of the reactions involves a displacement by dimethyl sulfoxide giving an alkoxysulfonium ion **1**, as was elucidated by Smith and Winstein at the same time, (3) and this species undergoes a 1,2 elimination assisted by base to give the carbonyl product (Eq. 2).

$$C_6H_5COCH_2Br \xrightarrow[25°]{(CH_3)_2SO} C_6H_5COCHO \qquad (1)$$

$$\underset{R^1CHR^2}{\overset{X}{|}} + (CH_3)_2S{=}O \xrightarrow{-X^-} \underset{\underset{\mathbf{1}}{R^1CHR^2}}{\overset{\overset{+}{O}S(CH_3)_2}{|}} \xrightarrow[-H^+,\,-(CH_3)_2S]{base} \underset{R^1CR^2}{\overset{O}{\|}} \qquad (2)$$
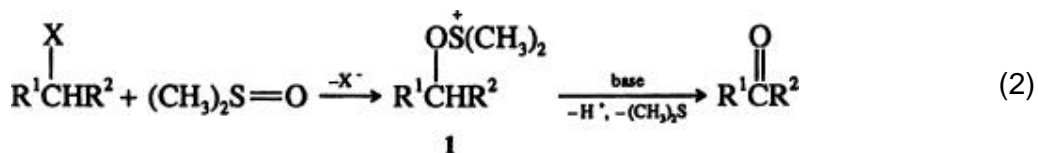
A few years later Pfitzner and Moffatt (4) made the serendipitous discovery that alcohols were oxidized at room temperature to carbonyl compounds by dimethyl sulfoxide, dicyclohexylcarbodiimide (DCC), and phosphoric acid (Eq. 3). This reaction was immediately recognized as an effective and mild procedure for sensitive substrates, and the extensive studies by this group and the development of alternative variations elsewhere have been the subject of several earlier reviews. (5-8)

$$\text{(3)}$$
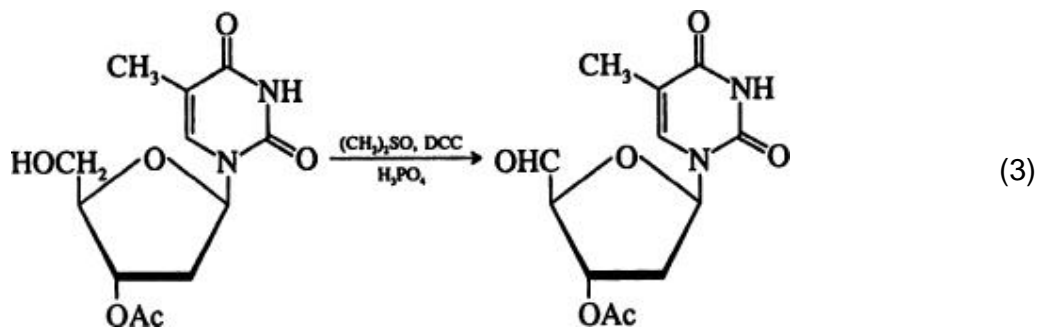
The course of the Moffatt procedure is summarized in Eqs. 4–6. (5, 9) The key intermediate in this process is the oxysulfonium ylide **4**, which appears to be common to all of the variations of dimethyl sulfoxide oxidations, and which reacts intramolecularly to give the products (Eq. 6).

$$RN{=}C{=}NR + H^+ \rightleftharpoons RNH\overset{+}{C}{=}NR \xrightarrow{(CH_3)_2SO} \underset{\textbf{2}}{RNH\overset{\overset{\displaystyle \overset{+}{O}S(CH_3)_2}{|}}{C}{=}NR} \qquad (4)$$

$$\textbf{2} + R^1R^2CHOH \xrightarrow{-H^+} \underset{\textbf{3}}{\text{image}} \longrightarrow RNH\overset{O}{\overset{||}{C}}NHR + CH_3\overset{+}{S}CH_2^- \overset{OCHR^1R^2}{\underset{\textbf{4}}{|}} \qquad (5)$$

$$\longrightarrow R^1CR^2 + CH_3SCH_3 \qquad (6)$$

4
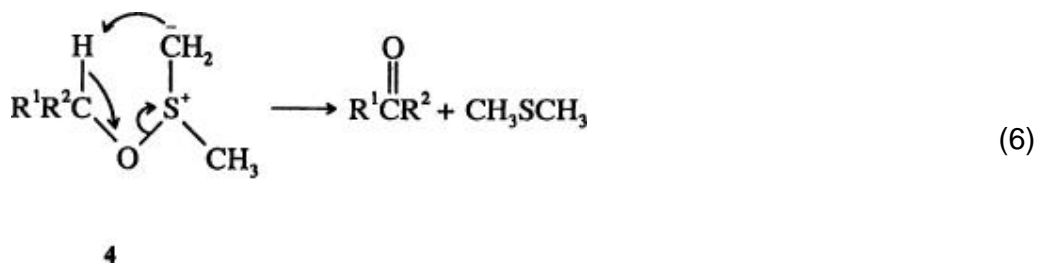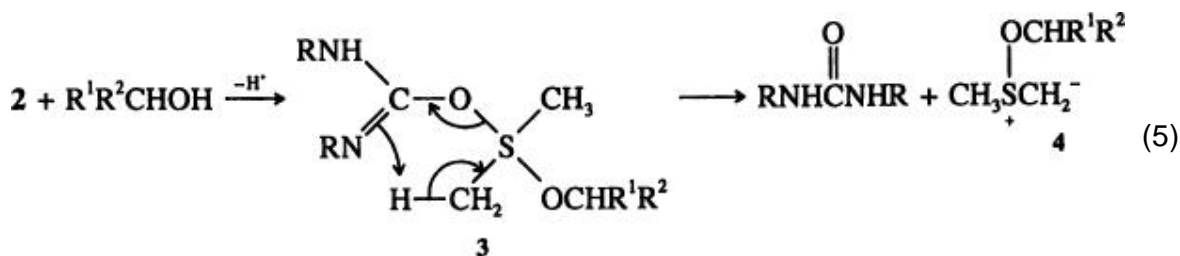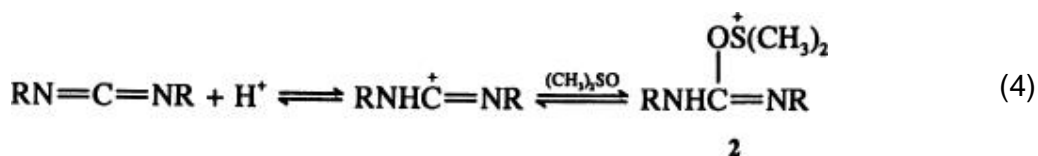
Other related procedures that were soon developed utilize dimethyl sulfoxide

activated by acetic anhydride, (10, 11) phosphorus pentoxide, (12) sulfur trioxide/pyridine complex, (13) and chlorine. (14) Reaction of alcohols with phosgene to give chloroformates **5** which react with dimethyl sulfoxide to give alkoxysulfonium ions **6**, followed by reaction with triethylamine, also effects oxidation (Eq. 7). (15, 16)

$$ROH \xrightarrow{COCl_2} R\overset{\overset{\displaystyle O}{\|}}{OCCl} \xrightarrow{(CH_3)_2SO} RO\overset{+}{S}(CH_3)_2 \xrightarrow{(C_2H_5)_3N} \begin{matrix} \text{carbonyl} \\ \text{products} \end{matrix} \qquad (7)$$

$$\underset{\textbf{5}}{} \qquad \underset{\textbf{6}}{}$$
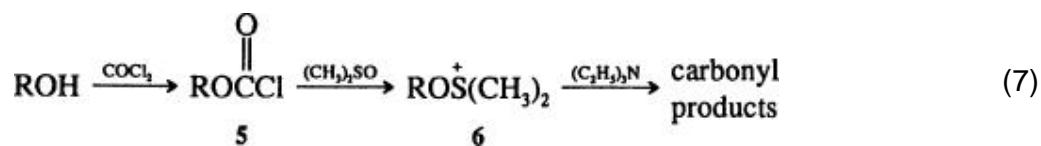
The reaction of the complexes of dimethyl sulfide and chlorine or *N*-chlorosuccinimide (NCS) with alcohols is proposed to give the same alkoxysulfonium complexes **6**, which are efficiently converted into carbonyl products upon addition of triethylamine. (17-19) Electrochemical activation of sulfides has also been successfully utilized. 20,20a

The activation of dimethyl sulfoxide is effected by many reagents, (8, 21-27) and these reactions as well as those involving activated sulfides evidently involve the alkoxysulfonium ion **6** (in almost all cases except the Moffatt procedure using DCC) and the decisive oxidation step which occurs via the alkoxysulfonium ylide **4** in all the reactions. Activation of dimethyl sulfoxide by oxalyl chloride, as developed by Swern and co-workers, (8, 22-27) has become the most used of these oxidation procedures, but several of the other methods are also convenient and efficient.

2. Mechanism

The mechanism of the dimethyl sulfoxide/DCC reaction has been carefully studied and the pathway of Eqs. 4–6 is well established. (5, 28-30) Oxygen transfer occurs from ^{18}O-labeled dimethyl sulfoxide, (28) but not from ^{18}O-labeled benzhydrol (11) to the product dicyclohexylurea. The reactions of n- $C_3H_7CD_2OH$ to give CH_3SCH_2D , (28) and of dimethyl sulfoxide-d_6 to give monodeuterodicyclohexylurea (29) and CD_3SCD_2H , (28) confirm the intervention of the ylide **4**, which transfers hydrogen intramolecularly (Eq. 6). Experiments using tritium-labeled substrates are also interpreted in terms of **4**. (31) Attempts to observe the intermediate **2** by ^1H NMR have been unsuccessful, so it is concluded that at equilibrium the concentration of this species is low (Eq. 4). (29)

Deuterium-labeling experiments confirm the pathway of Eq. 6 in the dimethyl sulfide/NCS procedure, (32) and this pathway is also proposed for the dimethyl sulfoxide/acetic anhydride method. (11)

The mechanism of dimethyl sulfoxide activation by oxalyl chloride has also been investigated in some detail, and formation of an initial adduct **7** which collapses to a dimethylchlorosulfonium species **8** is clearly implicated (Eqs. 8 and 9). (8, 23) Reaction of **8** with an alcohol at –78° produces the alkyoxysulfonium ion **6**, which is converted into the product by reaction with an amine base to give ylide **4**, which reacts as shown in Eq. 6.

$$(CH_3)_2SO \xrightarrow{COCl_2} (CH_3)_2\overset{+}{S}OC(O)C(O)Cl\ Cl^- \longrightarrow (CH_3)_2\overset{+}{S}Cl + Cl^- + CO_2 + CO \qquad (8)$$

$$\underset{7}{} \qquad\qquad \underset{8}{}$$

$$8 + ROH \longrightarrow RO\overset{+}{S}(CH_3)_2 \xrightarrow{base} \text{carbonyl products} \qquad (9)$$

$$\underset{6}{}$$
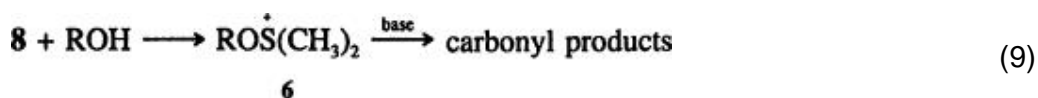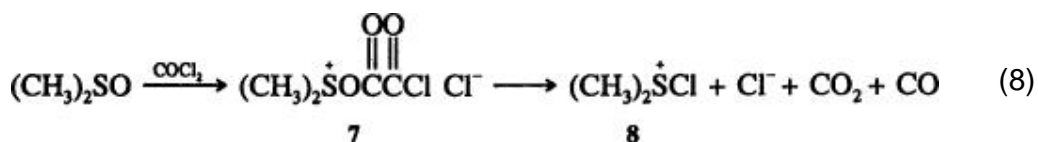
Formation of $(CH_3)_2\overset{+}{S}Cl$ (**8**) and its reaction with alcohols, as well as the

conversion of $ROS(CH_3)_2^+$ (**6**) into carbonyl products, are all quite rapid at –78°,

at which temperature such side reactions as formation of methylthiomethyl ethers are minimized.

The formation of methylthiomethyl ethers is proposed to involve formation of $CH_3SCH_2^+$, which alkylates the alcohol. (5, 23, 30) Crossover experiments confirm that intermolecular reactions are involved. (33) Intramolecular rearrangements (Eq. 10) involving the alkoxysulfonium ylide **4** would be equally probable in all the activation methods, since **4** is formed in each, but they are not observed. Therefore formation of $CH_3SCH_2^+$, possibly by dissociation of activated ylides, and alkylation (Eq. 11), appears to be the preferred pathway.

$$RO-\overset{Cl}{\underset{}{S}}\overset{CH_3}{\underset{CH_2^-}{\diagup}} \longrightarrow ROCH_2SCH_3 \tag{10}$$

4

$$\overset{+}{X}\overset{}{S}(CH_3)CH_2^- \xrightarrow{-X^-} CH_3\overset{+}{S}{=}CH_2 \xrightarrow{ROH} ROCH_2SCH_3 \tag{11}$$
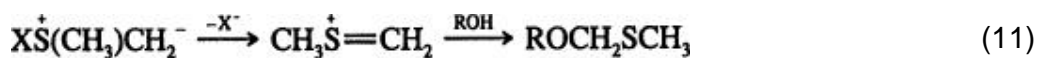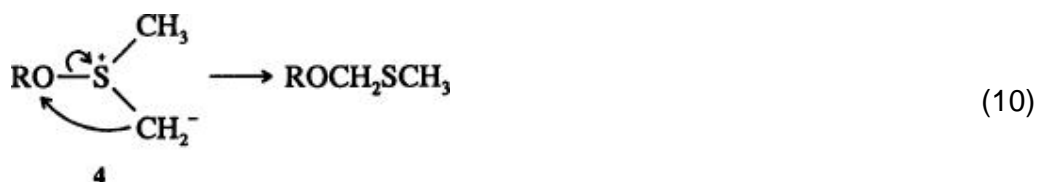
The active oxidants formed from dimethyl sulfide and chlorine or *N*-chlorosuccinimide are proposed to be chloro- or imidosulfonium species, respectively. (17)

$$(CH_3)_2\overset{+}{S}Cl\ Cl^- \qquad (CH_3)_2\overset{+}{S}N \qquad Cl^-$$
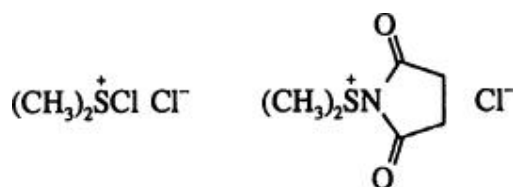
Alcohols react with these species to give $RO\overset{+}{S}(CH_3)_2$(**6**), and reaction with base gives the products (Eq. 9).

Several of the other dimethyl sulfoxide activation procedures require higher temperatures and longer reaction times; thus, acetic anhydride requires room temperature for several hours, (10, 11, 34) pyridine/sulfur trioxide requires periods up to 30–35 minutes at room temperature, (13) and phosphorus pentoxide requires up to 2 hours at 65° or 15 hours at room temperature. (12, 35) As noted below, the use of triethylamine increases the efficiency of this

procedure. One difference among these procedures is that the formation of methylthiomethyl ether byproducts is common in acetic anhydride activation, (10) but is much less prevalent with pyridine/sulfur trioxide. (13) This observation supports the idea that conversion of species $(CH_3)_2\overset{+}{S}X$, where the identity of X depends on the activator, to $CH_3SCH_2^+$ is responsible for the formation of the methylthiomethyl ethers.

The details of other activation processes are less extensively investigated than for DCC and oxalyl chloride, but formation of acyloxysulfonium ions **9**, which undergo displacement by alcohols (Eq. 12), is proposed as the intermediate for the reactions with acetic anhydride (Ac$_2$O). (11) Because room temperature is necessary for the formation of **9**, its reaction with alcohols to give **6**, and the conversion of **9** into $CH_3SCH_2^+$, may become competitive. Formation of $CH_3SCH_2^+$ may occur from **9** by an intramolecular 6-membered cyclic transition state, but this has not been established.

$$(CH_3)_2S\!=\!O + (CH_3CO)_2O \longrightarrow [(CH_3)_2\overset{+}{S}O_2CCH_3] \xrightarrow{\text{ROH}} (CH_3)_2\overset{+}{S}OR \qquad (12)$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad \mathbf{9} \qquad\qquad\qquad\qquad \mathbf{6}$$
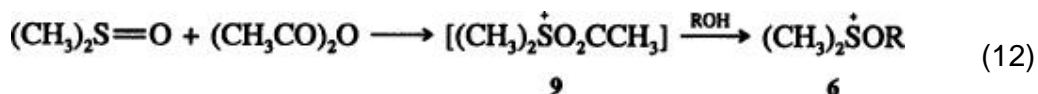
Acetyl bromide reacts rapidly with dimethyl sulfoxide at –60° to form an intermediate, while the reaction of acetyl chloride with dimethyl sulfoxide is much slower. (23) These reactive intermediates are long-lived at –60°, but react rapidly with alcohols. (23) Mechanistic studies suggest that although **9** is an intermediate in these reactions, (CH$_3$)$_2$SBr$^+$ and (CH$_3$)$_2$SCl$^+$ are also important intermediates in the reactions with acetyl bromide (36) and acetyl chloride. (37)

The alkylation of alcohols by $CH_3SCH_2^+$ is favored by most authors (5, 23) as a major route to the formation of the ethers ROCH$_2$SCH$_3$. The dissociation of ylides $X\overset{+}{S}(CH_3)CH_2^-$, where X is derived from the activator or the alcohol, is a plausible route to $CH_3SCH_2^+$, but several different species $X\overset{+}{S}(CH_3)CH_2^-$ may be involved and there may be nucleophilic assistance in the dissociative step. The low yields of the methylthiomethyl ethers found when either bulky alcohols or more crowded amines than triethylamine (except for the

N-chlorosuccinimide procedure) are used suggest that, in addition to the role of the amines as bases promoting oxidation (Eq. 13), they also have a nucleophilic role promoting methylthiomethyl ether formation. (23) However, the nucleophilic process proposed (Eq. 14) (23) requires further elaboration because of the ambiguity regarding the proton removal step and the fate of this proton.

$$RO\overset{+}{S}(CH_3)_2 \xrightarrow{(C_2H_5)_3N} RO\overset{+}{S}(CH_3)CH_2^- \longrightarrow \text{carbonyl products} \qquad (13)$$

$$\underset{6}{} \qquad\qquad\qquad \underset{4}{}$$

$$RO\overset{+}{S}(CH_3)_2 \ A^- \xrightarrow{(C_2H_5)_3N} RO-\overset{\overset{\displaystyle \overset{\delta^-}{N(C_2H_5)_2}}{\underset{\displaystyle}{|}}}{\underset{\displaystyle \underset{H}{\overset{|}{CH_2}}}{\overset{\delta^+}{S}CH_3 \ A^-}} \longrightarrow RO^- + CH_3\overset{+}{S}{=}CH_2 \qquad (14)$$
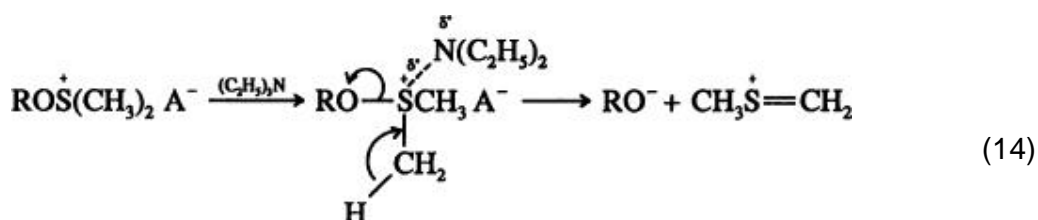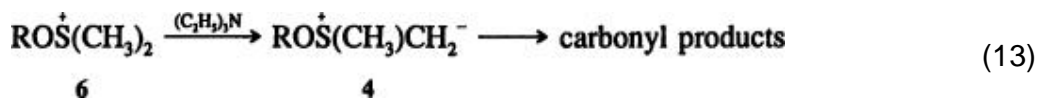
$A^- = \text{anion}$

Another possibility is an electrocyclic process whereby the RO group in Eq. 14 is the proton acceptor leading directly to ROH. Reactions of alcohols and amines with species $X\overset{+}{S}(CH_3)CH_2^-$, where X is derived from either the activator or the alcohol, also provide possible routes to methylthiomethyl ethers.

$$X\overset{+}{S}(CH_3)CH_2^- + ROH \longrightarrow HX + CH_3SCH_2OR$$

$$X\overset{+}{S}(CH_3)CH_2^- \xrightarrow{(C_2H_5)_3N} X^- + CH_3\overset{+}{S}{=}CH_2 \xrightarrow{ROH} CH_3SCH_2OR$$
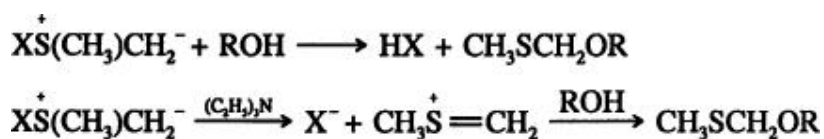
These bimolecular reactions leading to methylthiomethyl ethers would be disfavored by bulky alcohols or amines, and hence could explain the diminished yields of such ethers in these reactions. The conversion of the ylide **4** into carbonyl products involving conversion of a tetrahedral carbon to a less-hindered carbonyl group would also be favored for a bulky alcohol. These speculations are subject to experimental testing, and a detailed understanding of all the processes involved in the formation of methylthiomethyl ethers awaits further investigation.

The addition of boron trifluoride-etherate to the alkoxysulfonium ions at –50° followed by triethylamine gives high yields of methylthiomethyl ethers. The function of the boron trifluoride, not previously explained, (23) may be coordination of the boron trifluoride to oxygen in $\text{RO}\overset{+}{\text{S}}(\text{CH}_3)_2$ or ylide **4**, promoting dissociation to the alkoxy residue and thus enhancing ether formation. Protic acids also enhance formation of methylthiomethyl ethers, (11, 23) perhaps by a similar mechanism.

$$\overset{-}{\text{F}_3\text{B}}-\overset{\overset{\displaystyle \cdot}{|}}{\underset{\underset{\displaystyle R}{|}}{\text{O}}}-\overset{+}{\text{S}}(\text{CH}_3)_2 \xrightarrow{\ (\text{C}_2\text{H}_5)_3\text{N}\ } \text{RO}\overset{-}{\text{B}}\text{F}_3 + \text{CH}_3\overset{+}{\text{S}}{=}\text{CH}_2 \longrightarrow \text{ROCH}_2\text{SCH}_3$$
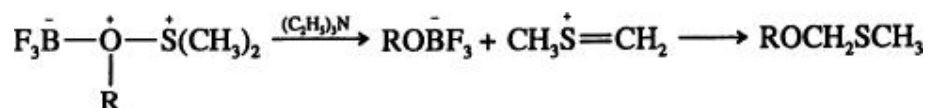
Competitive oxidation of mixtures of alcohols with less than an equivalent amount of dimethyl sulfoxide activated by oxalyl chloride leads to preferential oxidation of the less crowded and more electron-rich alcohols. (38) Further, there is a preference for oxidation of the first added alcohol when these are added in sequence, but this effect diminishes with time if the mixture is aged before addition of triethylamine. (38) The results are interpreted (38) as showing that alkoxysulfonium ions $\text{RO}\overset{+}{\text{S}}(\text{CH}_3)_2$ (**6**) are disfavored by R groups that are bulky or electron-withdrawing, and that **6** can undergo exchange with other alcohols. The reaction of **6** with triethylamine is much faster than equilibration. (38) An observed 2.6-fold preference for loss of a proton in oxidation of C_6H_5CHDOH , and the absence of an isotope effect in the competitive oxidation of $C_6H_5CHOHCH_3$ and $C_6H_5CDOHCH_3$, are consistent with these interpretations. (38) These studies indicate that there are good prospects for the development of selective oxidations of polyhydroxy compounds based on steric and electronic factors, but, as discussed in the section "Selective Oxidation of Polyols," there has been only limited progress in this direction.

3. Scope and Limitations

3.1. Oxidants
3.1.1. Sulfoxides and Sulfides

The most extensive examination of the effects of variation of the R groups of the activated sulfonium species R_2S^+X involves activation with *N*-chlorosuccinimide, but unfortunately this has appeared only incompletely in communication form and includes several reactivity trends that have not been plausibly explained. (39) Thus, diisopropyl sulfide (DIPS) with *N*-chlorosuccinimide is reported to oxidize primary alcohols to aldehydes at 0°, whereas the starting alcohols are recovered at –78°; the same reagents oxidize secondary alcohols to ketones at –78° and give the starting alcohols at 0° (Eqs. 15 and 16).

$$n\text{-}C_{12}H_{25}OH \xrightarrow[\text{NCS}]{\text{DIPS}} n\text{-}C_{11}H_{23}CHO \qquad \begin{array}{cc} \underline{0°} & \underline{-78°} \\ 90\% & 0\% \end{array} \qquad (15)$$

$$n\text{-}C_5H_{11}CHOHCH_3 \xrightarrow[\text{NCS}]{\text{DIPS}} n\text{-}C_5H_{11}COCH_3 \qquad 0\% \quad 88\% \qquad (16)$$
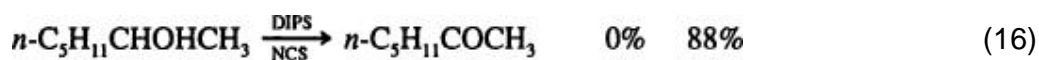
No convincing explanation of this unusual selectivity is advanced, but similar behavior is also observed with di-*sec*-butyl sulfide, methyl *tert*-butyl sulfide, and methyl phenyl sulfide, while di-*n*-butyl sulfide and methyl *sec*-butyl sulfide do not show selectivity. The diol **10** shows similar temperature-dependent selectivity (Eqs. 17 and 18). Further study of these reactions is clearly warranted to provide better understanding of these results.

$$(17)$$

$$10 \xrightarrow[\text{NCS, } -78°]{\text{DIPS}}$$

(18)
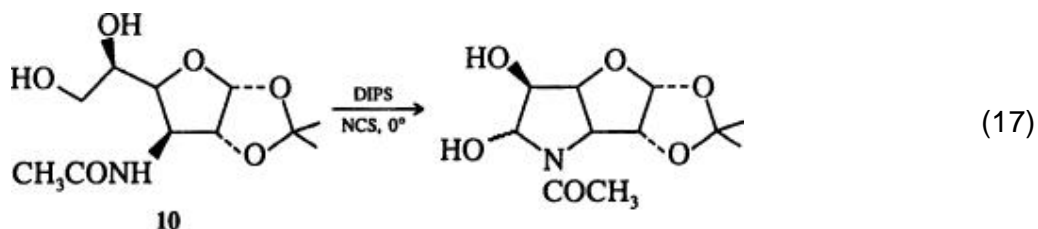
In another comparative study of different sulfides, some starting material is recovered in the oxidation of a hydroxyl lactone with dimethyl sulfide/N-chlorosuccinimide in toluene/methylene chloride, a result attributed (18) to possible insolubility of the sulfoxonium intermediate. Use of methyl phenyl sulfide/chlorine gives superior yields. (18)

(>90%)
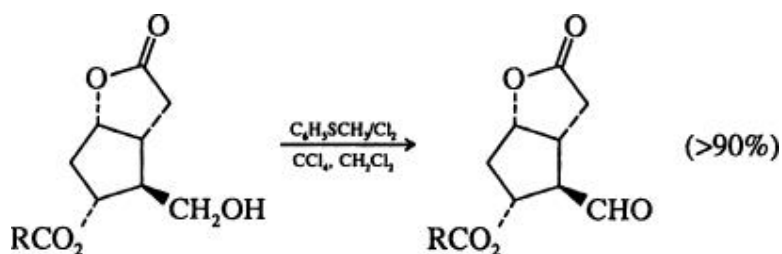
In other examples, activated dimethyl sulfide or dimethyl sulfoxide give equal or better yields than other sulfides or sulfoxides. (20, 21, 40, 41) Tetramethylene sulfoxide gives an 80% yield for the oxidation of yohimbine (11), compared with 93% with dimethyl sulfoxide. (11)

(93%)

11
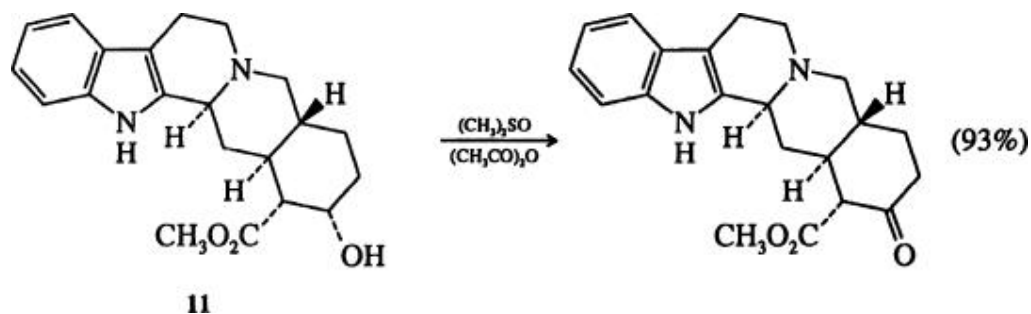
A polymer-supported sulfide reagent can be used with chlorine, but the 67% yield of benzaldehyde from benzyl alcohol using this reagent is not outstanding. (42)

Reaction of the pyranoside **12** with dimethyl sulfoxide/acetic anhydride gives the intermediate ketone **13** which slowly forms thioether **14** (Eq. 19), whereas similar byproducts are not formed in reactions using diethyl sulfoxide, tetramethylene sulfoxide, dibenzyl sulfoxide, or methyl phenyl sulfoxide. (43)

The intramolecular oxidation of the hydroxy sulfoxide **15** by reaction with sulfoxide activators (exact conditions not specified) (44) fails, perhaps because of steric factors in the intramolecular proton transfer. The intermolecular version of the same reaction on the corresponding sulfide also fails, a result

(19)
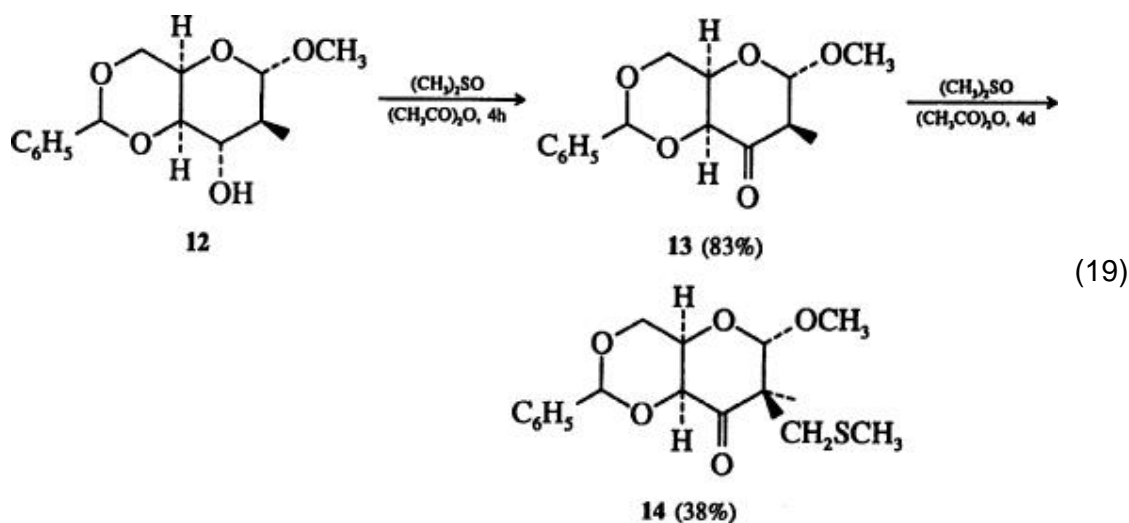
ascribed to possible displacement of dimethyl sulfoxide from the alkoxysulfonium intermediate by a neighboring sulfur atom. (44)
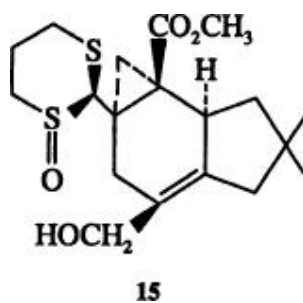
In sulfoxide **16** the pyridyl nitrogens might act as bases in intramolecular reactions so that oxysulfonium ylides would not be intermediates, thus avoiding methylthiomethyl ether formation. (45) However, the transition state for this process would involve a six-membered ring, as opposed to the usual five-membered ring in the oxidation step (Eq. 6), and the combination of **16**

with trifluoromethanesulfonic anhydride does not oxidize either benzoin or cholestanol. (45)
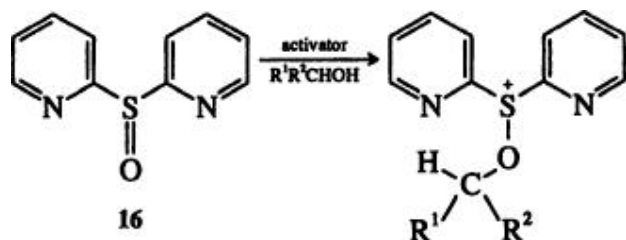
In summary, dimethyl sulfoxide and dimethyl sulfide are by far the most used sulfoxide and sulfide oxidants, respectively, and no consistent advantages for other reagents have been established.

3.1.2. Selenium-Based Oxidations

The complex of dimethyl selenide with *N*-chlorosuccinimide oxidizes a variety of primary and secondary alcohols to the corresponding aldehydes and ketones, and also oxidizes benzoin and hydrobenzoin to benzil. (46) The oxidation of allyl alcohols without formation of allylic chlorides is particularly noteworthy as methyl sulfide/*N*-chlorosuccinimide often gives these as the major products. (46) The order of decreasing reactivity for selenides is $(CH_3)_2Se > C_6H_5SeCH_3 > (C_6H_5)_2Se$, and for bases is 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) $>$ $(C_2H_5)_3N$ $>$ $NaHCO_3$.

Reaction of β -hydroxy selenide **17** proceeds without added dimethyl selenide, although the reaction may be intermolecular, while selenide **18** gives the elimination product in 97% yield. (46) Both reactions can be viewed as eliminations.
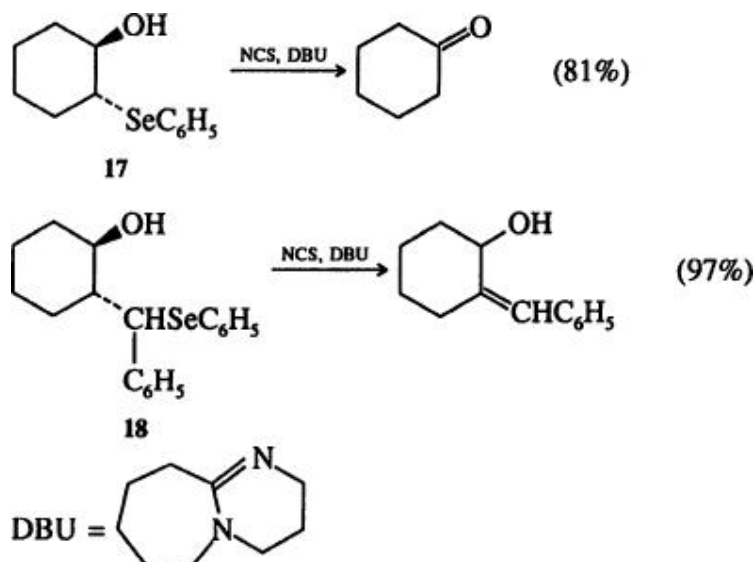
Dimethyl selenoxide is an effective reagent for oxidation of alcohols to carbonyl compounds, (47) and both this reagent and potassium benzeneselenite are effective in Kornblum-like oxidations of benzylic halides to substituted benzaldehydes. (47)

Other related reagents that effect the oxidation of alcohols to carbonyl compounds are bis(4-anisyl) telluroxide, (48) benzeneselenic anhydride, (49) and dimesityl diselenide/*tert*-butyl hydroperoxide. (50, 51)

3.2. Activators
3.2.1. Carbodiimides
Carbodiimide activation of dimethyl sulfoxide has been reviewed in detail, (5) and only the salient features are mentioned here. Dicyclohexylcarbodiimide (DCC) is by far the most used diimide, and excess reagent can be conveniently converted by oxalic acid into the highly insoluble dicyclohexylurea which is removed by filtration. However, sometimes complete removal of the urea is difficult; in these cases diethylcarbodiimide (DEC) or diisopropylcarbodiimide (DIPC) can be used, although the former sometimes fails to promote complete oxidation. (5) A comparison of the efficiencies of these oxidants is shown in Eq. 20. (52)

$$\text{DCC (47\%)}$$
$$\text{DIPC (60\%)} \quad (20)$$
$$\text{DEC (53\%)}$$
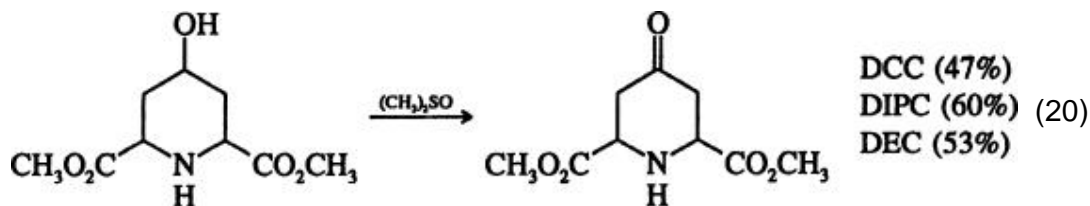
The workup of these reactions can be expedited by using water-soluble carbodiimides, including methyl-1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide toluenesulfonate or methanesulfonate (**19**, CMC), (52) or 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (**20**). (53)

19   **20**
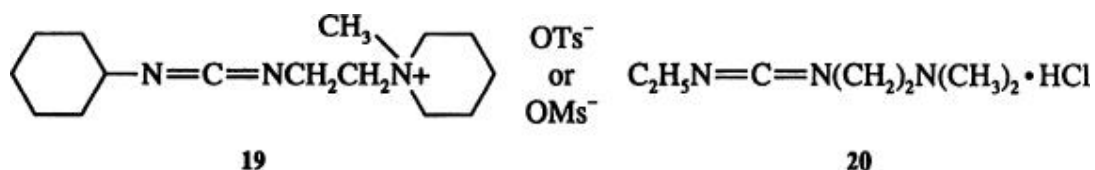
Some related activators that resemble carbodiimides include the ynamine *N,N*-dimethylamino-1-propyne and the ketenimine (4-tolyl)imino-2,2-diphenylethene $[(C_6H_5)_2C = C = NC_6H_4CH_3\text{-}4]$. (54)

Polymer-attached isopropylcarbodiimide gives a 95% yield of benzaldehyde from benzyl alcohol. 55,55a This reagent gives a yield of 90% in the reaction of Eq. 20, and is superior to dimethyl sulfoxide/phosphorus pentoxide and dimethyl sulfoxide/acetic anhydride. (52)

To facilitate purification of sensitive aldehydes in the presence of dicyclohexylurea, they are frequently converted into more stable derivatives and later regenerated. (5) Examples include diethyl acetals, (56) diphenylimidazolidenes, dinitrophenylhydrazones, and nitromethane adducts, but the extra protection/deprotonation steps constitute a definite inefficiency.

3.2.2. Acid Halides and Anhydrides
The activation of dimethyl sulfoxide by a wide range of reagents has been studied and reviewed, (8, 23) and a particularly extensive comparison of these is given for the oxidation of 1-decanol and 2-octanol in Table A. The acid halide and anhydride activators most frequently used are oxalyl chloride, (22, 26) trifluoroacetic anhydride (TFAA), (24, 25, 27) sulfur trioxide/pyridine complex, (13) acetic anhydride, (10) and trifluoromethanesulfonic anhydride. (45) Activation of dimethyl sulfoxide with trifluoroacetic anhydride or oxalyl

chloride usually gives better yields than the other procedures, and oxalyl chloride has the advantages of lower cost and toxicity and avoids the problem of trifluoroacetate formation. (8)

Table A. Comparison of Activators of Dimethyl Sulfoxide (23)

Substrate	Activator	Solvent	Temp. (°C)	Time (h)	R^1R^2C $=$ O	ROH	$ROCH_2SCH_3$	RX^a
					Products (%)			
1-Decanol	$(CH_3CO)_2O$	$(CH_3)_2SO$	25	27	27	1	56	6.7
	Pyridine/SO_3	"	25	0.5	91	0.6	6.3	—
	$(CH_3)_2S$, NCS	Toluene	−25	1.5	94	0.7	2.5	0
	"	CH_2Cl_2	−25	1.5	58	21	20	0
	$(CH_3SO_2)_2O$	HMPA	−20	0.25	69	16	12	—
	Cyanuric chloride	" , CH_2Cl_2	−20	0.5	73	14	8.5	—
	C_6H_5COCl	"	−20	0.25	29	40	26	0.4
	"	CH_2Cl_2	−60	0.75[b]	97	0.3	0.8	2
	"	"	−60	0.25	25	16	1	59
	CH_3SO_2Cl	HMPA, CH_2Cl_2	20	0.75	62	2.8	4.5	6.5
	p-$CH_3C_6H_4SO_2Cl$	"	5	1.25	72	14	10	—
	$(CF_3CO)_2O$	CH_2Cl_2	−50	0.5	56	—	8	24

	Reagent	Solvent	Temp	Time				
	$(COCl)_2$	"	−60	0.25	97	1	1.8	0
	$SOCl_2$	"	−60	0.25	76	12	4.6	tr[c]
	PCl_3	"	−30	0.25	45	18	23	tr
	$POCl_3$	"	−30	0.25	43	24	26	tr
	CH_3COBr	"	−60	0.25	58	34	7	tr
2-Octanol	$(CH_3CO)_2O$	$(CH_3)_2SO$	25	30	30	0.8	62	2.9
	Pyridine, SO_3	"	25	0.5	93	tr	4.2	—
	$(CH_3)_2S$, NCS	Toluene	−25	1.5	95	0.7	3.2	0
	", "	CH_2Cl_2	−25	1.5	61	21	19	0
	$(CH_3SO_2)_2O$	HMPA	−15	0.25	84	8	5.1	—
	Cyanuric chloride	HMPA, CH_2Cl_2	−15	0.5	82	10	3.2	—
	C_6H_5COCl	" , "	−20	0.25	28	45	22	tr
	CH_3SO_2Cl	" , "	20	0.75	77	3.3	2.5	1.3
	$p\text{-}CH_3C_6H_4SO_2Cl$	" , "	5	1.25	90	2.7	2.2	—
	$(CF_3CO)_2O$	CH_2Cl_2	−50	0.5	78	—	5	14
	$(COCl)_2$	"	−60	0.25	98	1.4	0.8	0
	$SOCl_2$	"	−60	0.25	88	4.3	3.2	1.5
	PCl_3	"	−30	0.25	59	22	16	0
	$POCl_3$	"	−30	0.25	52	27	19	0

| CH$_3$COBr | " | –60 | 0.25 | 70 | 22 | 5 | 5 |
| CH$_3$COCl | " | –20 | 0.25 | 40 | 54 | 7 | — |

[a]The product resulted from a substitution reaction.
[b]The alcohol was added 30 minutes after (CH$_3$)$_2$SO and C$_6$H$_5$COCl were mixed.
[c]tr designates trace.

To moderate the activation of dimethyl sulfoxide, and to minimize the formation of methylthiomethyl ethers and other byproducts, reactions with oxalyl chloride or trifluoroacetic anhydride are usually carried out at low temperatures (–60°), which can be a disadvantage with large-scale reactions or poorly soluble substrates. The latter problem is encountered in the oxidation of long-chain alcohols, but can be circumvented by using higher temperatures. The oxalyl chloride and trifluoroacetic anhydride reagents are satisfactory for most substrates, including carbohydrates. (26, 57-64)

The side reaction of trifluoroacetate formation can be significant with trifluoroacetic anhydride activation. For example, 24% of 1-decyl trifluoroacetate is formed in the oxidation of 1-decanol by dimethyl sulfoxide and trifluoroacetic anhydride when the reaction mixture is allowed to warm to room temperature before adding triethylamine. (27) In some oxidations significant amounts of trifluoroacetates are formed at –60°. (27)

The byproduct 4-(diethylamino)-1,1,1-trifluorobut-3-en-2-one is formed in small quantities (£8%) in some oxidations with dimethyl sulfoxide/trifluoroacetic anhydride followed by treatment with triethylamine. (64a) This product appears to arise from a single electron transfer reaction of trifluoroacetic anhydride with triethylamine, and is obtained in 33% yield when the oxidation procedure is carried out in the absence of alcohol. (64a)

$$(CF_3CO)_2O \xrightarrow[\text{2. }(C_2H_5)_3N]{\text{1. }(CH_3)_2SO,\ -60°} (C_2H_5)_2NCH=CHCOCF_3 \qquad (33\%)$$
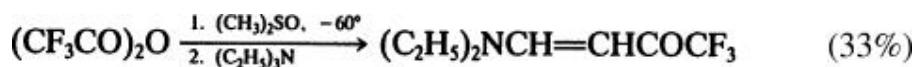
It is preferable to use trifluoroacetic anhydride instead of oxalyl chloride to activate dimethyl sulfoxide for oxidizing a dithiane to avoid formation of a dithiane monosulfoxide. (64b)

Phenyl dichlorophosphate is a promising new activator that is usually as effective as oxalyl chloride and is superior for the oxidation of phenylethanol. (64c)

$$C_6H_5CH_2CH_2OH \xrightarrow[-10 \text{ to } 25°, \ 75 \text{ min}]{C_6H_5OP(O)Cl_2} C_6H_5CH_2CHO \qquad (62\%)$$
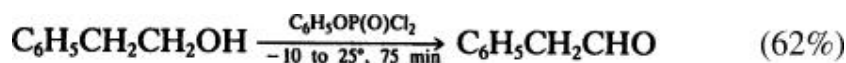
The sulfur trioxide complex with pyridine is frequently used for the activation of dimethyl sulfoxide, and the yields of methylthiomethyl ethers are low (4–5% from *n*-decanol and 2-octanol). (23) The reaction and workup are straightforward, but the use of triethylamine at 25° provides a possible avenue for side reactions, and the yields are usually not as good as those with oxalyl chloride or trifluoroacetic anhydride. The reaction of dimethyl sulfoxide with liquid sulfur trioxide produces a complex observable by ^{1}H NMR, whose structure is formulated as $(CH_3)_2S^+OSO_3^-$, (65) and this complex presumably reacts with alcohols to give ROS$^+$ $(CH_3)_2$ (**6**). Although these oxidations are usually run in dimethyl sulfoxide solvent, 6.5:1 dimethyl sulfoxide/tetrahydrofuran can also be used. (64d)

Acetic anhydride is also frequently used for the activation of dimethyl sulfoxide, but has the potential for forming acetates from alcohols or enolizable carbonyl groups, as well as for forming methylthiomethyl ethers. It also requires long reaction times (12–24 hours), (11) since it reacts with dimethyl sulfoxide slowly at room temperature. (65) Yohimbine (**11**) is conveniently oxidized on a 2.5-mol scale with this activator. (11)

The reaction of dimethyl sulfoxide with phosphorus pentoxide leads to immediate formation of a complex observable by ^{1}H NMR and formulated as $(CH_3)_2S^+O(P_2O_5)_n^-$, (65) which evidently reacts with alcohols to give **6**.

Addition of triethylamine to the original procedure (12) for oxidation with phosphorus pentoxide-activated dimethyl sulfoxide gives efficient conversion of alcohols to aldehydes or ketones at room temperature at scales ranging from 0.1 to 64 g of alcohol. 65a,b

$$n\text{-}C_{16}H_{33}OH \xrightarrow[2. \ (C_2H_5)_3N]{1. \ (CH_3)_2SO, \ P_2O_5} n\text{-}C_{15}H_{31}CHO \qquad (83\%)$$
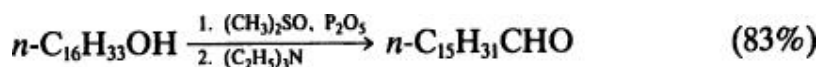
Activation of dimethyl sulfoxide by the chloroformate of the alcohol to be oxidized is proposed to occur as shown in Eq. 21. (15)

$$ROCCl \xrightarrow{(CH_3)_2SO} RO\overset{O}{\underset{(CH_3)_2S+}{\diamond}}O \xrightarrow{-CO_2} RO\overset{+}{S}(CH_3)_2 \qquad (21)$$
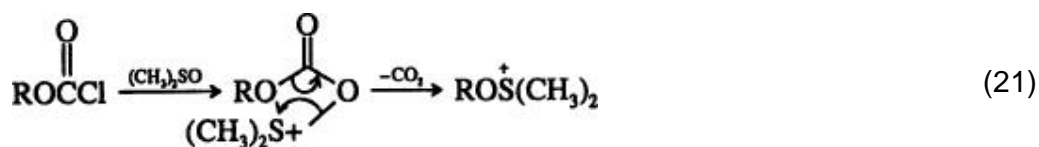
This mechanism implies that the oxygen of the alcohol is retained in the product, and the oxidation of *n*-butanol, 2-butanol, isobutanol, and 2,2-dimethylpropanol in 57–78% yields by this procedure is consistent with this pathway, since a displacement process is unlikely for the latter substrate. These reactions are carried out at room temperature, and the addition of epoxides such as 1,2-epoxypropane to act as acid scavengers gives improved yields of oxidized products. (16) Because the procedure for formation of the chloroformates involves the use of phosgene, (15) and because there are no apparent advantages to this procedure compared with other methods, its use is not recommended.

3.2.3. Halogens and Halosuccinimides

Reaction of dimethyl sulfide with *N*-chlorosuccinimide to form an active oxidant is a widely used procedure, (17-19) and as discussed in the mechanism section evidently involves an imidosulfonium species, whereas dimethyl sulfide and chlorine produce $(CH_3)_2S^+Cl\ Cl^-$. The reaction of chlorine with dimethyl sulfoxide produces a complex formulated as $(CH_3)_2S^+(O)Cl\ Cl^-$, which is also an effective oxidant but is rarely used. Since this reagent can also effect the addition of chlorine to alkenes, (14) it is often unsuitable for oxidation of hydroxyalkenes.

β-Keto alcohols in which the α carbon bears two hydrogen atoms react with dimethyl sulfoxide/*N*-chlorosuccinimide to form dimethylsulfonium ylides, which can be reduced to 1,3-dicarbonyl compounds with zinc in acetic acid. (66a)

$$C_6H_5CHOHCH_2COCH_3 \xrightarrow[NCS]{(CH_3)_2S} C_6H_5COCS(CH_3)_2COCH_3$$
$$\xrightarrow[CH_3CO_2H]{Zn} C_6H_5COCH_2COCH_3 \quad (97\%)$$
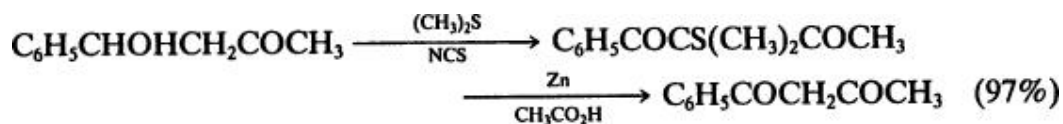
Reactions of alcohols with dimethyl sulfoxide and bromine, *N*-chlorosuccinimide, or *N*-bromosuccinimide at 50° lead to formation of methylene acetals, in which the methylene group is derived from dimethyl sulfoxide by Pummerer rearrangement and displacement. (67, 68)

$$(CH_3)_2\overset{+}{S}OR \xrightarrow{-H+} CH_3SCH_2OR \xrightarrow{Br_2} CH_3\overset{+}{S}(Br)CH_2OR \xrightarrow{ROH} (RO)_2CH_2$$
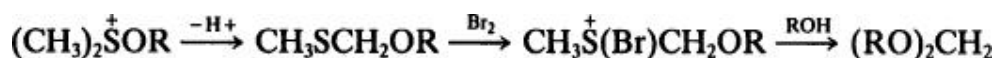
3.2.4. Oxygen

The use of oxygen and dimethyl sulfoxide at 190° for the oxidation of alcohols was reported some time ago, (69) but this reaction has seldom been used subsequently, and the specific roles of free-radical and oxysulfonium pathways have not been differentiated. More recently a report has appeared on the use of dimethyl sulfoxide and air at 150–160° for the conversion of secondary alcohols to ketones. (70)

Oxidation of α -hydroxy ketone **21** occurs with 10:1 dimethyl sulfoxide/methanol at 55°. (71) The reaction is "extremely sluggish" when oxygen is rigorously excluded and it appears that the latter is the active oxidant.

21   (80%)
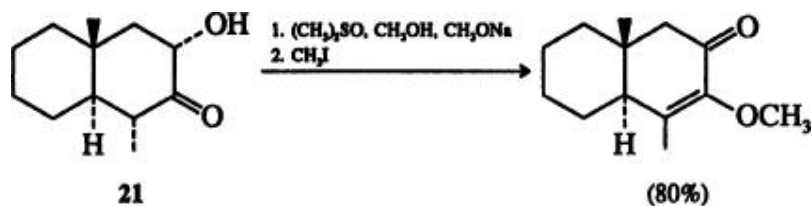
3.2.5. Electrochemical

Electrochemical oxidation of sulfides $RSCH_3$ (R = CH_3, n- C_8H_{17}, C_6H_5) can be used as an activating step in the oxidation of secondary alcohols such as 2-octanol to ketones in yields up to 99%. 20,20a These reactions are proposed 20,20a to involve formation of the same oxysulfonium intermediates $RO\overset{+}{S}(CH_3)R^1$ implicated in the oxidations with activated dimethyl sulfoxide or dimethyl sulfide/N-chlorosuccinimide.

3.3. Amine Bases

Triethylamine is the most commonly used base for the last step of the oxidation process, but for reactions with dimethyl sulfoxide/trifluoroacetic anhydride the use of diisopropylethylamine (DIPEA) often gives higher yields of carbonyl products and lower amounts of methylthiomethyl ethers and trifluoroacetates (Table B). The latter base is also effective with sulfur trioxide (71a) and oxalyl chloride activation. (72) 2,2,6,6-Tetramethylpiperidine is also very effective in the formation of cyclopentanone using dimethyl sulfoxide/trifluoroacetic anhydride, (27) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) is utilized in oxidations with dimethyl selenide/*N*-chlorosuccinimide. (46)

Table B. Effect of Amine on the Oxidation of Alcohols (23)

Substrate	Oxidant	Solvent	Amine	Time (h)	Products (%)		
					$R^1R^2C = O$	ROH	$ROCH_2SCH_3$
n-Decanol	$(CH_3)_2SO$, $(CF_3SO_2)_2O$, $-15°$	$(CH_3)_2SO$, HMPA	$C_2H_5N(CH_3)_2$	0.5	45	28	24
			$(C_2H_5)_3N$		68	18	13
			$(C_2H_5)_2NC_6H_{11}$		92	3	2
			$(i\text{-}C_3H_7)_2NC_2H_5$		94	2	2
n-Decanol	$(CH_3)_2SO$, cyanuric chloride, $-15°$	CH_2Cl_2, HMPA	$C_2H_5N(CH_3)_2$	0.5	47	32	18
			$(C_2H_5)_3N$		80	11	8
			$(C_2H_5)_3NC_6H_{11}$		93	5	3
			$(i\text{-}C_3H_7)_2NC_2H_5$		95	3	1
2-Octanol	$(CH_3)_2S$, NCS, $-20°$	CH_2Cl_2	$C_2H_5N(CH_3)_2$	1.5	56	30	16
			$(C_2H_5)_3N$		59	23	18
			$(C_2H_5)_2NC_6H_{11}$		60	23	17

Treatment of a diol with oxalyl chloride/dimethyl sulfoxide followed by DBU at –78° gives a sensitive dicarbonyl derivative which is cyclized by the base to the desired product. (72a)

(25%)
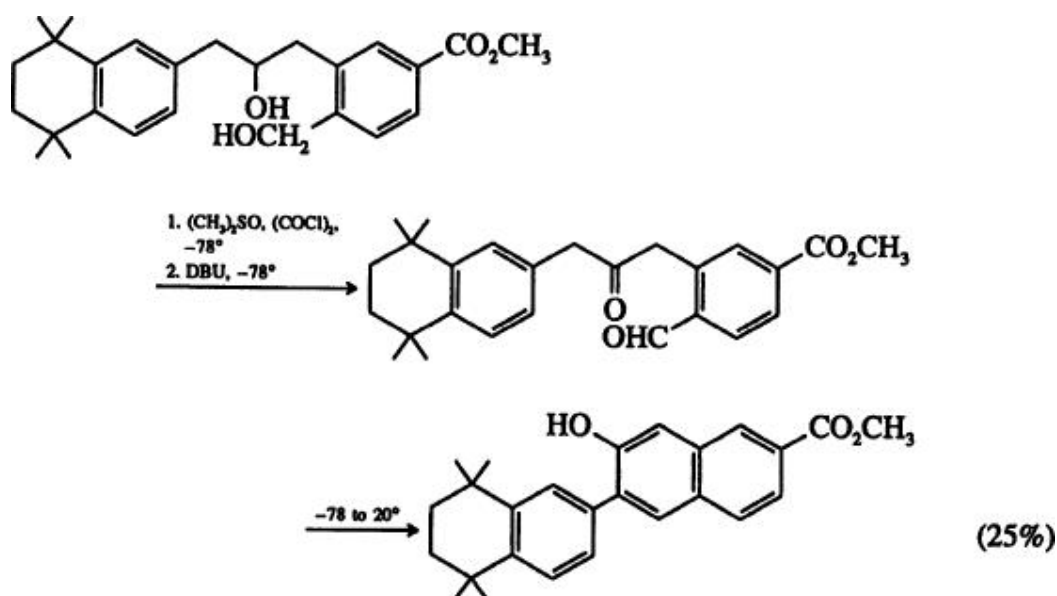
A principal reason for the use of hindered bases is to minimize enolization of the product, which results in epimerization or racemization. This problem is particularly acute with aldehydes, and diisopropylethylamine is frequently utilized for this reason, (72-74) as discussed further in the section "Side Reactions."

In another interesting reaction (see Eqs. 32 and 33) the use of diisopropylethylamine instead of triethylamine enhances an intramolecular cyclization but suppresses an allylic chlorination. (75)

3.4. Alcohol Substrates
3.4.1. Tertiary Alcohols
In a number of examples, primary or secondary alcohols are successfully oxidized while tertiary hydroxy functions in the same molecule are undisturbed. In some instances, however, elimination of tertiary hydroxyls to form alkenes is

observed. A number of examples are listed in the section "1,2 Elimination to Alkenes," and another example is shown in Eq. 22. (76) Isolation of methylthiomethyl ethers from tertiary alcohols is rare. (77)

(22)

Ar = 4-CH$_3$OC$_6$H$_4$ (59%)   (16%)
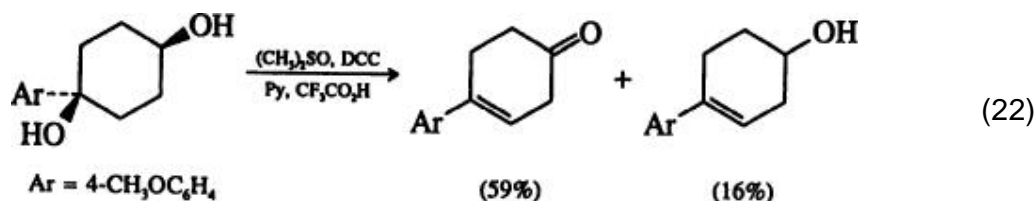
3.4.2. Primary and Secondary Alcohols
3.4.2.1. Oxidation
The oxidation of primary and secondary alcohols to the corresponding carbonyl compounds is very general. With dimethyl sulfoxide activated by oxalyl chloride, it is uncommon for these substrates to fail to react or for significant side reactions to occur. Activation of dimethyl sulfoxide by trifluoroacetic anhydride usually also gives efficient oxidation, although trifluoroacetate formation is sometimes significant. (24)

Among the exceptional cases where clean oxidation is not observed is allyl alcohol, which does not give efficient formation of acrolein with dimethyl sulfoxide/trifluoroacetic anhydride even though other allylic alcohols react successfully. (27) Trifluoroacetate formation may predominate here, but this has not been established.

2-Phenylethanol and 2-phenyl-1-propanol give 23 and 38% yields of the aldehydes, respectively, and 39 and 58% respective recoveries of starting material, using dimethyl sulfoxide/oxalyl chloride. (26) However 2-indanol and *trans*-2-phenyl-1-cyclohexanol give 95% yields of the corresponding ketones, (26) and 1-phenyl-2-propanol and 2-(1-naphthyl)ethanol give greater than 90% yields of carbonyl products with dimethyl sulfoxide/oxalyl chloride. (78) Thus the cause of the inefficiency of oxidation of some β -arylethanols is not known.

Many alkynyl alcohols are successfully oxidized using dimethyl sulfoxide. (22, 79-86)

$$\text{HC} \equiv \text{C(CH}_2)_3\text{OH} \xrightarrow[\text{2. (C}_2\text{H}_5)_3\text{N}]{\text{1. (CH}_3)_2\text{SO, (COCl)}_2} \text{HC} \equiv \text{C(CH}_2)_2\text{CHO (100\%)}^{22}$$
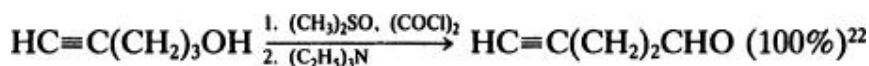
Formation of products with the structural units RCOC ≡ CH, RC ≡ CCH$_2$COR′,

and $CH_2 = C = CHCH_2CHO$ fails, (22, 26, 27) for example with $CH_3C \equiv CCH_2CHOHCH_3$ (22) and $n\text{-}C_4H_9CHOHC \equiv CH$. (27) It has been suggested that the triethylamine base plays an important role in this failure by destroying the reactant or product. (26) Quenching of the reaction mixture with water instead of triethylamine leads to recovery of the starting alcohols in some cases. (26)

Successful oxidations are listed in the tables of many compounds containing sulfur, silicon, or phosphorus atoms, as well as complexed transition metals, nitroxyl groups, polyene functions, and other sensitive groupings. In some reactions transition metal oxidants attack sulfur, and dimethyl sulfoxide based oxidations avoid this problem. *N*-Protected 2-amino aldehydes that are structurally related to amino acids can also be prepared from the alcohols by dimethyl sulfoxide oxidations. (87-100)

Some examples in which side reactions do occur are listed in the section "Side Reactions of Other Functional Groups."

As noted in the section "Overoxidation" the conversion of primary alcohols into carboxylic acids by reaction with activated dimethyl sulfoxide is rare. Sometimes it is convenient to carry out this transformation by first converting the alcohol into an aldehyde using activated dimethyl sulfoxide, and then using another oxidant to convert the aldehyde into the carboxylic acid. (101-103)

3.5. Side Reactions
3.5.1.1.1. Product Isomerization by Enolization
Generation of aldehydes and ketones in the presence of bases always presents the possibility that product isomerization may occur by enolization. However, there are many examples in the tables where enolization that could conceivably cause racemization of an optically active substrate, or isomerization to a more stable product, does not occur.

Thus, in the oxidation of **22** using activation with pyridine/sulfur trioxide, no more than 0.1% racemization occurs, whereas chromic oxide in pyridine/methylene chloride and silica gel supported chromate produce 5 and 22% racemization, respectively. (104)
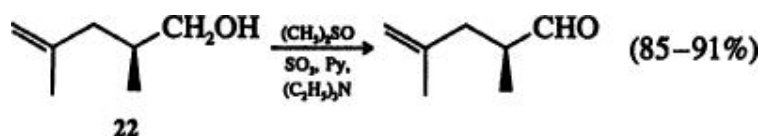
However, oxidation of the cyclobutanol **23** with dimethyl sulfoxide, sulfur trioxide/pyridine, and triethylamine gives the epimerized ketones **24a** (32%) and **24b** (16%). (105)
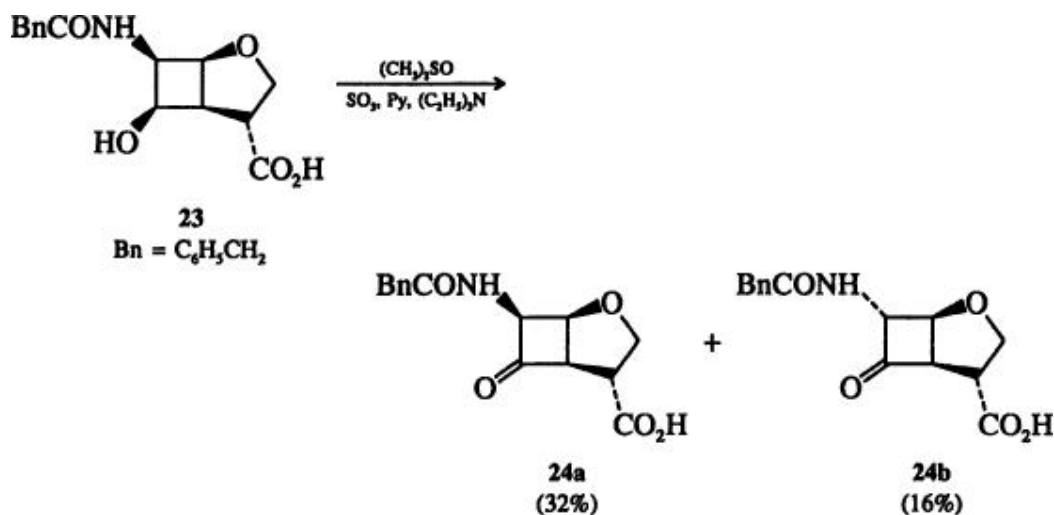
Oxidation of alcohol **25** using dicyclohexylcarbodiimide activation gives the aldehyde in 44% yield and only 82% retention of optical purity. (106) For comparison, chormic acid oxidation of **25** gives complete racemization. (106)

$$(S)\text{-}t\text{-}C_4H_9CH(CH_3)CH_2OH \xrightarrow[\text{Py, } CF_3CO_2H]{(CH_3)_2SO, \text{ DCC}} (S)\text{-}t\text{-}C_4H_9CH(CH_3)CHO$$

25   (44%)
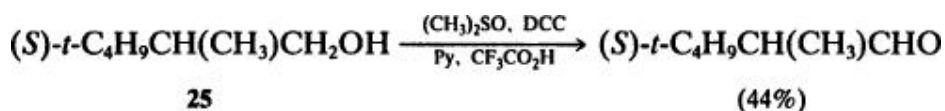
The low temperatures used with oxalyl chloride activation of dimethyl sulfoxide help to suppress enolization, and no more than 8% racemization is observed in the oxidation of **26**. (107)

However, epimerization in the product does occur during oxidation of alcohol **27**. (108) This is attributed to a unique ring opening and reclosure, but
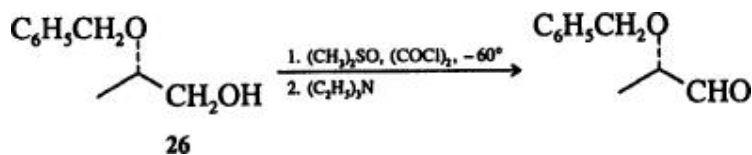
there is no convincing evidence for this proposal, and enolization caused by the triethylamine is the more likely cause.
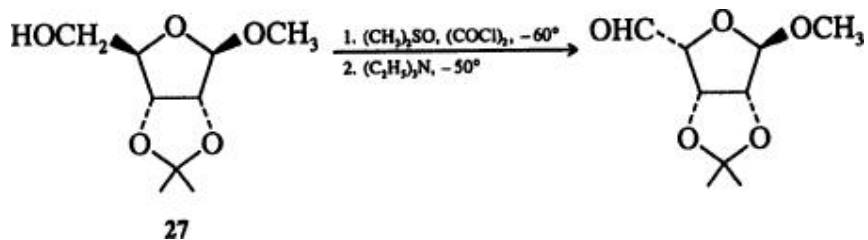
Another example illustrates the normal resistance to racemization during the dimethyl sulfoxide/oxalyl chloride oxidation. (109)
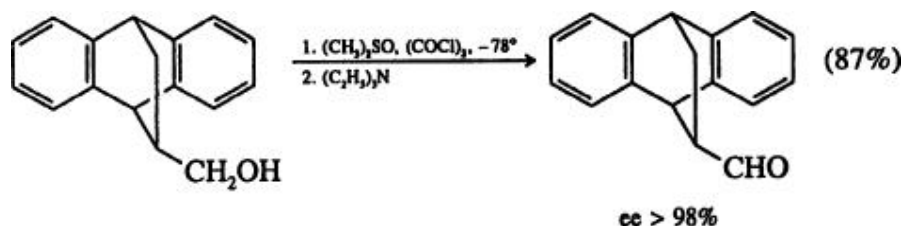
Hindered amine bases, particularly diisopropylethylamine (DIPEA), can minimize racemization if the product is a sensitive aldehyde. (72-74) Thus in the oxidation of alcohol **28**, followed by oxidative removal of the phenylboronate protecting group and spontaneous cyclization to the lactol, no diastereomeric products are found. (72)
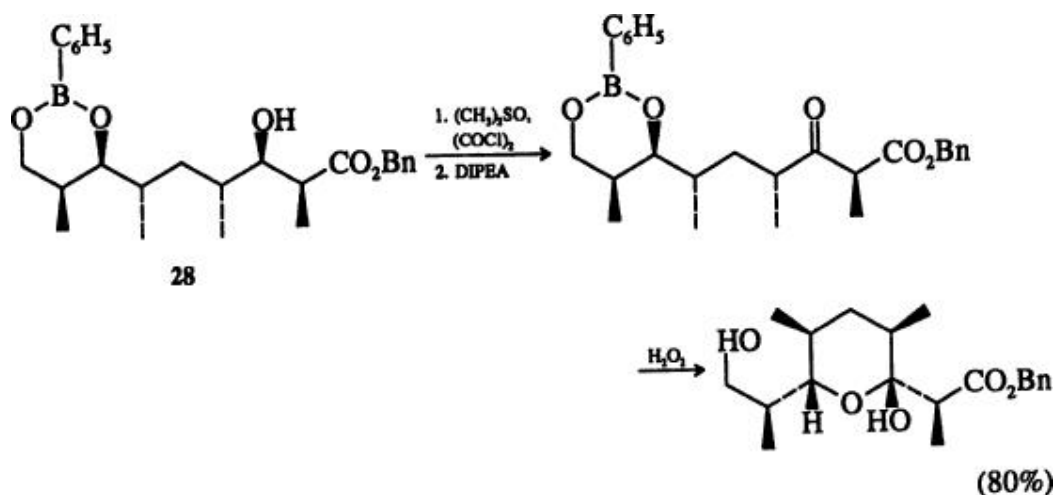
The use of DIPEA, cold acidic workup, and buffered wash gives a good yield of a sensitive aldehyde. (109a)

$$\text{(CH}_3)_2\text{SO, (COCl)}_2 \xrightarrow[\text{2. DIPEA}]{\text{1. (CH}_3)_2\text{SO, (COCl)}_2} \text{(92\%)}$$
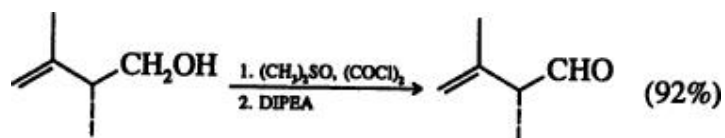
Another approach to protecting a product aldehyde from racemization by triethylamine involves removal of the base by extraction of the solution with aqueous sodium bisulfate prior to concentration. (110)
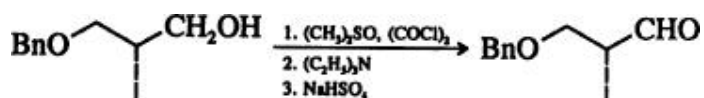
The use of pH 7 phosphate buffer and hexane extraction are effective in preventing racemization of sensitive aldehydes by the product triethylammonium hydrochloride. (111) Tetramethylurea also serves as a buffer for the dimethyl sulfoxide/trifluoroacetic anhydride procedure. (112)

$C_6H_5CH_2OCH_2O$ —— (with $Si(CH_3)_3$ group) ...CH$_2$OH

1. $(CH_3)_2SO$, $(COCl)_2$
2. $(C_2H_5)_3N$, 0°
3. phosphate buffer, hexane extraction

$C_6H_5CH_2OCH_2O$ —— (with $Si(CH_3)_3$ group) ...CHO (>72%)

OAB

t-$C_4H_9(CH_3)_2SiO$ ... OH, N_3

1. $(CH_3)_2SO$, $(CF_3CO)_2O$
2. $[(CH_3)_2N]_2CO$ $(C_2H_5)_3N$, −78°

OAB

t-$C_4H_9(CH_3)_2SiO$ ... O, N_3 (>80%)
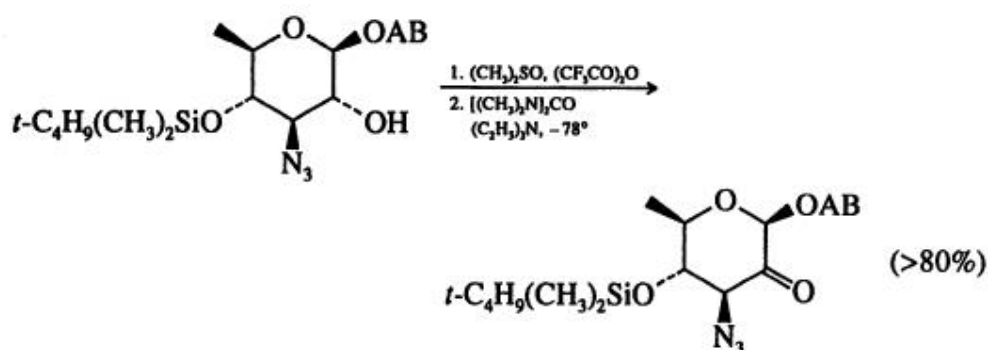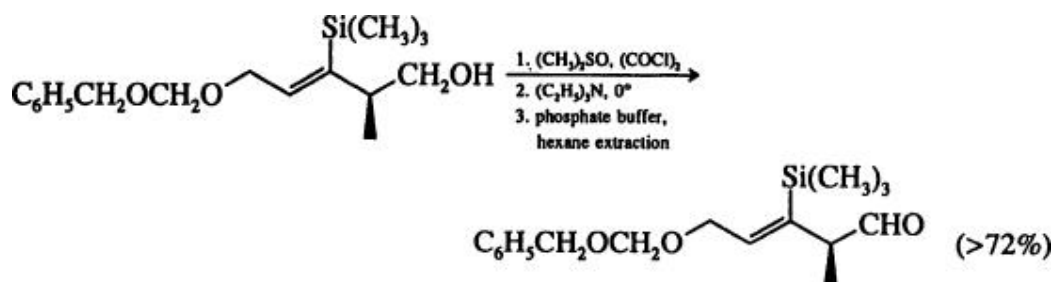
AB = Amphoteronolide B protected by the group t-$C_4H_9(CH_3)_2Si$

Some substrates with β , γ double bonds that can be isomerized by enolization to form α , β -unsaturated carbonyl products undergo this rearrangement, (113-115) but this is rare and only appears to be favored where disubstituted double bonds are converted to trisubstituted double bonds.

There are many examples where isomerization of β , γ - to α , β -unsaturated systems does not occur. (116-126)

$(81\%)^{113}$

$(65\%)^{114}$

$(80\%)^{115}$

$(—)^{116}$

$(80\%)^{117}$
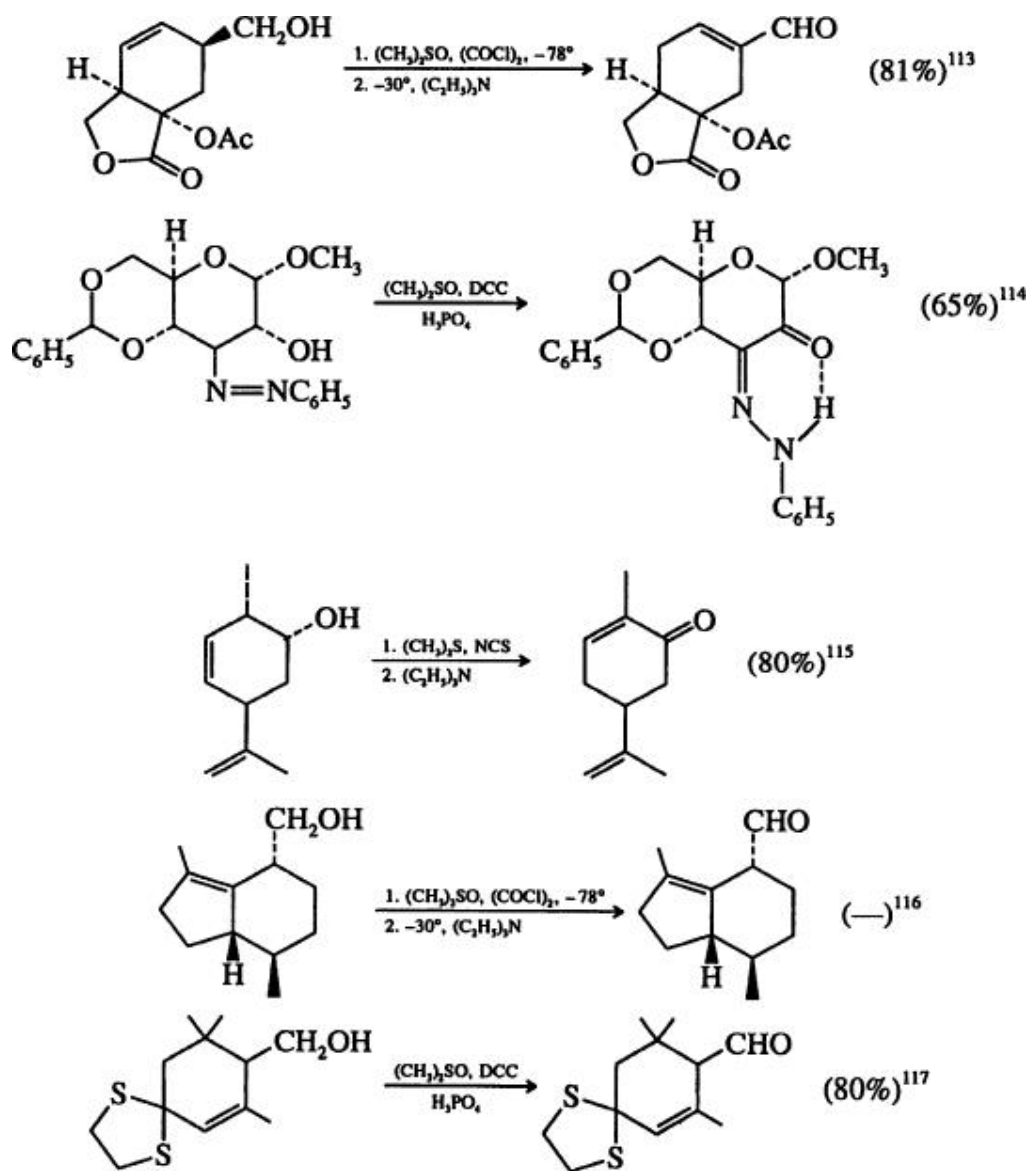
The formation of a ketone with four β , γ double bonds is notable, even though isomerization to bridgehead double bonds is improbable. (124)

(90%)
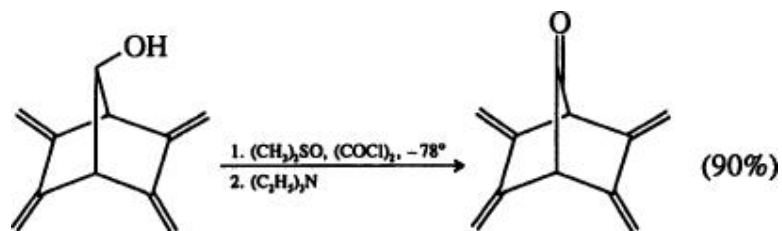
The use of dimethyl sulfoxide/oxalyl chloride at –60° followed by diisopropylethylamine as the base may be helpful in suppressing rearrangement of β , γ double bonds where this is a problem.

3.5.1.1.2. 1,2 Elimination to Alkenes

Elimination to give alkenes is a potential side reaction of the oxysulfonium intermediates, and can occur by the E1 process of dissociation to carbocations (Eq. 23), by an E2 process involving base reacting with the alkoxysulfonium ion, or by base attack to give oxysulfonium ylides, which undergo elimination through six-membered transition states (Eq. 24) as opposed to the five-membered transition states involved in oxidations.

$$\text{H}-\underset{|}{\overset{|}{\text{C}}}-\underset{|}{\overset{|}{\text{C}}}-\text{O}\overset{+}{\text{S}}(\text{CH}_3)_2 \xrightarrow{-(\text{CH}_3)_2\text{SO}} \text{H}-\underset{|}{\overset{|}{\text{C}}}-\text{C}\overset{+}{\diagup} \xrightarrow{-\text{H}^+} \diagdown\text{C}=\text{C}\diagup \tag{23}$$

29

$$\textbf{29} \xrightarrow{(\text{C}_2\text{H}_5)_3\text{N}} \left[\begin{array}{c}\text{CH}_3\\ \bar{\text{C}}\text{H}_2-\overset{+}{\overset{|}{\text{S}}} \\ \text{H} \qquad \text{O}\\ \diagup\text{C}-\text{C}\diagdown\\ | \qquad |\end{array}\right] \longrightarrow \diagdown\text{C}=\text{C}\diagup + (\text{CH}_3)_2\text{SO} \tag{24}$$
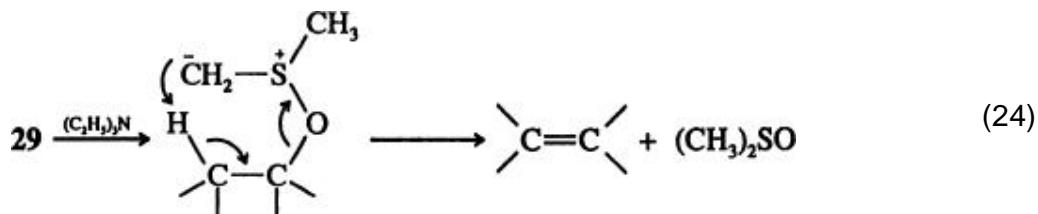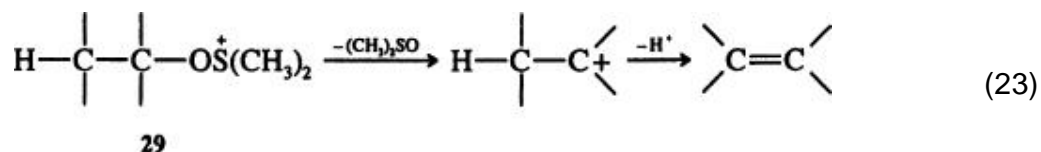
An example of such an elimination is shown in Eq. 25. (38) It is notable that elimination of the tertiary 17-hydroxy group does not occur, even though an α , β -unsaturated carbonyl system would be formed.

(25)
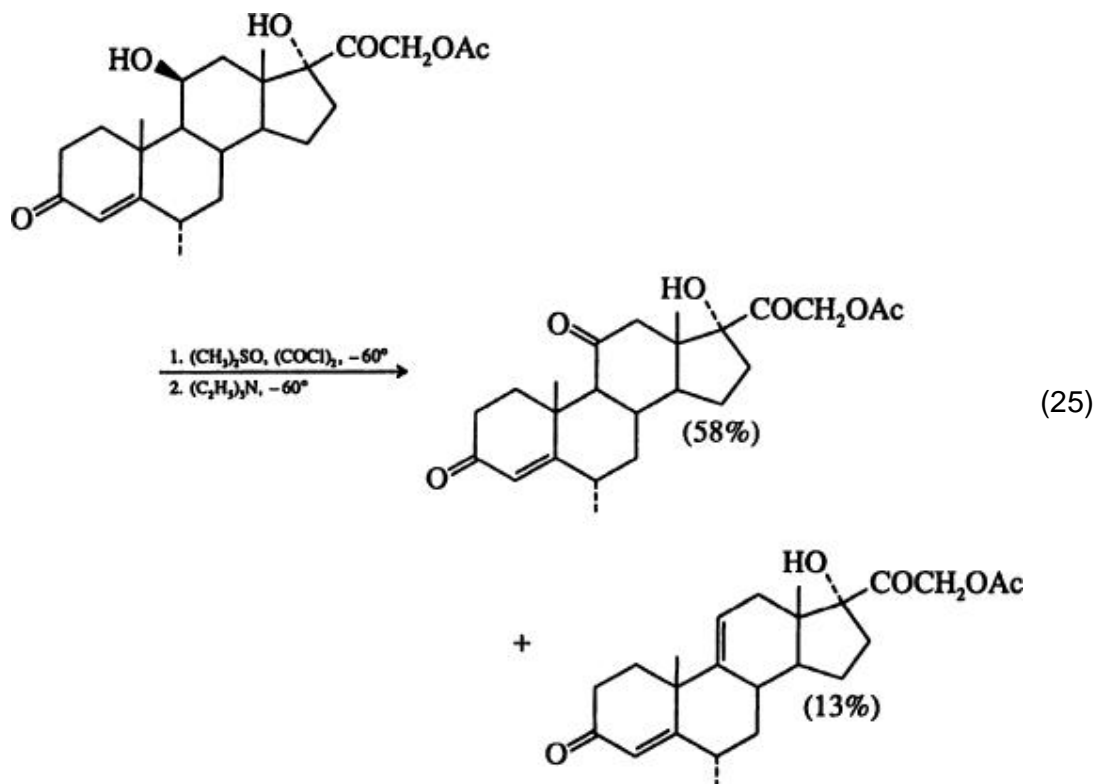
Such eliminations are relatively uncommon and, even in a series of β -keto alcohols, are not observed with oxalyl chloride activation, but only with trifluoroacetic anhydride activation. (127)

$$n\text{-}C_6H_{13}CHOHCH_2COCH_3 \xrightarrow[(C_2H_5)_3N]{(CH_3)_2SO}$$

$$n\text{-}C_6H_{13}COCH_2COCH_3 + n\text{-}C_6H_{13}CH=CHCOCH_3$$

(COCl)₂ activation	(69%)	(—)
(CF₃CO)₂O activation	(50%)	(33%)
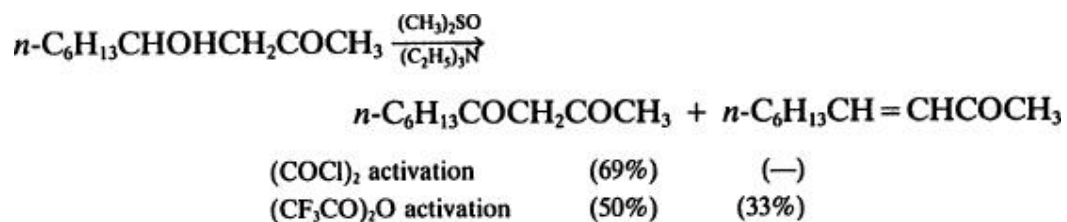
Treatment of allylic alcohol **30** with dimethyl sulfide/*N*-chlorosuccinimide causes elimination of the hydroxy group, but the product structure was not identified. (128)

30
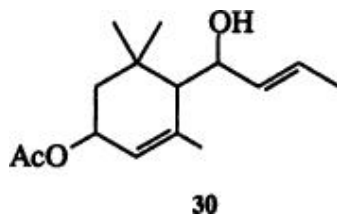
1,4 Elimination is the predominant reaction of allylic alcohol **30a**, and some rearranged alcohol is also formed. (129)

30a

(23%)

(42%)   (12%)
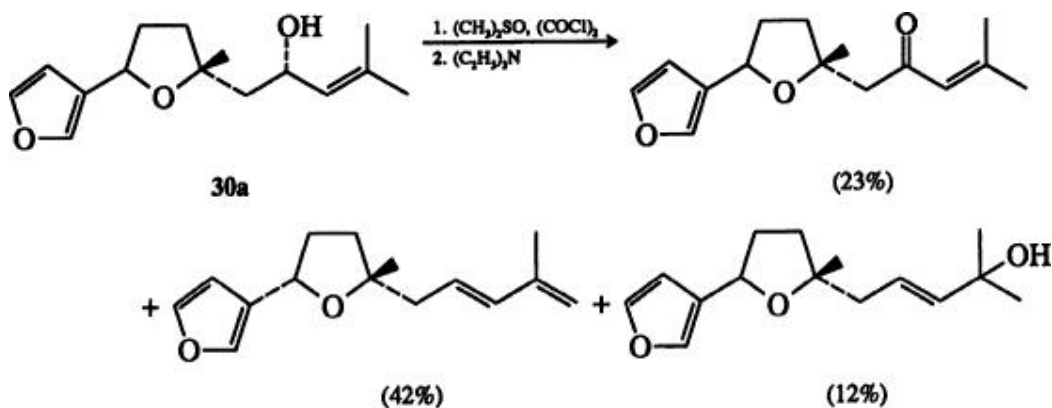
Treatment of the heterocyclic alcohols **31** (130) and **32** (131) with activated dimethyl sulfoxide causes elimination, although **32** does not react at −70°. (131) Oxidation of alcohol **31** is successful using chromic acid in acetone. (130)

1-Phenyl-2-propanol undergoes some elimination under rather drastic conditions. (69)

$$C_6H_5CH_2CHOHCH_3 \xrightarrow[190°]{(CH_3)_2SO,\ O_2} C_6H_5CH_2COCH_3\ +\ C_6H_5CH=CHCH_3$$

(25%)   (36%)

31

32

(82%)[131]
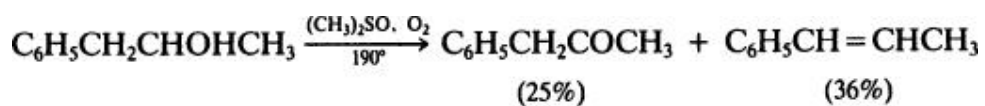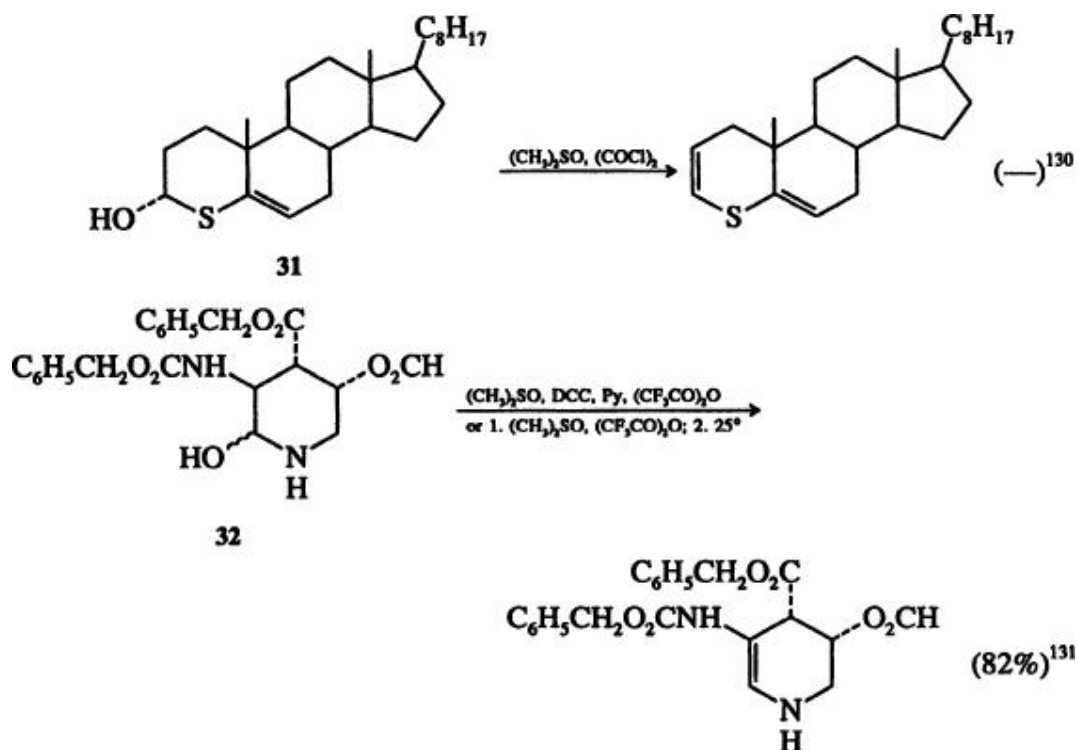
Oxidation of the primary alcohol **33** with dimethyl sulfoxide/dicyclohexylcarbodiimide gives the diene **34** in 72% yield, evidently through a 1,4-elimination pathway. (132) Oxidation to the unrearranged aldehyde is effected by pyridinium chlorochromate. (132)

33

(72%) **34**
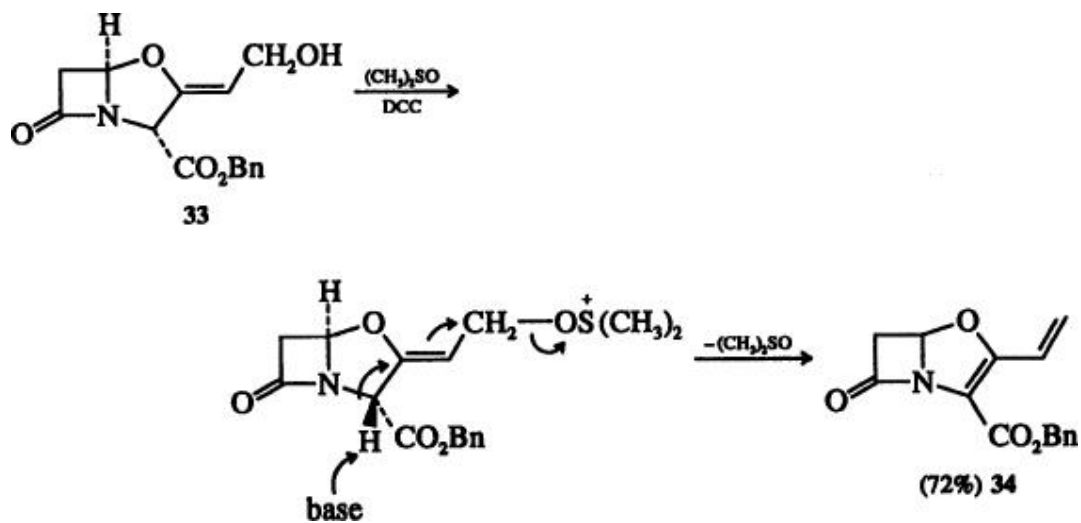
The oxidation of the tertiary lactol **35** is believed to proceed by elimination,

followed by attack of the activated sulfoxonium ion on the intermediate alkene to give a vinyl sulfide via the intermediate **36** (Eq. 26). (41)

(26)
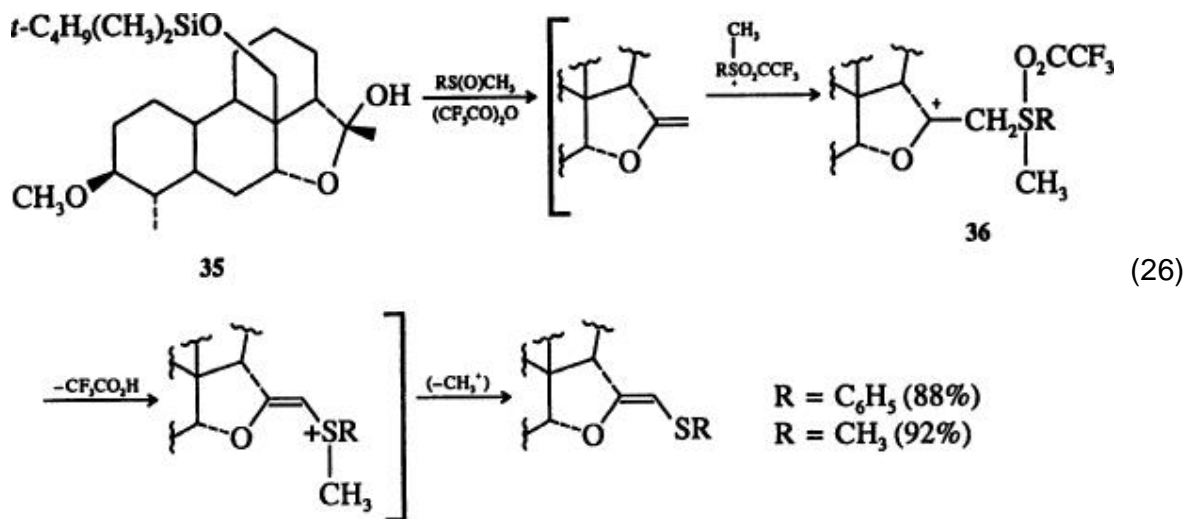
An example of lactol elimination is shown in Eq. 27. (30)

(27)
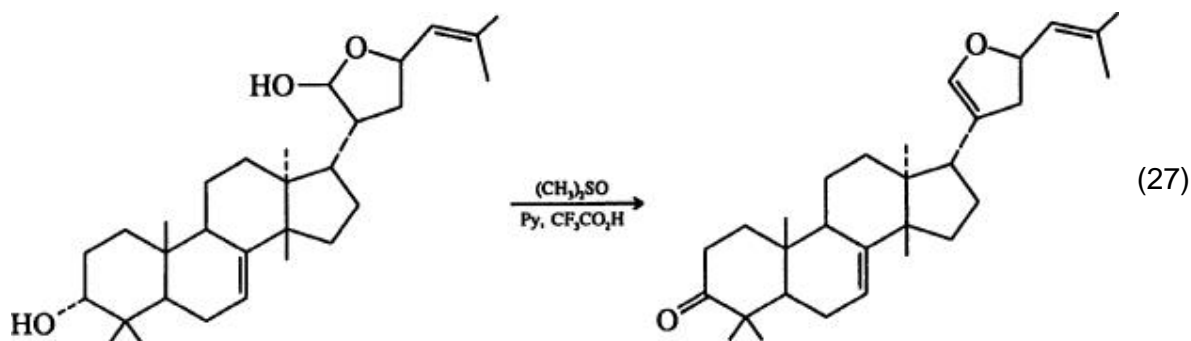
Although activated sulfoxides may form tertiary alkoxysulfonium ions in the presence of tertiary alcohols, the alcohols are usually recovered unchanged from the reaction; evidently the alkoxysulfonium ions revert to the alcohols during workup. There is evidence for the generation of *tert*-butoxysulfonium ions from the reaction of *tert*-butyl bromide with dimethyl sulfoxide, and it appears that nucleophiles and bases react at sulfur to displace the *tert*-butoxide unit. (133-135)

$$(CH_3)_2SO + t\text{-}C_4H_9Br \longrightarrow t\text{-}C_4H_9O\overset{+}{S}(CH_3)_2$$
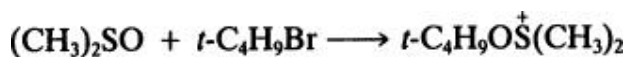
The tertiary alkoxysulfonium ion generated by reaction of dimethyl sulfoxide with tosylate **37** leads to an alkene. (136)
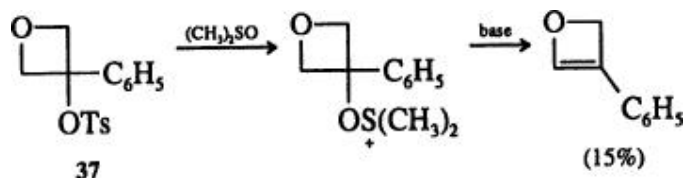
Attempted oxidation of alcohol **38** with dimethyl sulfoxide activated by dicyclohexylcarbodiimide or sulfur trioxide results in dehydration to **39**, whereas dimethyl sulfide/*N*-chlorosuccinimide or dimethyl sulfoxide/oxalyl chloride give the α , β -unsaturated aldehyde **40**; the latter result is attributed to formation of the mono-oxidation product **41**, which is converted into aldehyde **40** by oxidation of enol **42**. (137)
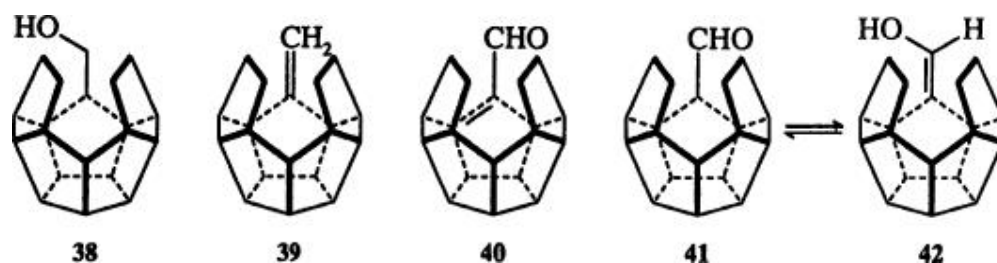
1,2 Elimination with cleavage of a carbon–carbon bond and formation of a carbocationic species can evidently occur with some strained alcohols; thus it is proposed that isoborneol (**43**) is converted into camphene by the path shown in Eq. 28. (25) Rearrangement does not occur below –65°, and camphor is formed in >90% yield. (25)

(28)

(85%)
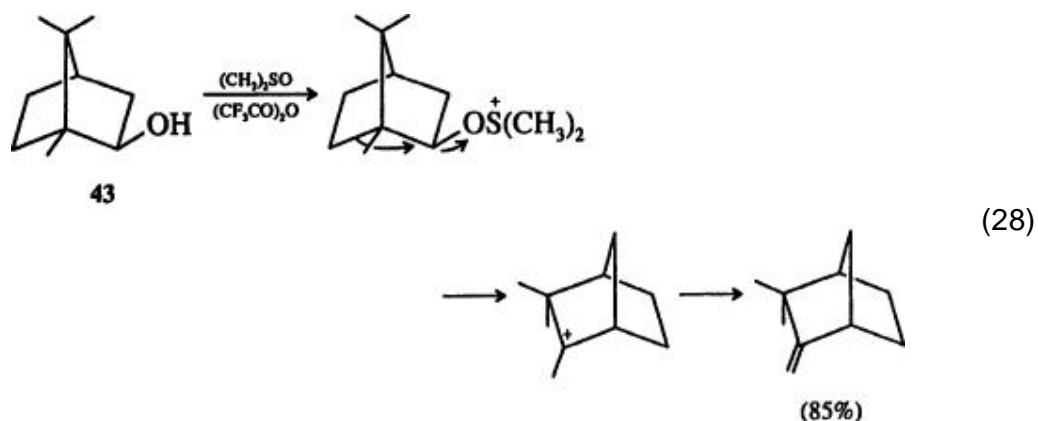
Cyclopropylmethanol and cyclopropylethanol give the corresponding carbonyl compounds on treatment with dimethyl sulfoxide/trifluoroacetic anhydride. (27) With dimethyl sulfoxide containing boron trifluoride at 170°, alcohol **44** undergoes dehydration whereas **45** gives a ring-opened carbonyl compound. (38) It appears likely that under these stringent conditions the dehydrations and ring cleavages shown involve acid-catalyzed formation of carbocations which are captured by dimethyl sulfoxide.

Cyclopropyl ring opening also occurs on reaction of alcohol **46** with dimethyl sulfoxide/oxalyl chloride, forming **47** in 25% yield as determined by gas chromatography. (139) The exact stage of the reaction at which ring opening occurs is not known; one possibility is that complexation of an initially formed aldehyde with chlorodimethylsulfonium ion promotes rearrangement. (139)
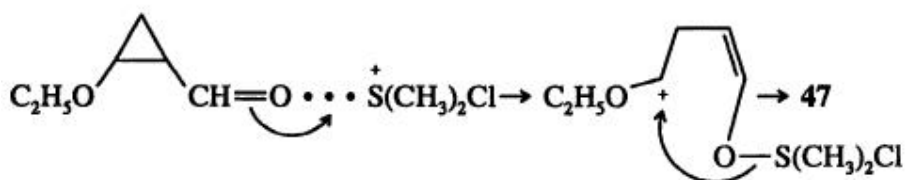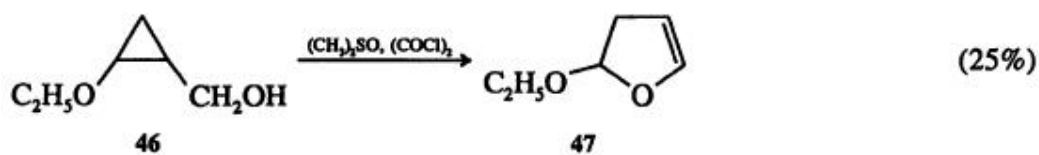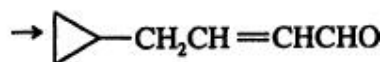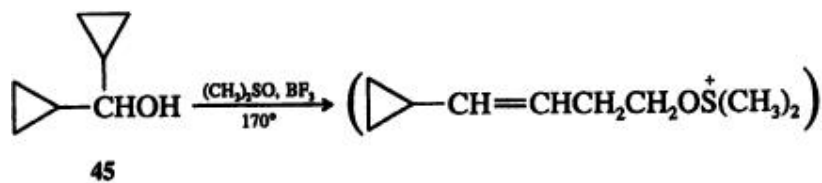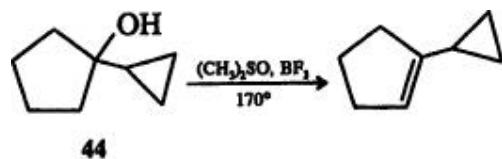
Carbinol **48** is converted into enal **49** in 50% yield by reaction with dimethyl sulfoxide, acetic anhydride, and potassium carbonate. (140)
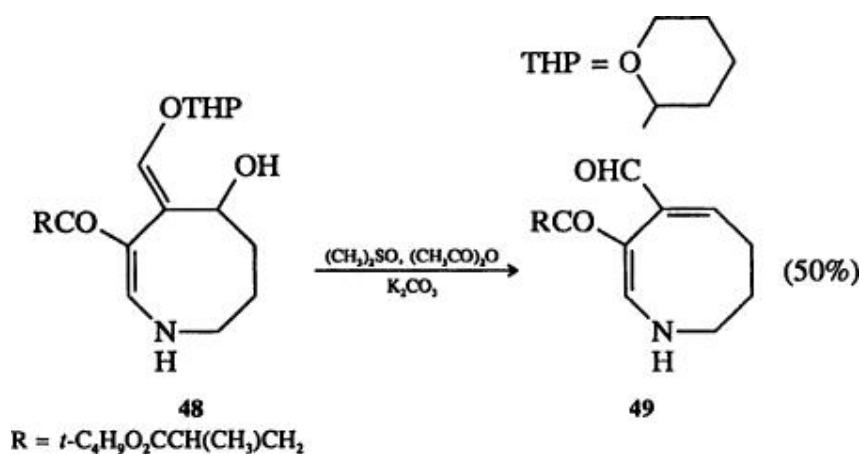
3.5.1.1.3. 3,4 Elimination to α , β -Unsaturated Carbonyl Compounds

Oxidation of carbohydrates with good leaving groups beta to the incipient carbonyl often involves concomitant elimination with formation of α , β -unsaturated carbonyl products. (141-153) The leaving groups are typically acetate or benzoate and elimination to give exocyclic methylene groups usually does not occur. (35, 147)
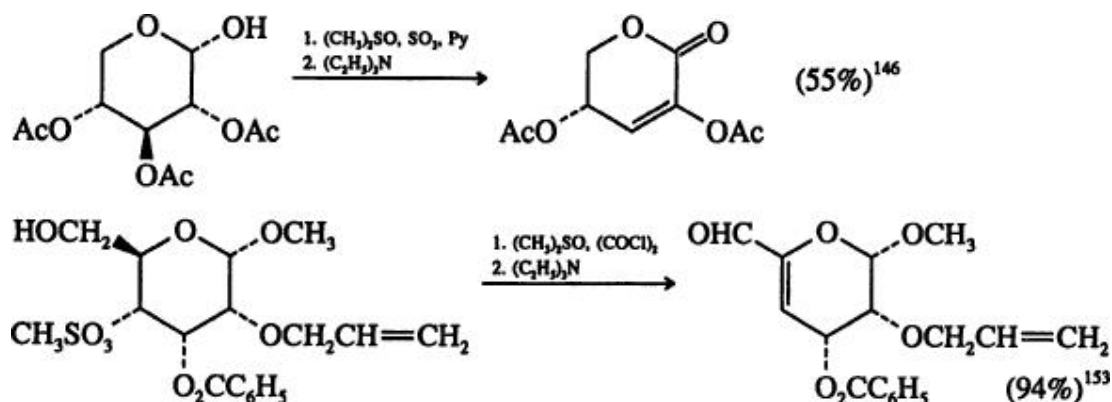
A similar elimination from diol **50** probably involves acid catalysis by the pyridinium trifluoroacetate (142) or simply elimination of the oxysulfonium group β to the carbonyl group.
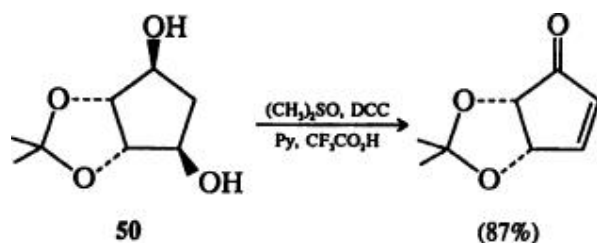
Elimination also occurs when a β -keto sulfone to generated at 10°. (154)
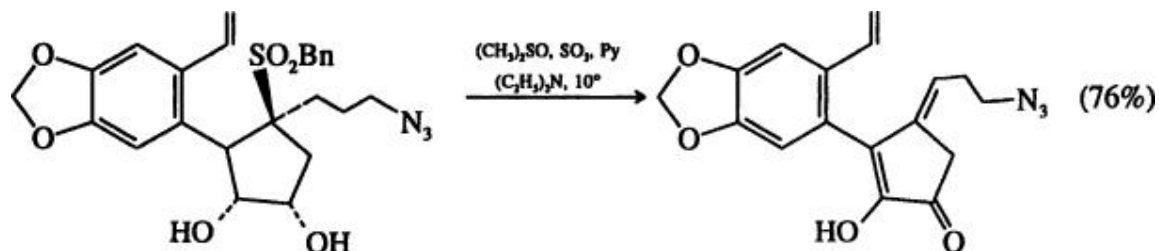
3.5.1.1.4. Formation of Methylthiomethyl Ethers

Methylthiomethyl ethers are common byproducts in the oxidation procedure and, as shown in Table A, (23) are best avoided by using dimethyl sulfoxide/oxalyl chloride at –60°, dimethyl sulfoxide/sulfur trioxide–pyridine at 25°, or dimethyl sulfide/N-chlorosuccinimide at –25°. In the reaction of cyclohexylmethanol with dimethyl sulfide/N-chlorosuccinimide, the methylthiomethyl ether yield at –25° is less than 1% in toluene, 18% in methylene chloride, and 45% in 1/1 methylene chloride/dimethyl sulfoxide. (17) This side reaction is most serious with the dimethyl sulfoxide/acetic anhydride procedure at 25°, and is usually of little consequence with dimethyl sulfoxide activated by trifluoroacetic anhydride or oxalyl chloride, (18, 22-24, 26, 27) probably because of the very low temperatures (ca. –60°) used. Interestingly, this side reaction is less prevalent when diisopropylethylamine is used as a base instead of triethylamine. (23, 27)

On rare occasions tertiary alcohols form thiomethylmethyl ethers under the conditions of the reaction. (77)

$(\sim 100\%)^{77}$

R = CH$_2$SCH$_3$
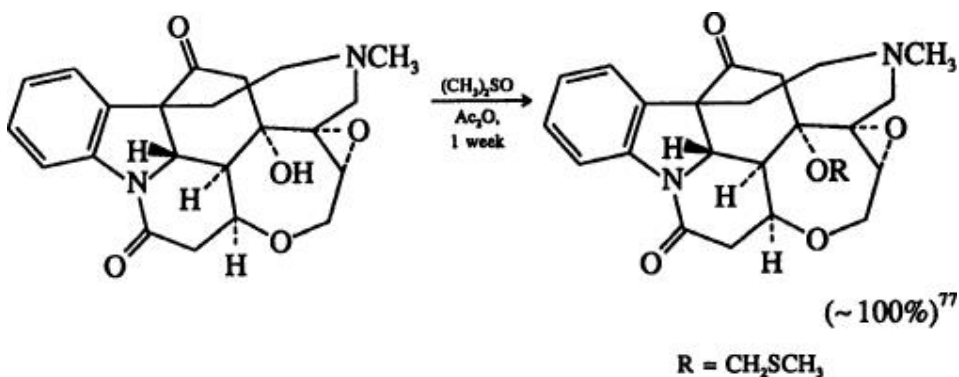
3.5.1.1.5. Substitution

Because sulfoxides are rather good leaving groups there is potential competition between oxidation and substitution whenever alkoxysulfonium ions are generated, and the latter path is favored by the presence of good nucleophiles or reactive substrates. This behavior has been exploited for the development of a widely used synthesis of allylic and benzyl halides by reaction of the corresponding alcohols with dimethyl sulfide and N-chlorosuccinimide or N-bromosuccinimide. (155) The procedure is the same as the oxidation method, except that the triethylamine is omitted. (17)

$$C_6H_5CH_2OH \xrightarrow[\text{CH}_2\text{Cl}_2, \ -20^\circ]{\text{(CH}_3)_2\text{S, NCS}} [C_6H_5CH_2O\overset{+}{S}(CH_3)_2Cl^-] \longrightarrow C_6H_5CH_2Cl$$

<div align="right">(>95%)</div>
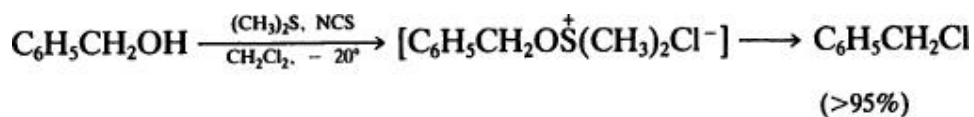
Temperature can play an important role in determining which reaction path is followed. Thus benzhydrol with dimethyl sulfoxide/oxalyl chloride gives benzophenone in 98–100% yield at –60°, but at –20° the ketone yield drops to 34% and significant conversion to the chloride occurs. (26)

Oxidation of diol **51** gives the dialdehyde when the reaction is carried out in dry dimethyl sulfoxide with oxalyl chloride, but if the dimethyl sulfoxide is moist the chloro aldehyde **52** resulting from chloride displacement on the allylic hydroxy group is obtained in 40% yield. (156)
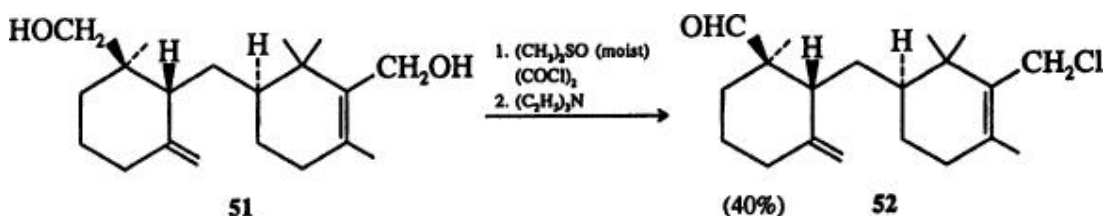
Treatment of allylic alcohols with dimethyl sulfoxide/oxalyl chloride without base gives allylic chlorides in good yields. (157)
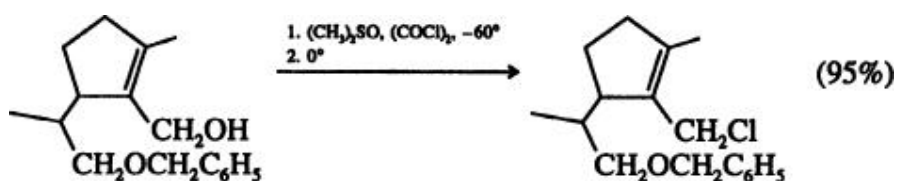
Alcohols can also serve as nucleophiles. Thus reaction of an equimolar mixture of 1-(4-anisyl)ethanol and 1-phenylethanol with 0.5 equivalent of dimethyl sulfoxide/oxalyl chloride gives a mixture of ketones and ethers. (38) The latter are evidently formed by attack of the excess alcohol on an incipient 4-anisylethyl carbocation (Eq. 28a). (38)

$$4\text{-}CH_3OC_6H_4CHOHCH_3 + C_6H_5CHOHCH_3 \xrightarrow[\text{2. } (C_2H_5)_3N]{\text{1. } (CH_3)_2SO, (COCl)_2}$$

$$C_6H_5COCH_3 \ (24\%) + 4\text{-}CH_3OC_6H_4CH(CH_3)OCH(CH_3)C_6H_5 \ (6\%)$$

$$+ \ 4\text{-}CH_3OC_6H_4COCH_3 \ (24\%) + [(4\text{-}CH_3OC_6H_4CH(CH_3)]_2O \ (4\%) \quad (28a)$$

$$4\text{-}CH_3OC_6H_4CH[O\overset{+}{S}(CH_3)_2]CH_3 \xrightarrow[-(CH_3)_2SO]{ROH}$$

$$4\text{-}CH_3OC_6H_4CH(OR)CH_3$$
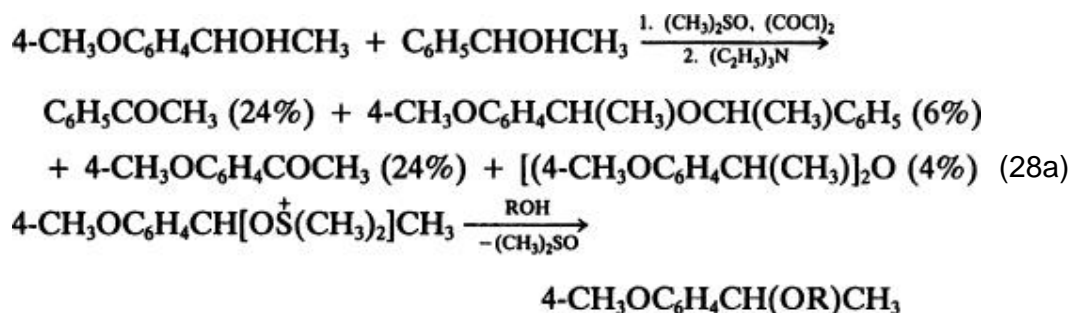
Trifluoroacetate esters are formed when alcohols are treated with dimethyl sulfoxide/trifluoroacetic anhydride at –60° and the reaction mixture is warmed to room temperature before addition of the amine. (24, 27) With 1-cyclopropylethanol the yield of trifluoroacetate is 86% by this procedure, but when triethylamine is added at –60° the yield of ketone is 60–75%. Significant amounts of trifluoroacetates are formed from some alcohols even when the triethylamine is added at –50° (*n*-decanol, 35%; cyclohexanol, 39%). (24)

Intramolecular nucleophilic displacement of the sulfoxonium group as the sulfoxide can occur when a neighboring group is suitably disposed, but the addition of triethylamine prevents displacement from taking place (Eqs. 29–31). (158, 159)

(29)

(93%)

(30)

(95%)

(31)

(−)
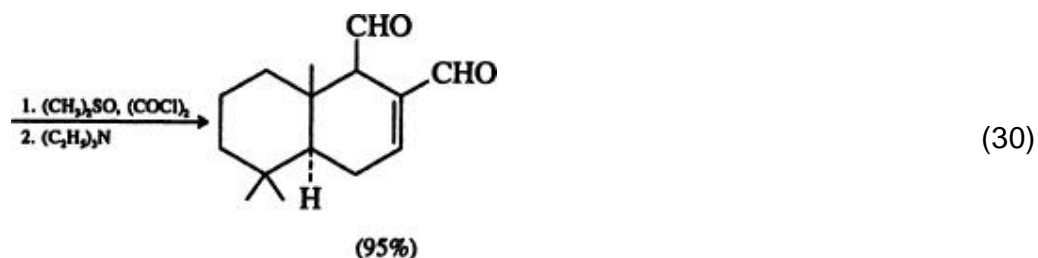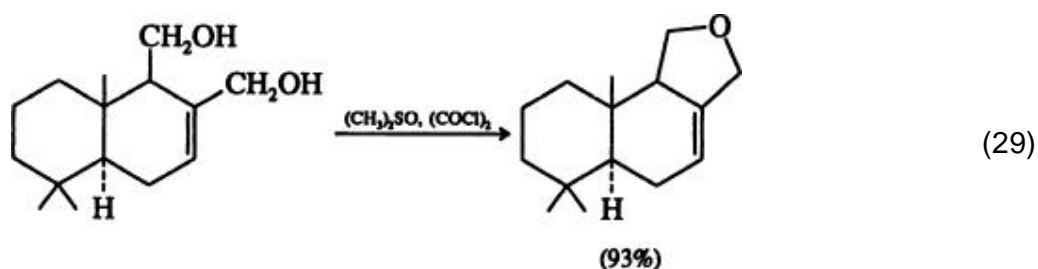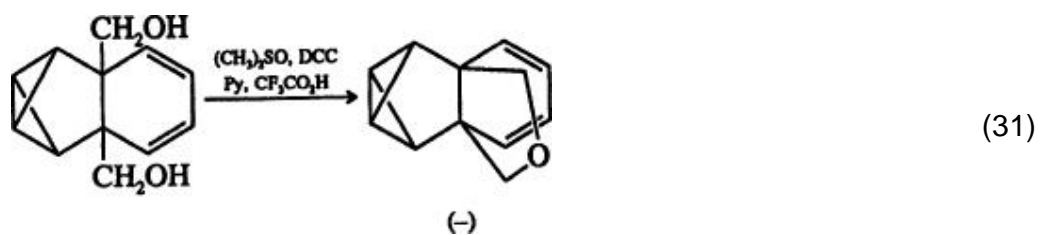
Some displacement is observed in the reaction of alcohol **53** using diisopropylethylamine (Eq. 32). (75) On the other hand, use of triethylamine results in chlorination of the tertiary alcohol (Eq. 33). (75) Chlorination via an $S_N i$ process is conceivable, but the amine dependence is puzzling.

(32)

(33)
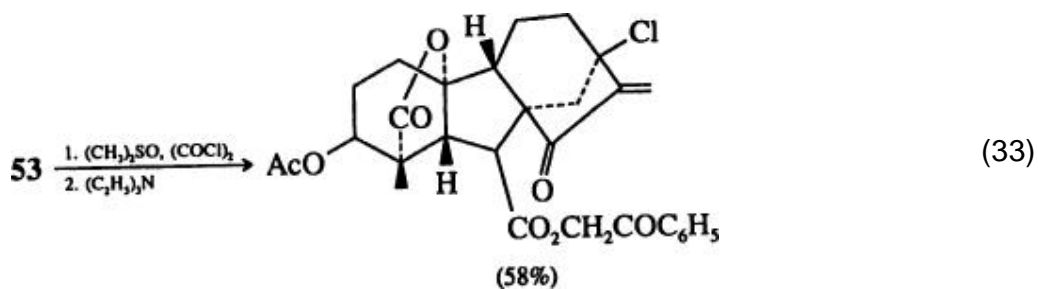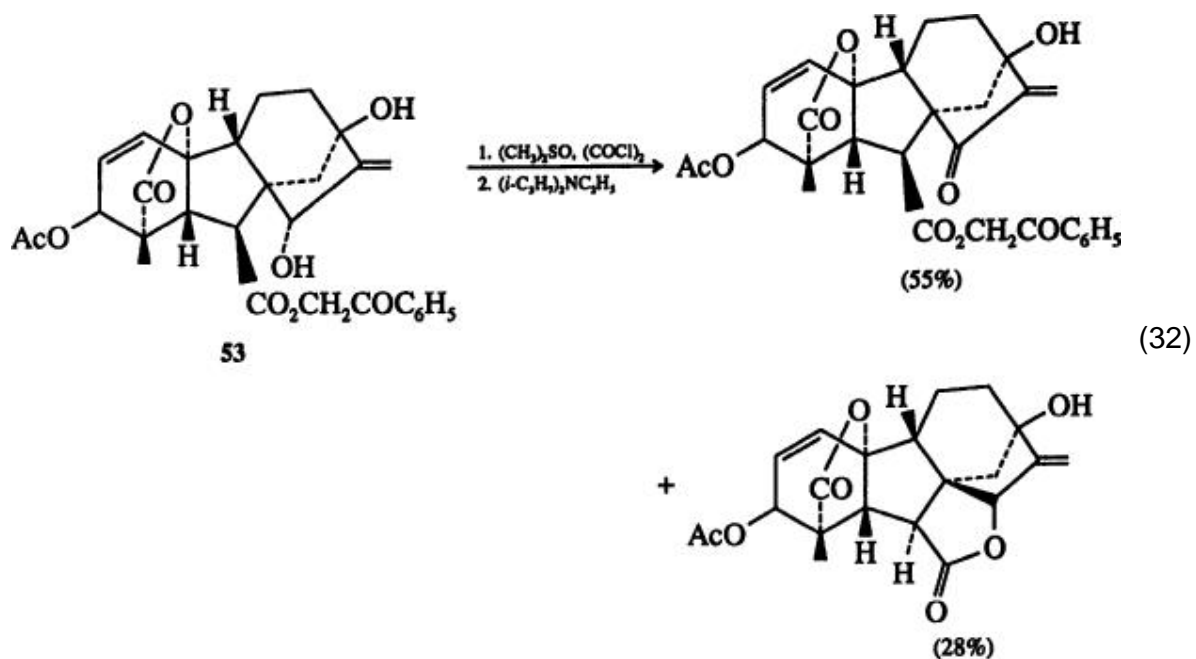
Normal oxidation of intermediate **54** occurs at –78°, but at 0° the amido nitrogen participates in cyclization; the adjacent furan ring strongly favors departure of dimethyl sulfoxide and carbocation formation, and with a 5-methoxy group on the furan ring cyclization occurs even at –60°. (160) In the case of alcohol **55** even an aromatic ring seems to be sufficiently nucleophilic to induce cyclization. (161)
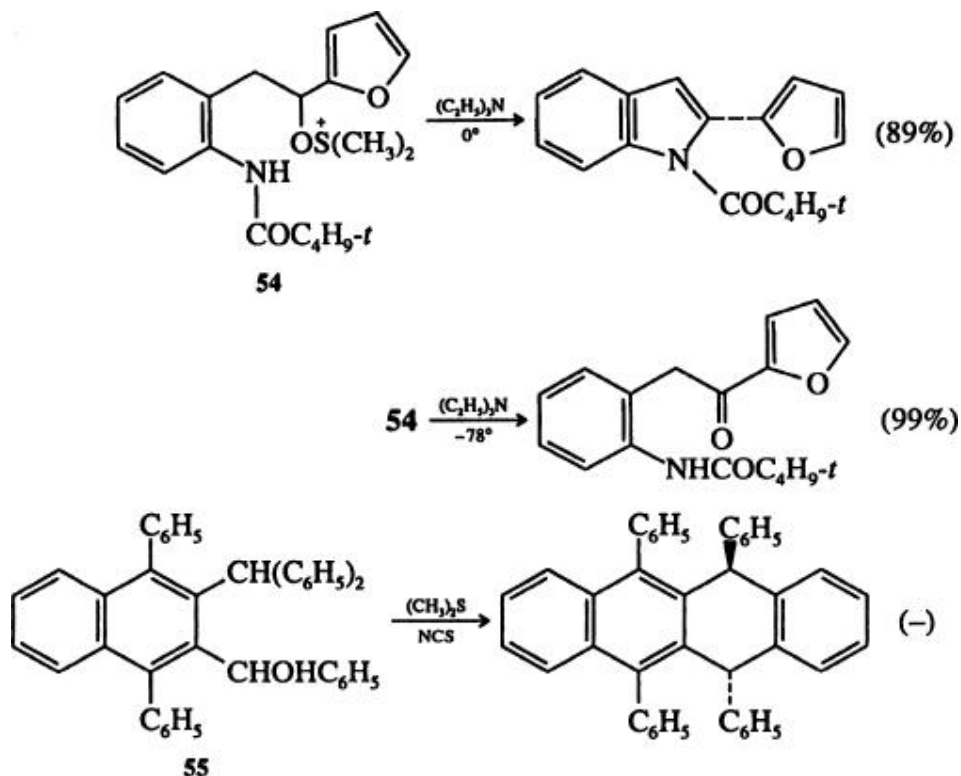
3.5.1.1.6. Further Reactions of the Carbonyl Products

Cyclization can also occur by initial oxidation to a carbonyl product which undergoes cyclization and dehydration. (162, 163)

(70%)

(79%)
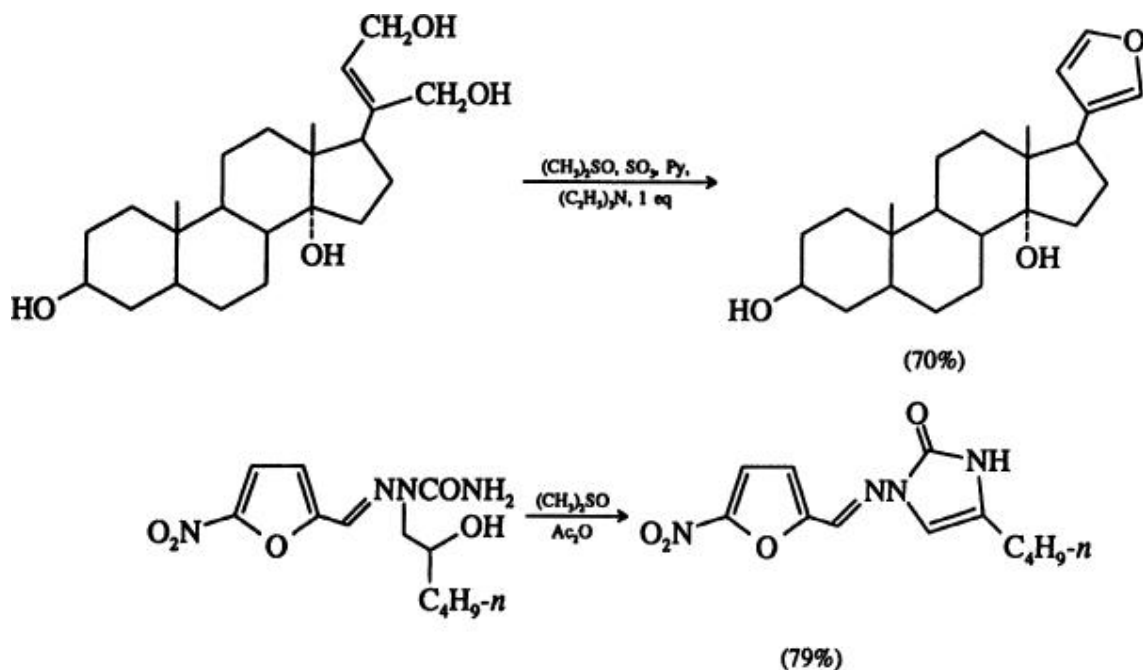
Alcohol **56**, on treatment with dimethyl sulfoxide/sulfur trioxide, undergoes cyclization with carbon–carbon bond cleavage, whereas it undergoes normal oxidation with dicyclohexylcarbodiimide. (164)

(58%)
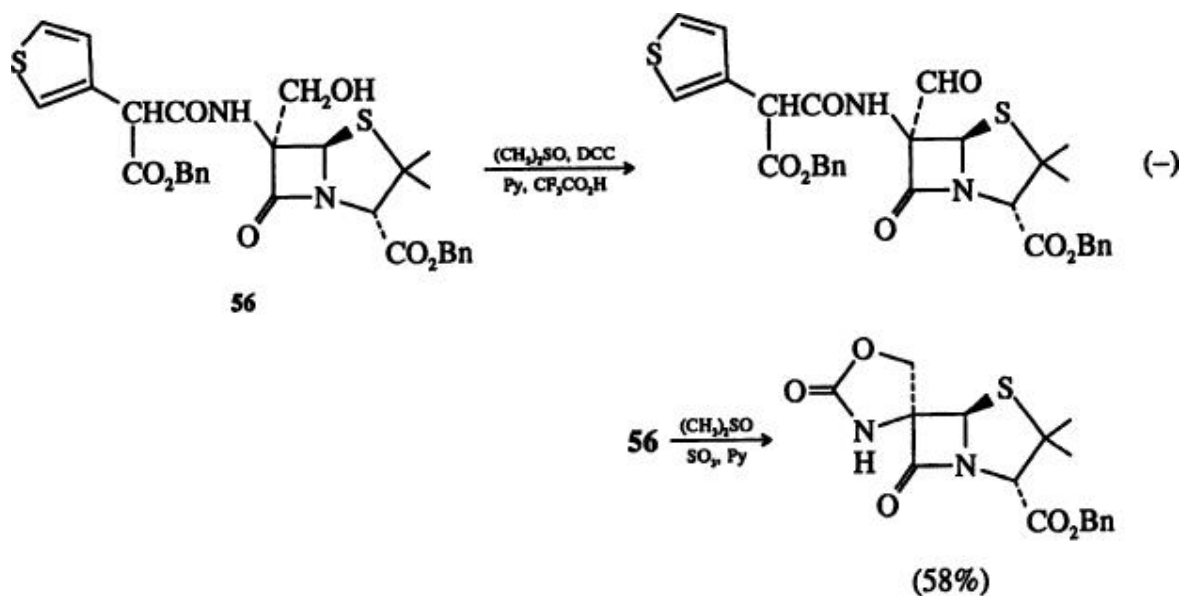
Another example in which the carbonyl group generated by oxidation reacts intramolecularly involves cyclization with a phosphorus ylide. (165)

R = $C_6H_5CH_2$ (64%)
R = $C_6H_5OCH_2$ (30%)
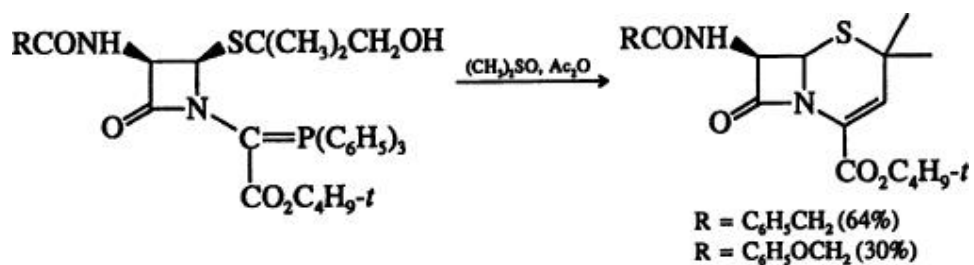
Methanethiol formed during the reaction can add to the carbon–carbon double bond of a product enone (Eq. 34). (166)

(34)

(51%)
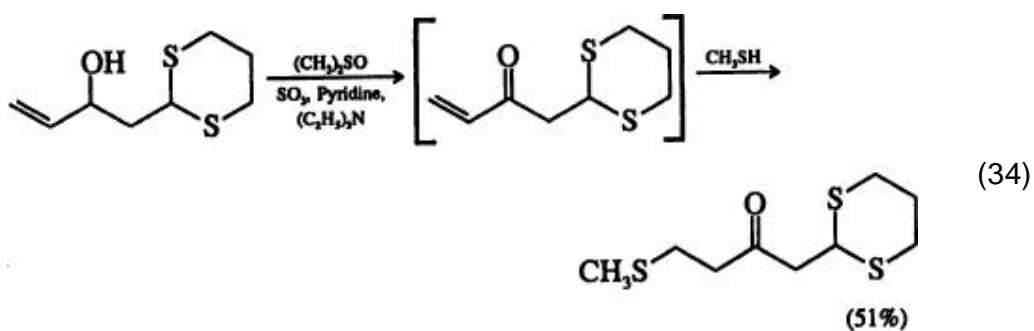
Cyclization is also involved in the reaction of Eq. 35. (167)

(35)
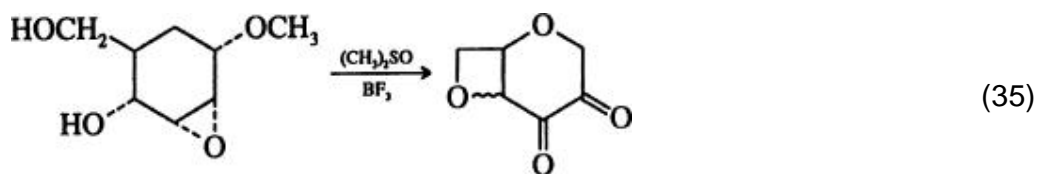
Nonaqueous workup prevents hydration of aldehydes prone to this reaction. 168,168a

$$C_6H_5CH_2OCH_2CH_2OH \xrightarrow[\text{2. } (C_2H_5)_3N]{\text{1. } (CH_3)_2SO, (COCl)_2} C_6H_5CH_2OCH_2CHO$$
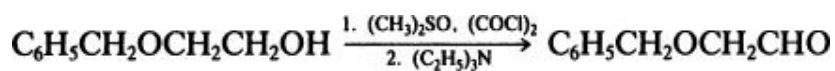
The product ketones may react with excess dimethyl sulfoxide/oxalyl chloride to give a -chloro ketones. (168b) These reactions evidently involve attack of positive chlorine from a species such as $(CH_3)_2SCl^+$ on the enolized ketone. (168b)
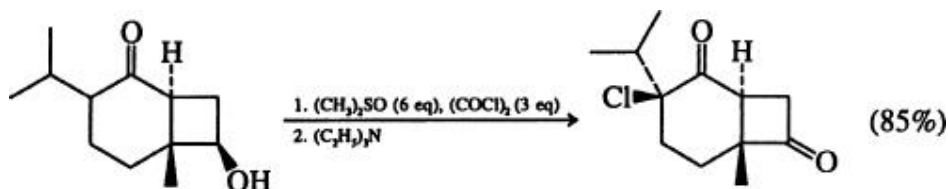
3.5.1.1.7. Side Reactions of Other Functional Groups

Many functional groups are inert to the conditions of dimethyl sulfoxide-based oxidations, but in some cases side reactions involving such groups occur on attempted oxidations of alcohols.

Reaction of the alcohol **57** with dimethyl sulfoxide/oxalyl chloride gives the chloro aldehyde **58** in 80% yield (Eq. **36**), (169) whereas the carbinol epimeric at C-16 undergoes normal oxidation under the same conditions. (170) Reaction of **57** with dimethyl sulfoxide/sulfur trioxide also gives the unchlorinated aldehyde in 80% yield. (169)

(36)
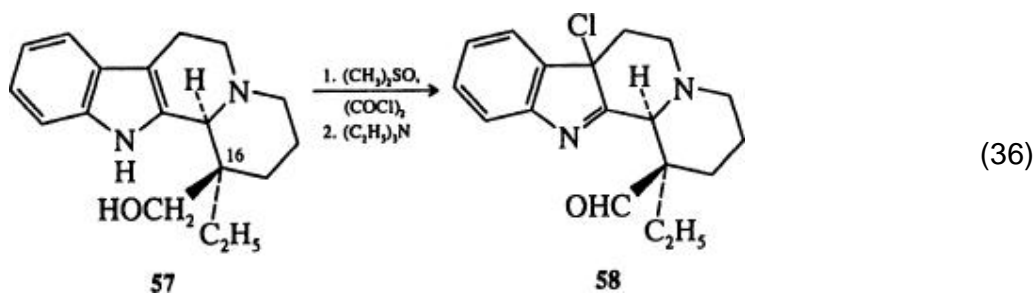
Hydroxy nitroxides are successfully oxidized using dimethyl sulfoxide (171-174) even though there is a report that nitroxides are not stable to dimethyl sulfoxide/oxalyl chloride. (171) Dimethyl sulfide/*N*-chlorosuccinimide is also effective. (171, 173)

$(100\%)^{171}$

$(69\%)^{172}$
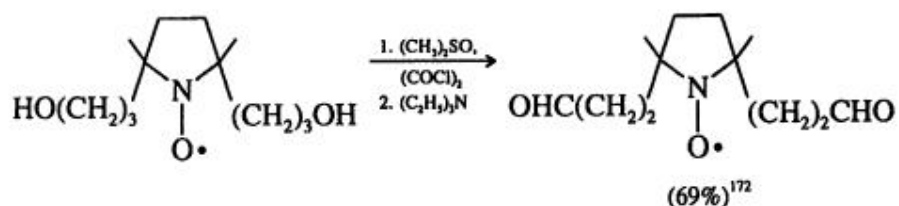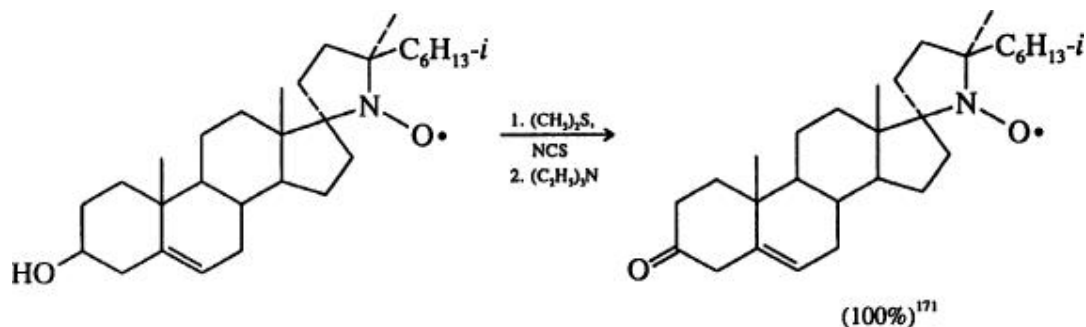
Trimethylsilyl and triethylsilyl ethers of primary and secondary alcohols give the corresponding carbonyl compounds on treatment with dimethyl sulfoxide/oxalyl chloride followed by triethylamine. 174a,b The reaction occurs at –60°, but higher yields are obtained at –30°. The reaction appears to involve cleavage of the silyl ether by chloride ion and adventitious hydrogen chloride to give the free alcohol, which is then oxidized. *tert*-Butyldimethylsilyl and *tert*-butyldiphenylsilyl ethers are unaffected under these conditions and are frequently used to protect hydroxy groups during oxidations with dimethyl sulfoxide/oxalyl chloride.

(83%)
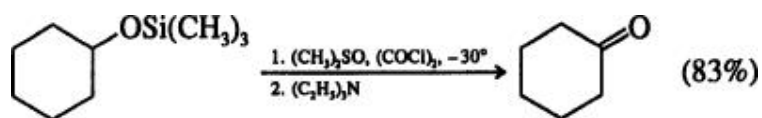
Amines are converted into imines by treatment with dimethyl sulfoxide/ oxalyl chloride in a nitrogen analog of alcohol oxidation. (174c)

$$(C_6H_5CH_2)_2NH \xrightarrow[\text{2. }(C_2H_5)_3N]{\text{1. }(CH_3)_2SO,\ (COCl)_2} C_6H_5CH=NCH_2C_6H_5 + (C_6H_5CH_2)_2NCH_2SCH_3$$

<div align="center">(63%)   (37%)</div>

<div align="center">(88%)   (11%)</div>
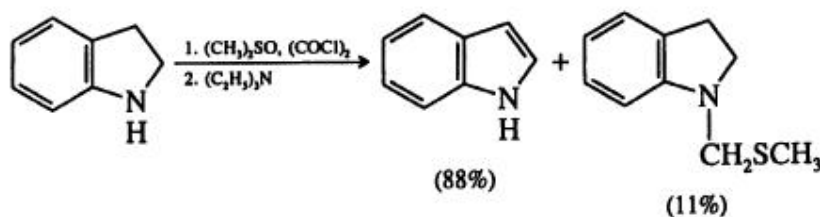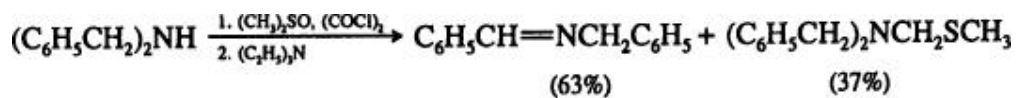
Pyrrole and indole undergo ring substitution on reaction with dimethyl sulfoxide/*N*-chlorosuccinimide (174d) or dimethyl sulfoxide/trifluoroacetic anhydride. (174e)

<div align="center">(84%)</div>
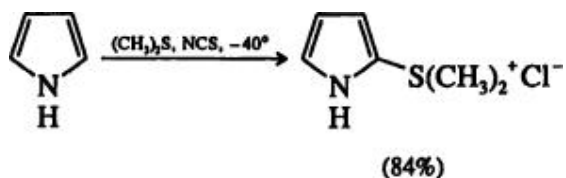
Phenols react with dimethyl sulfoxide/dicyclohexylcarbodiimide and a proton source (Eq. 37), (175-177) and this is a potential side reaction in the oxidation of phenolic alcohols.

(37)
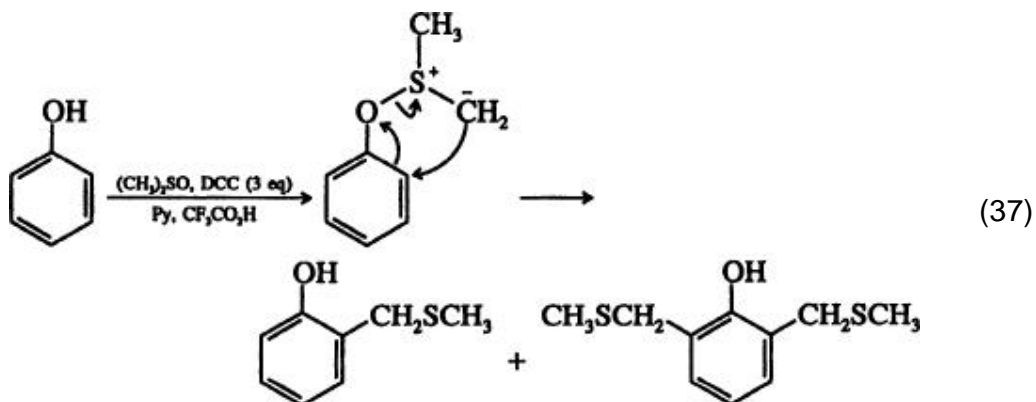
Phenol, phenyl ethers, and anilines can undergo ring halogenation in reactions

with bromodimethylsulfonium or chlorodimethylsulfonium chloride, which is another possible side reaction in oxidations of alcohols containing activated aryl rings (Eq. 38). (178)

$$\text{(38)}$$
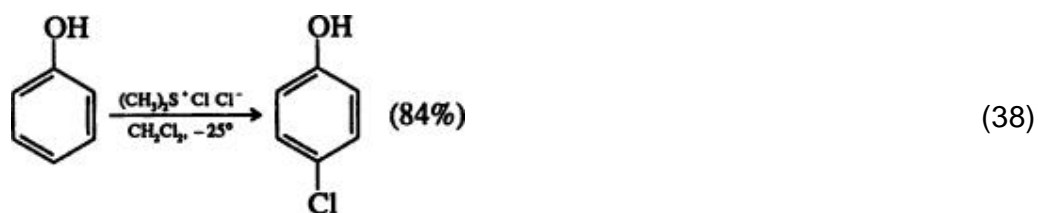
The reaction of enols such as dimedone with dimethyl sulfoxide/dicyclohexylcarbodiimide gives stable ylides, and presumably involves transfer of dimethyl sulfide from activated dimethyl sulfoxide either directly to carbon to give ylide **59**, or first to oxygen followed by rearrangement to **59** (Eq. 39). (179)

3.5.1.1.8. Overoxidation
Further oxidation of the initial carbonyl products resulting from the conversion of alcohols into aldehydes and ketones to the oxidation level of carboxylic acids is seldom observed. One potential mechanism for

$$\text{(39)}$$

59
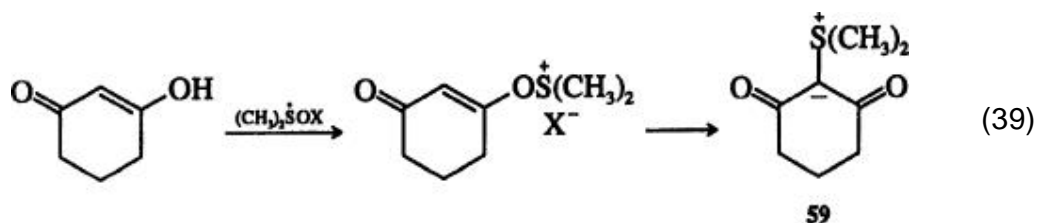
this process involves enolization of the carbonyl compound followed by formation of a vinyl sulfoxonium species (Eq. 40) and 1,2 elimination to a ketene (Eq. 41) or 1,4 elimination to an α , β -unsaturated carbonyl compound (Eq. 42).

$$\text{(40)}$$

$$\xrightarrow{\text{1,2 elimination}} R_2CH\overset{\overset{\displaystyle R}{|}}{C}{=}C{=}O \xrightarrow{H_2O} R_2CH\overset{\overset{\displaystyle R}{|}}{C}HCO_2H \qquad (41)$$

$$\xrightarrow{\text{1,4 elimination}} R_2C{=}\overset{\overset{\displaystyle R}{|}}{C}CHO \qquad (42)$$
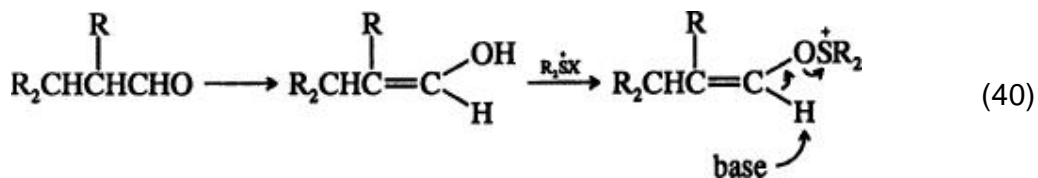
Apparently ketene formation has not been proven, but an indication of the 1,4 elimination path is noted for a potential dodecahedrane precursor (see p. 324). (137)

Oxidation of alcohol **60** with dimethyl sulfoxide/trifluoroacetic anhydride gives **61** in 79% yield. (180) This could occur by first forming the saturated ketone followed by enolization and further oxidation, although initial formation of the allyl alcohol is also possible. (180)
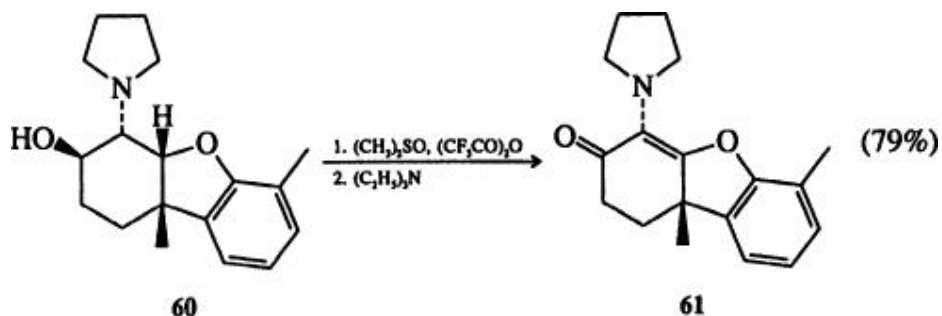
Other similar examples are known, although evidence to differentiate autoxidation from the enolization–oxidation pathway is not available. (181-184)

Reaction of hydroxy benzoate **62** involves the sequence of oxidation, enolization, rearrangement to a hydroxy enol benzoate, and further oxidation to the final product. (185) Such ester rearrangements are well known in carbohydrates.
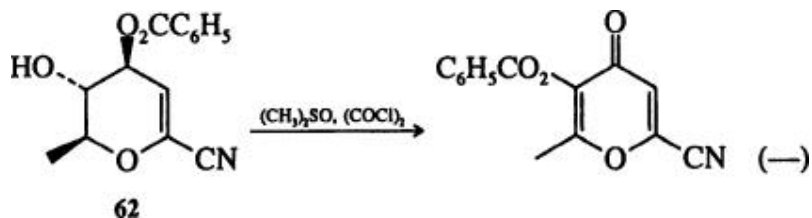
The oxidation of the primary alcohol **63** to an acid may involve air oxidation of an initial aldehyde product. (186)
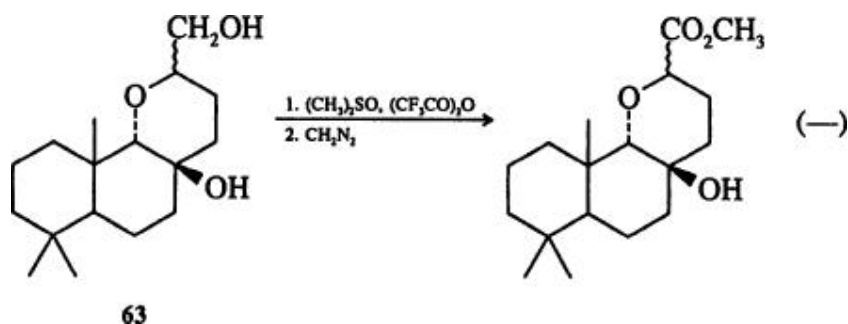
The oxidation of lactols to lactones is another way for dimethyl sulfoxide oxidations to provide the oxidation level of carboxylic acids (Eq. 43). (187, 188)
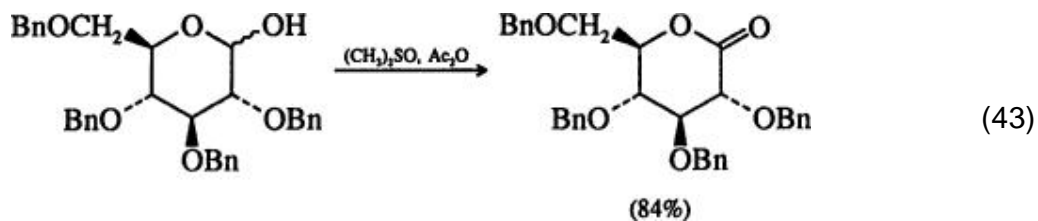
A procedure for oxidation of aldehydes to carboxylic acids and their derivatives involves treatment of the bisulfite adducts of aldehydes with dimethyl sulfoxide/acetic anhydride to give the acyl derivatives, which can be hydrolyzed with base to give carboxylic acids (Eq. 44). Reaction with methoxide gives methyl esters, and with amines gives amides. (189)

$$RCHO \xrightarrow{\text{NaHSO}_3} R\overset{\overset{\displaystyle OH}{|}}{C}HSO_3Na \xrightarrow[\text{Ac}_2\text{O}]{\text{(CH}_3)_2\text{SO}} R\overset{\overset{\displaystyle O}{||}}{C}SO_3Na \xrightarrow[\text{2. H}^+]{\text{1. K}_2\text{CO}_3} RCO_2H \qquad (44)$$
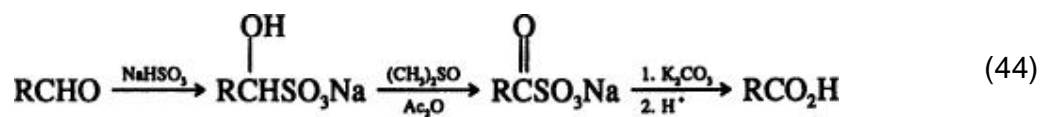
Addition of methanol and bromine to aldehydes formed by dimethyl sulfoxide/oxalyl chloride oxidation also gives methyl esters. (189a) Oxidation of cyanohydrins with dimethyl sulfoxide/oxalyl chloride gives acyl cyanides, which are converted to esters on treatment with alcohols. (189b)

3.6. Diols, Ketols, and Polyols

3.6.1.1. Oxidation of 1,2-Diols and Ketols

The oxidation of 1,2-diols with dimethyl sulfoxide and related reagents is particularly effective since there is no tendency for cleavage of the carbon–carbon bond between the two oxygenated centers, which often occurs with chromium(III) or copper(II) oxidants. (190, 191) Compounds in which one oxygenated carbon is tertiary give hydroxy carbonyl products, whereas when both oxygenated carbons bear hydrogens, 1,2-dicarbonyl products are generally formed. Reagents that are effective for the former conversion include dimethyl sulfide/*N*-chlorosuccinimide, (17) methyl phenyl sulfide/chlorine, (19) dimethyl sulfoxide/oxalyl chloride, 191,191a and dimethyl sulfoxide/sulfur trioxide-pyridine. (191b) Reagents used for the latter conversion include dimethyl sulfoxide/dicyclohexylcarbodiimide, (191c) dimethyl sulfoxide/oxalyl chloride, (191d) dimethyl sulfide/*N*-chlorosuccinimide, (191c) and dimethyl sulfoxide/sulfur trioxide-pyridine. (154) Conversion of α -keto secondary alcohols into 1,2-diketones can be effected with dimethyl sulfoxide/phosphorus pentoxide (190) or dimethyl sulfoxide/trifluoroacetic anhydride. (191f)

$$ C_6H_5CHOHCHOHC_6H_5 \xrightarrow[\text{2. } (C_2H_5)_3N]{\text{1. } (CH_3)_2SO, (COCl)_2} C_6H_5COCOC_6H_5 \quad (90\%)^{26} $$
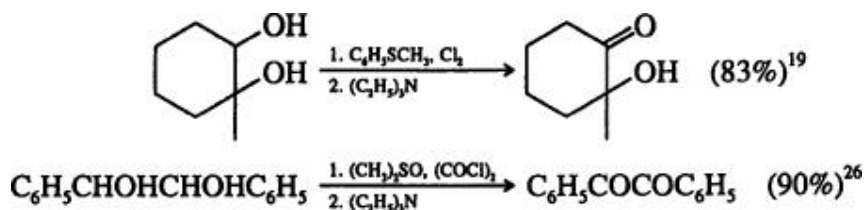
Dimethyl sulfoxide/trifluoroacetic anhydride is reported to be more effective than other reagents, including dimethyl sulfoxide/oxalyl chloride, for the oxidation of vicinal diols to α -dicarbonyl compounds, particularly when halogen is present in the molecule.
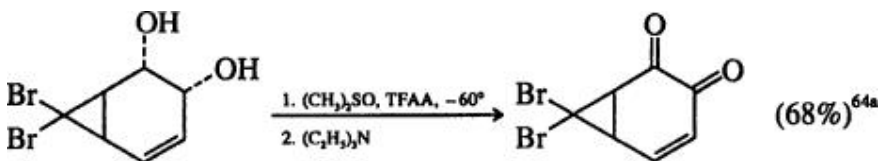
Hydroquinones are oxidized to the corresponding quinones by several activation procedures. 175,191c,192–196
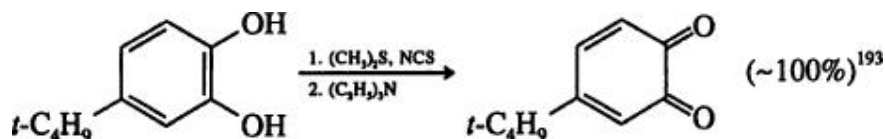
These oxidations differ from those of other alcohols in that carbon–hydrogen bond cleavage does not occur. Moreover, oxidation succeeds if dimethyl sulfide is omitted from the dimethyl sulfide/*N*-chlorosuccinimide procedure.

Some 1,4-dihydroxyquinones give the corresponding pulvinic acid dilactones. (197)
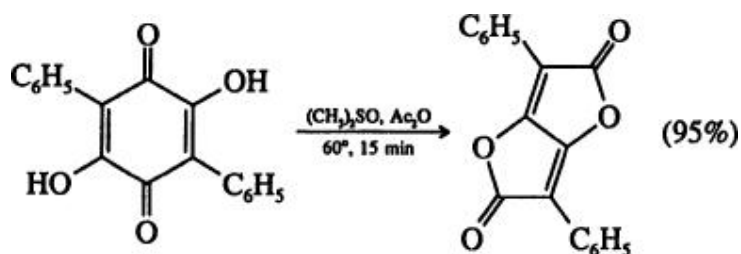
3.6.1.2. Selective Oxidation of Diols and Polyols

When two or more potentially oxidizable hydroxy groups are present in a molecule, the selective oxidation of one or more of these groups has been achieved in only a few instances. Thus specific hydroxy carbonyl compounds are not obtained in oxidations of polyols **64** (198) and **65**, (199) whereas diol **66** is selectively oxidized at the 3-position in the presence of diethylcarbodiimide (DEC). (200)

64

65

(50%)

66
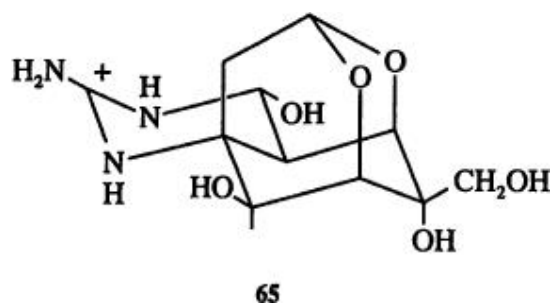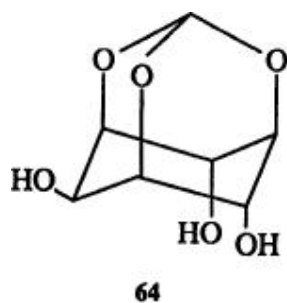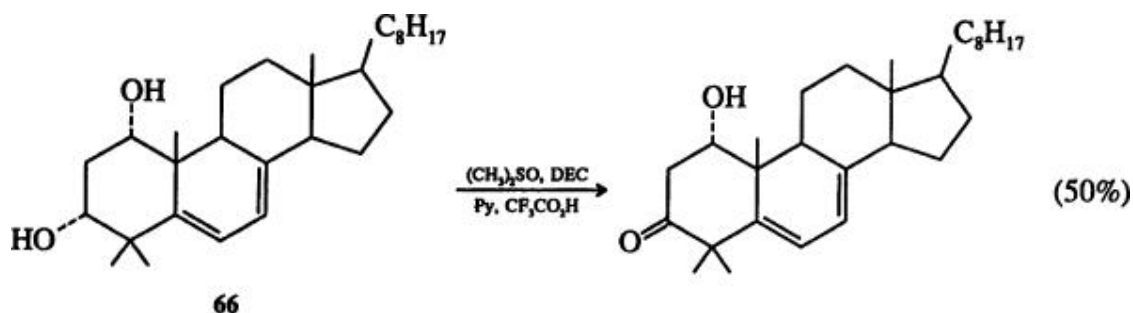
Diol **67** reacts with neither dimethyl sulfide/*N*-chlorosuccinimide nor dimethyl sulfoxide/dicyclohexylcarbodiimide, but addition of **67** to 1.67 equivalents of trifluoroacetic anhydride and excess dimethyl sulfoxide at –60° followed by warming and addition of 5% hydrochloric acid gives **68** in 84% yield, along with 12% of starting material. (201) This selectivity is attributed to the reaction of the ethereal oxygen acting intramolecularly as a base to remove the axial hydrogen in the bis(sulfoxonium) salt **67a**. Another example of this phenomenon has been observed. (202)

67

68 (84%)

67a   (R = CO₂CH₃)

69

70
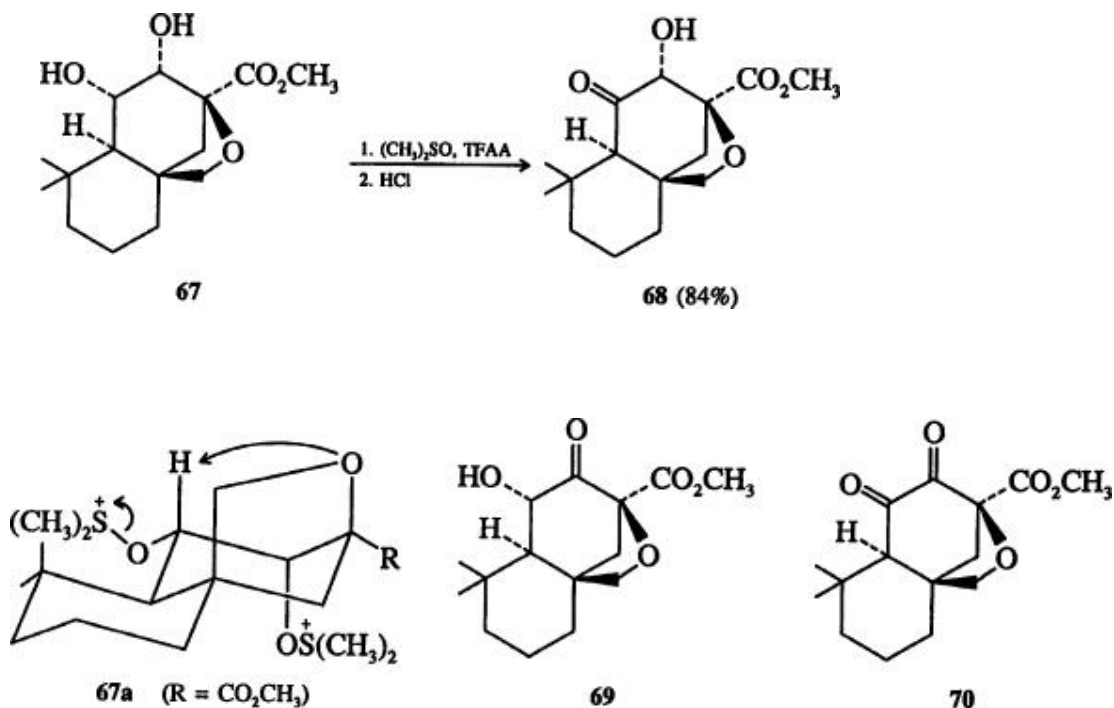
Oxidation of diol **67** with excess dimethyl sulfoxide/trifluoroacetic anhydride followed by triethylamine gives dione **70** in 78% yield, and use of dimethyl sulfoxide/trifluoroacetic anhydride or dimethyl sulfoxide/oxalyl chloride gives

mixtures of **68**, **69**, and **70**. The failure to achieve oxidation with dimethyl sulfide/N-chlorosuccinimide or dimethyl sulfoxide/dicyclohexylcarbodiimide evidently reflects the inability of these reagents to form the requisite sulfoxonium intermediates.

Oxidation of a polycyclic diol with 1.1 molar equivalents of oxidant shows significant selectivity. (203)
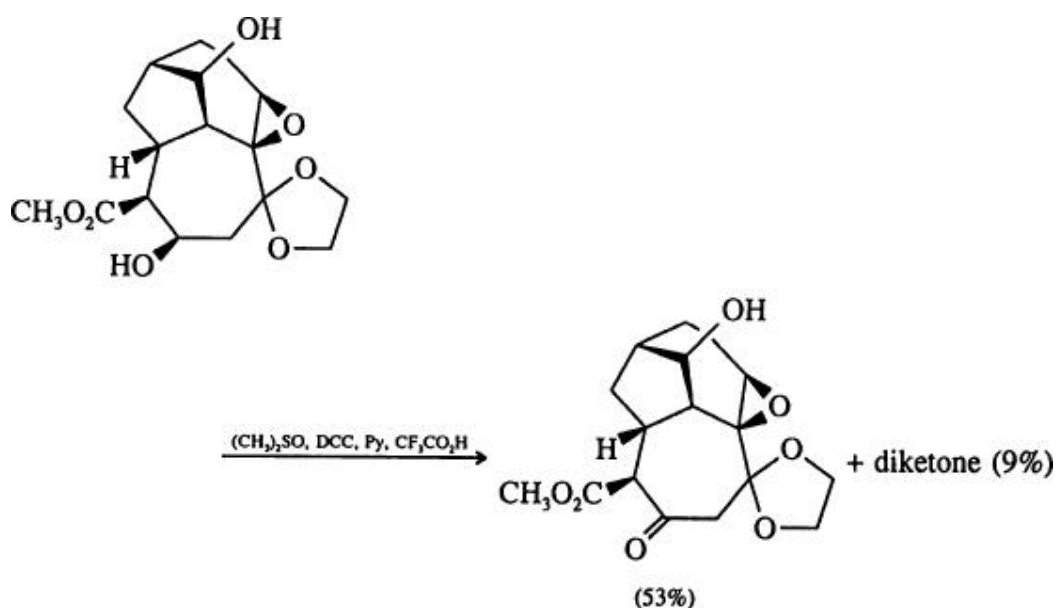
Trimethylsilyl ethers of primary and secondary alcohols are oxidized to carbonyl compounds by dimethyl sulfoxide/oxalyl chloride, (174a) and reaction of methyl cholate 3,12-bis(trimethylsilyl ether) with 1 equivalent of oxalyl chloride and dimethyl sulfoxide followed by removal of the residual silyl ether groups gives a 74% yield of the 12-hydroxy-3-keto compound along with 14% of the diol and 4% of the 3,12-diketo compound. (174a)

$$\begin{array}{c}\text{1. } (CH_3)_2SO,\ (COCl)_2 \\ \hline -60\ \text{to}\ -40° \\ \text{2. } (C_2H_5)_3N \\ \text{3. } HCl,\ CH_3OH \end{array}$$

(74%)
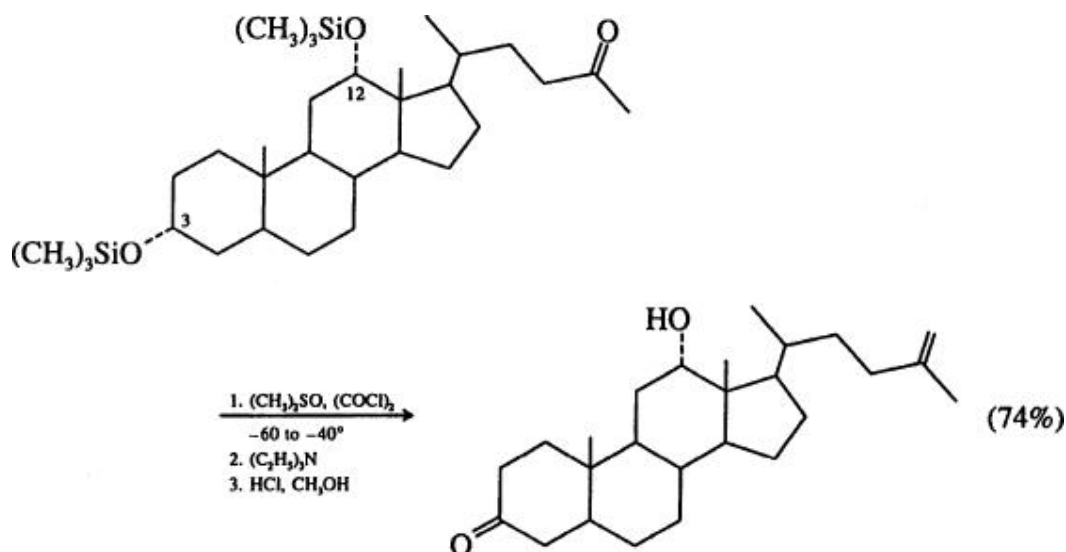
Selective oxidation of the diol is less effective, giving the 3-keto compound in 40% yield, together with 12% of the 3-hydroxy-12-keto product as well as some 3,12-diketo compound and starting material. (174a)

Oxidation of a 21-membered macrolide 9,10-diol precursor to FK-506 (partial structure shown) with dimethyl sulfoxide/oxalyl chloride (204a) resulted in oxidation of only one hydroxy group, proposed as that on C-10 on the basis of the 2D ^{1}H NMR spectrum. (204b) A second treatment with dimethyl sulfoxide/oxalyl chloride was necessary to effect complete oxidation. These results may be specific to this particular macrolide structure. (204b)
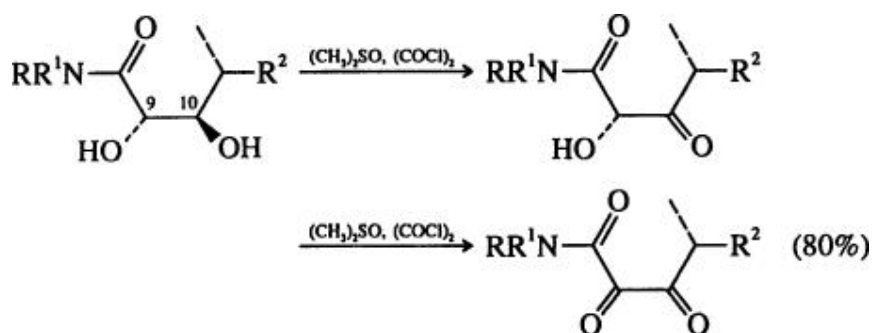
3.6.1.3. Oxidation of Polymeric Alcohols

6-*O*-Tritylamylose (**71**) reacts with dimethyl sulfoxide/acetic anhydride to form **72** with oxidation occurring almost exclusively at C-2 and approximately 50% methylthiomethyl ether formation at C-3. (204, 205)

71   72
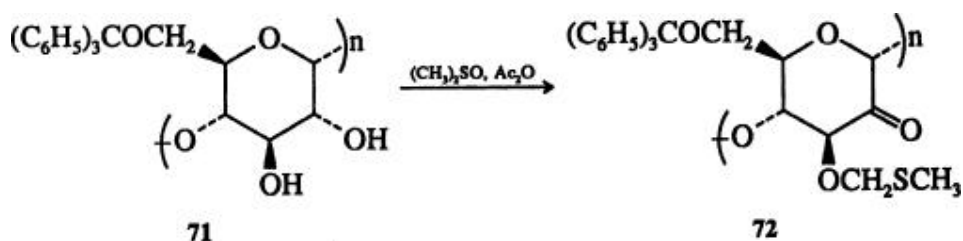
Reaction of mono- or oligosaccharides such as methyl α -D-glucopyranoside, sucrose, or trehalose with phosphorus pentoxide in dimethyl sulfoxide results in polymerization to phosphorylated glycans. (206)

Methanolysis of permethylated polysaccharides gives methyl trimethylglucopyranosides, which can be oxidized to carbonyl compounds with dimethyl sulfoxide/phosphorus pentoxide. (207)

6-O-Tritylcellulose is oxidized by dimethyl sulfoxide/acetic anhydride or by dimethyl sulfoxide/dicyclohexylcarbodiimide/pyridine/trifluoroacetic acid. The product contains 0.6–0.8 carbonyl group per pyranose ring, and oxidation occurs mainly at C-2. (204, 208) Cotton is also extensively oxidized by dimethyl sulfoxide/acetic anhydride. (209)

The polystyrene-bound alcohol **73** is effectively oxidized by dimethyl sulfoxide/oxalyl chloride, and the side chain can be cleaved from the polymer and isolated in 43% overall yield from **73**. (210) However, the related polystyrenebound alcohol **74** is not oxidized by either dimethyl sulfoxide/dicyclohexylcarbodiimide or dimethyl sulfoxide/trifluoroacetic anhydride, a result ascribed to possible poor swelling of the polymer in the solvents used. (211)

73

74
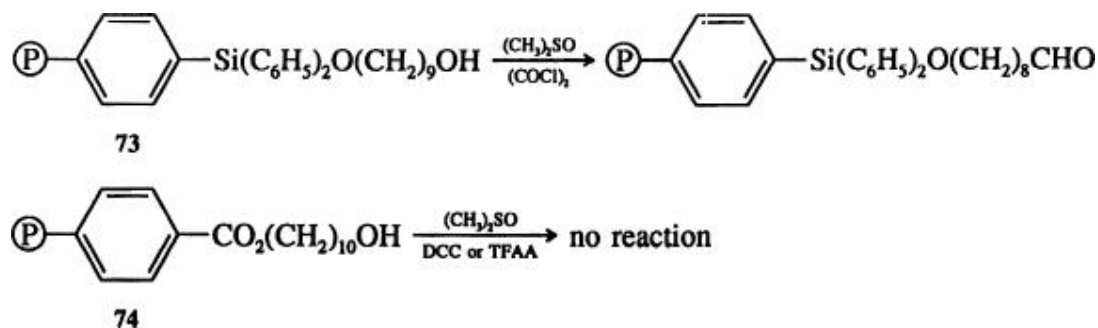
Poly(*p*-ethynylbenzyl alcohol) is efficiently oxidized to the poly(aldehyde) by dimethyl sulfoxide/oxalyl chloride. (211a)

3.7. Nonalcohol Substrates

3.7.1.1. Kornblum Oxidation of Halides and Tosylates

This process (Eqs. 1 and 2) (1, 2) involves a displacement of halide or tosylate by dimethyl sulfoxide to give an oxysulfonium ion which is then converted to a carbonyl compound.
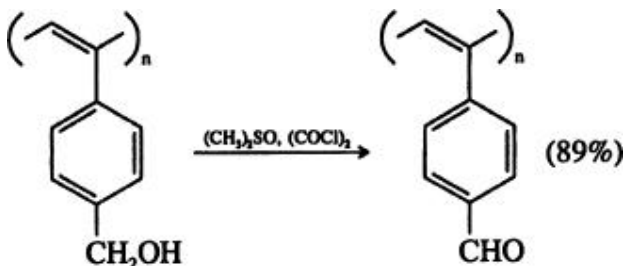
Since this reaction has only limited current synthetic application, no effort has been made to compile a comprehensive list of citations.

An extension of this procedure involves generating the bromide in situ by reaction of activated CH groups with halogens (Eq. 45) (212) or hydrogen halides (Eq. 46). (213) The latter example apparently differs from the Kornblum reaction and involves the successive formation of $ArCOCH_2Br$, $ArCOCH_2OH$, and $ArCOCHBrOH$. (213) Another variation utilizes bis(4-methoxyphenyl) selenoxide with sodium bicarbonate in acetonitrile at 75° or in refluxing tetrahydrofuran (Eq. 47). (214)

$$4\text{-}BrC_6H_4COCH_3 \xrightarrow[\text{H}_2\text{O, 55°}]{(CH_3)_2SO,\ HBr} 4\text{-}BrC_6H_4COCH(OH)_2 \quad (86\%) \tag{46}$$

$$C_6H_5CH_2Br + (4\text{-}CH_3OC_6H_4)_2SeO \longrightarrow C_6H_5CHO \quad (93\%) \tag{47}$$
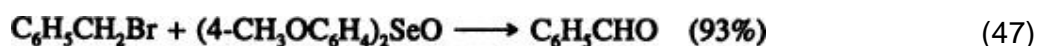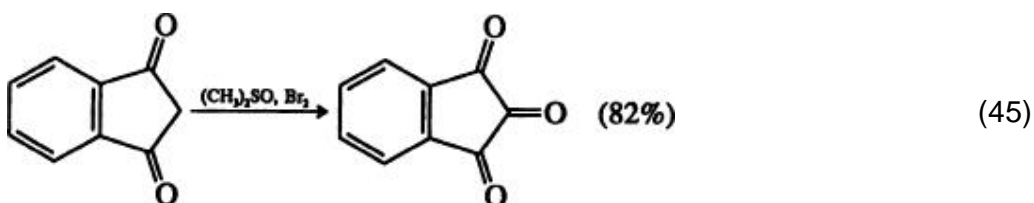
Dimethyl sulfoxide evidently attacks toluenesulfonate **75** at the homoallylic double bond, leading to formation of cyclopropyl products (Eq. 48). (215)

(48)

(60%)   (30%)
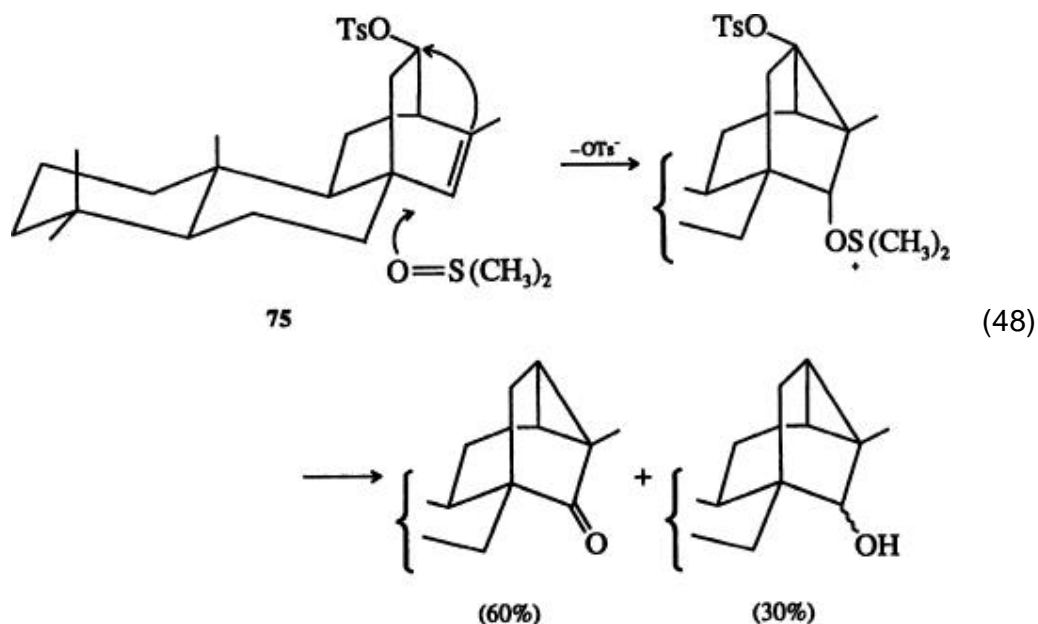
Primary and secondary alcohols react with 2-fluoro-1-methylpyridinium toluenesulfonate in dimethyl sulfoxide to give carbonyl compounds. This process occurs by a variation of the Kornblum pathway in which 2-alkoxypyridinium salts are formed initially and undergo displacement by dimethyl sulfoxide to give alkoxysulfonium ions, which react further with triethylamine to give carbonyl products. (216)

(49)
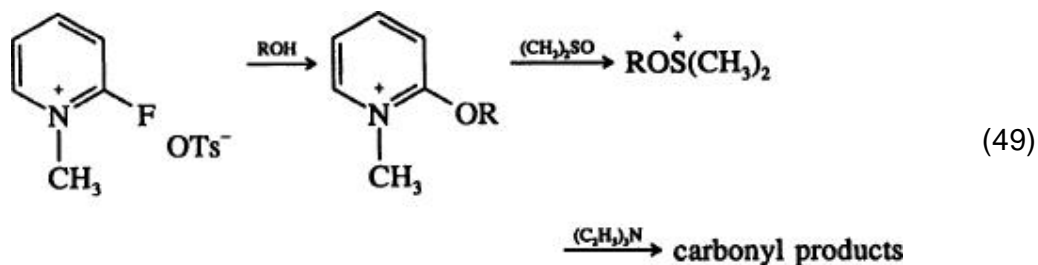
3.7.1.2. Alkenes

Carbon–carbon double bonds in the oxidation substrates are sometimes subject to attack; examples already cited include attack by electrophilic chlorine (Eq. 37) (178) of electrophilic sulfur (Eqs. 26 (41) and 39 (179)), as well as nucleophilic attack by sulfur (Eq. 34) (166) and by the oxygen of

dimethyl sulfoxide in a vinylogous example of the Kornblum oxidation (Eq. 48). (215) The reaction of Eq. 50 involves attack by an electrophilic reagent such as the sulfur of $(CH_3)_2\overset{+}{S}X$ to give **76**, which undergoes further displacement by dimethyl sulfoxide and oxidation. (217)
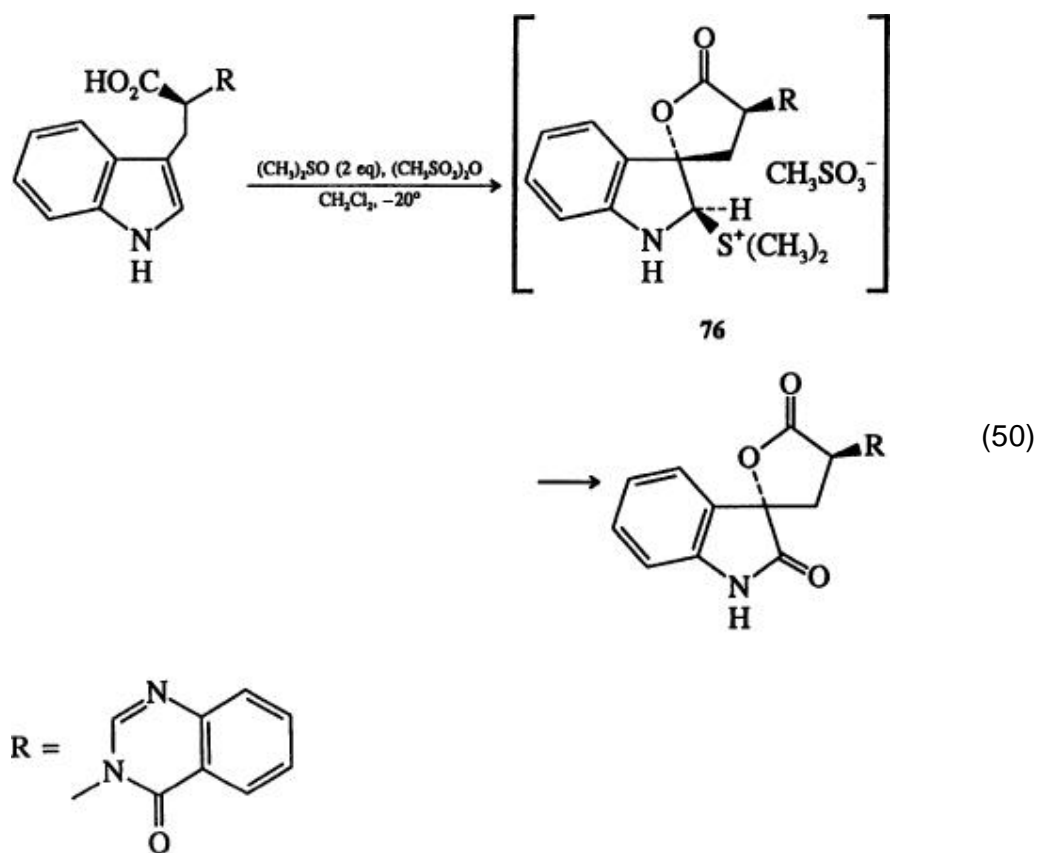
3.7.1.3. Oxidation of Carboxylic Acids

Electrolysis of substituted phenylacetic acids in dimethyl sulfoxide in the presence of sodium hydride followed by addition of sodium bicarbonate leads to substituted benzaldehydes. Evidently this reaction involves formation of an intermediate sulfoxonium adduct which then forms the aldehyde under the basic conditions. (218) When the aryl group is phenyl or 4-nitrophenyl, large amounts of bibenzyls are formed, evidently reflecting the decreasing stability of the benzyl carbocations.

$$ArCH_2CO_2H \xrightarrow{-2e^-} Ar\overset{+}{C}H_2 \xrightarrow{(CH_3)_2SO} ArCHO\overset{+}{S}(CH_3)_2 \longrightarrow ArCHO$$
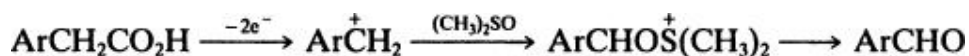
3.7.1.4. Epoxides

Epoxides are normally inert to the conditions of most of the dimethyl sulfoxide oxidation procedures, including dimethyl sulfide/*N*-chlorosuccinimide, (219) and there are numerous examples in the tables where epoxy carbonyl compounds are formed from epoxy alcohols. However, if ring opening is induced, oxidation products are produced. Thus, when epoxides react with the thioanisole/chlorine complex in methylene chloride followed by addition of triethylamine, α -chlorocarbonyl compounds are obtained in high yield. (203) The intervention of β -chloroalkoxysulfonium ions **77** is indicated, since β -chlorocarbinols are obtained if the initial adducts are treated with aqueous sodium bicarbonate instead of triethylamine. (220)
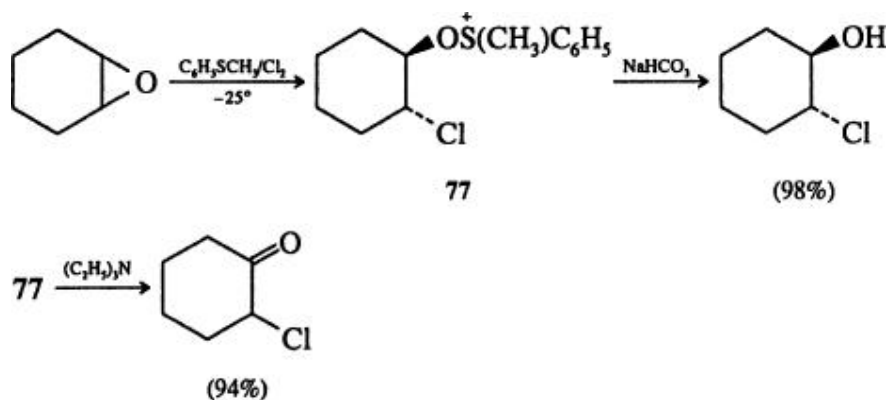
Epoxides react with dimethyl sulfoxide in the presence of boron trifluoride or trifluoroacetic acid to give α -hydroxyalkoxysulfonium salts, the dimethyl sulfoxide evidently acting as the nucleophile. (221-223) These salts can react further to give glycols and α -ketols. (222, 223)
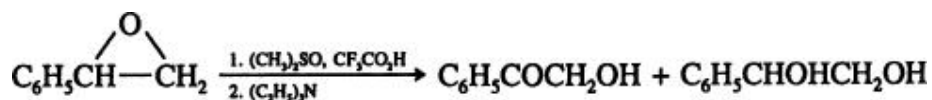
4. Comparison with Other Methods

General reviews (224-228) compare the many procedures for the oxidation of alcohols to aldehydes and ketones. Besides activated dimethyl sulfoxide, the most widely used for this purpose are chromium(VI), (229, 230) activated manganese dioxide, (231, 232) and silver carbonate on Celite. (228, 231-235) Other common oxidants are permanganate, (236-238) lead tetraacetate, (228, 239, 240) cerium(IV), (241, 242) and ruthenium(VIII). (228, 243-245) Other processes include metal-catalyzed dehydrogenations or oxidations, (228, 246, 247) enzyme-catalyzed reactions, (248) and the Oppenhauer oxidation. (249, 250) Dimethyl sulfoxide, chromium(VI), manganese dioxide, or silver carbonate on Celite are effective for the oxidation of almost every primary or secondary alcohol to the aldehyde or ketone, and other oxidants do not seem to have any advantages over these except in specialized applications. Accordingly, these reagents are discussed in most detail. A recently reported iodine(V) reagent is also finding application. (250a) An extensive computer-assisted evaluation of 21 oxidation reagents, *which does not include dimethyl sulfoxide*, is available. (250b)

4.1. Chromium(VI) Oxidations

This group of procedures is widely used for the conversion of alcohols into aldehydes and ketones. They generally oxidize acetylenic alcohols and β-phenylethanol derivatives, two classes that are sometimes not effectively oxidized by dimethyl sulfoxide. They are also effective at room temperature and are adaptable to large-scale operations.

Problems that sometimes occur with chromium(VI) oxidants are overoxidation of aldehydes to carboxylic acids, oxidation of heteroatoms such as sulfur and selenium, cleavage of 1,2- and 1,3-dihydroxy compounds or β-carbonyl alcohols, hazards associated with the use and disposal of the reagents, difficulties in product isolation because of the formation of insoluble chromium salts, and the moderately high cost of these reagents.

A recent monograph dealing exclusively with chromium oxidants has appeared and provides a detailed description of these reagents. (229)

Chromic acid generated from chromium trioxide in acidic solution has long been used as an oxidant. One of the most commonly used of these procedures is due to Jones, (251) which uses chromic acid in aqueous sulfuric acid and acetone, and is satisfactory for large-scale conversion of secondary alcohols to ketones. The procedure is simple and relatively free of side reactions, but for sensitive compounds other procedures are more commonly employed. *Organic Syntheses* describes procedures for conversion of cyclooctanol to cyclooctanone (252) and nortricyclanol to nortricyclanone. (253)

Two-phase systems using an aqueous phase containing chromic and sulfuric acid and an organic phase help prevent overoxidation and side reactions; methylene chloride is widely used as the organic phase, (254) and diethyl ether is even more effective. (255)

A catalytic system using 2–5 mole % of the chromate ester **78** and 2 equivalents of peracetic acid is effective in the oxidation of alcohols to aldehydes and ketones. (256)

The oxidant **78** resembles $(t\text{-}C_4H_9O)_2CrO_2$, formed from chromyl chloride (CrO_2Cl_2), pyridine, and *tert*-butyl alcohol, and used as stoichiometric oxidant. (257)

78
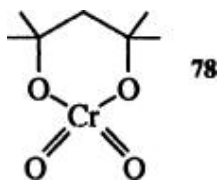
The Sarett reagent is a complex of chromic oxide in pyridine, (258) but is better utilized in the modification by Collins using methylene chloride as the cosolvent. (259-261) These reagents efficiently oxidize many alcohols to aldehydes and ketones, but have the drawbacks of the labor involved to prepare the reagents, their occasional tendency to overoxidize primary alcohols, the flammability of the Sarett reagent, the need for excess reagent, the slowness of the reaction, and inconvenient workup.

4-(Dimethylamino)pyridinium chlorochromate is readily prepared by the reaction of chromium trioxide in cold dilute hydrochloric acid with 1 equivalent of 4-dimethylaminopyridine. (262) This reagent oxidizes benzylic or allylic alcohols to carbonyl compounds at room temperature, including the selective oxidation of these alcohols in the presence of nonactivated alcohols. The long reaction times required (ca. 15 hours) are a disadvantage in the use of this reagent.

Pyridinium dichromate $[(C_5H_5NH^+)_2Cr_2O_7^{2-}]$ is formed from the reaction of chromium trioxide with pyridine in water. (263, 264) This reagent is widely used and offers the advantages of commercial availability (Aldrich, Alfa, Fluka), low flammability, and effectiveness in near stoichiometric amounts. The reagent is satisfactory for large-scale oxidations, and while it oxidizes primary alcohols to carboxylic acids in dimethylformamide, in methylene chloride

oxidation stops at the aldehyde stage. The reactions are typically carried out at 0 or 25° with reaction times of 1–24 hours.

The chromium trioxide/3,5-dimethylpyrazole complex (**79**) (265) is another effective chromium(VI) oxidant, and in one specific application gives efficient oxidation of 1-octyn-3-ol, (265) while dimethyl sulfoxide/oxalyl chloride gives an intractable residue with this same substrate. (22, 27)

79
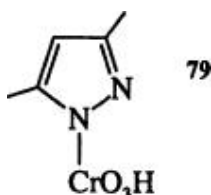
The chromium(VI) reagent that is now most commonly used in the oxidation of sensitive alcohols to aldehydes and ketones is pyridinium chlorochromate $(C_5H_5NH^+ \ ClCrO_3^-)$, (230, 266) which is readily made from pyridine, hydrochloric acid, and chromium trioxide. It is commercially available (Aldrich, Fluka), air-stable, and reacts rather rapidly with most alcohols to give the desired products in high yield with ease in handling, except sometimes in the workup. The reaction proceeds rapidly in refluxing methylene chloride and gives near-quantitative yields with stoichiometric amounts of reagent. (267) This reagent is mildly acidic, and even though the use of sodium acetate buffer is recommended (267) for acid-sensitive compounds, it is not always effective.

Molecular sieves catalyze the oxidation of carbohydrate alcohols by both pyridinium chlorochromate and pyridinium dichromate, (268) and the activity of the latter oxidant is particularly enhanced by adding a mixture of freshly activated molecular sieves and anhydrous acetic acid. (269)

Other chromium(VI) reagents include chromium peroxide (270) and zinc dichromate dihydrate. (271) A number of polymer-supported chromium(VI) reagents have been prepared on Amberlyst A26 anion exchange resin, (272) polyvinylpyridine, (273, 274) silica gel, (275) silica–alumina, (276) alumina, (277) or graphite. (278) Many of these are also commercially available (Alfa, Aldrich, Fluka). Phase-transfer conditions have also been developed. (279)

Several alcohols for which chromium(VI) oxidants are significantly better than activated dimethyl sulfoxide are **30**, (128) and **80–83**. The reasons for the comparative advantage in these examples are difficult to assess, but the general lability of some of these substrates is a contributing factor.

HOCH₂ structure with OCH₃

80[280] **81**[281] **82**[282]

83[283]
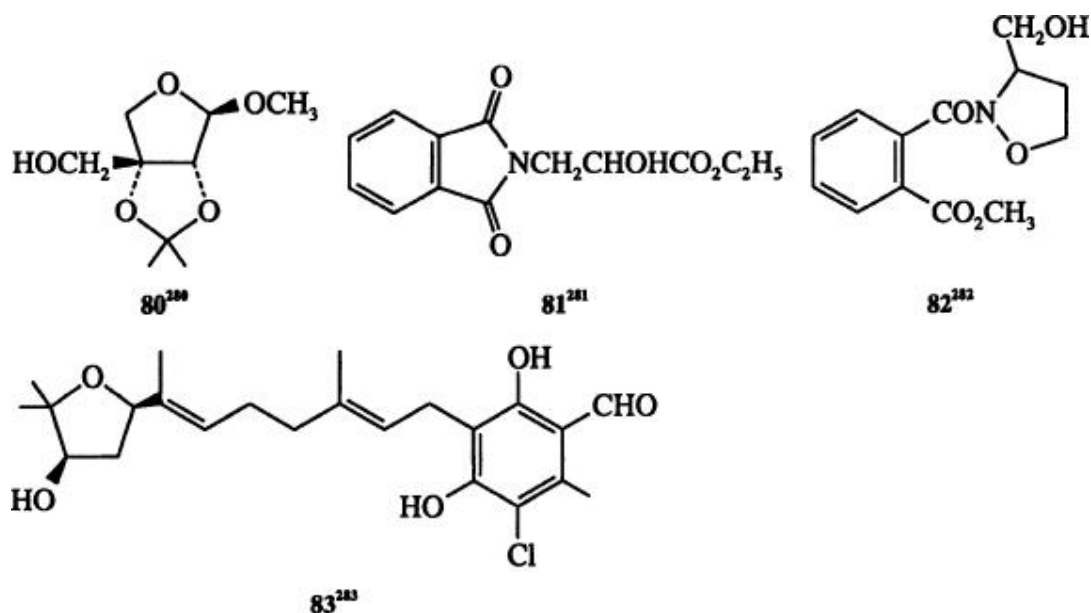
Allylic rearrangement as depicted in Eq. 51 is a reaction sometimes observed with chromium oxidants that has little analogy in dimethyl sulfoxide oxidations. (284)

$$\text{[structure]} \xrightarrow[\text{CH}_2\text{Cl}_2]{\text{C}_5\text{H}_5\text{NH}^+\text{ClCrO}_3^-} \text{[structure]} \quad (98\%) \quad (\text{Eq. 51})^{284}$$

(51)
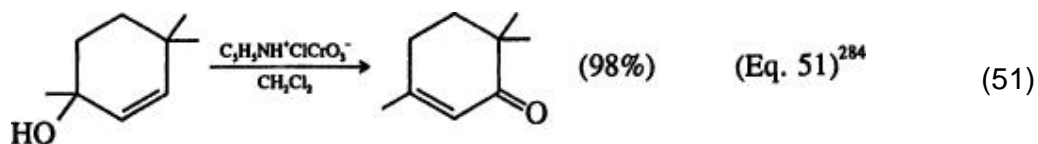
4.2. Other Oxidants

Silver carbonate on Celite is a commercially available reagent (Alfa Products) that is also easily prepared and readily oxidizes primary or secondary alcohols to aldehydes or ketones, respectively, in high yields with a simple workup procedure. (228, 233-235) This reagent is especially reactive toward allylic hydroxy groups, which can be selectively oxidized in the presence of secondary alcohols. Silver carbonate fails in certain cases (*vide infra*), (96, 285, 286) and is costly for large-scale reactions.

Allylic alcohols are more reactive in this procedure, making possible some impressively selective oxidations (Eq. 52). This reagent is also effective for alkynyl alcohols. (287)

$$\text{(70\%)} \qquad \text{(Eq. 52)}[287] \qquad (52)$$
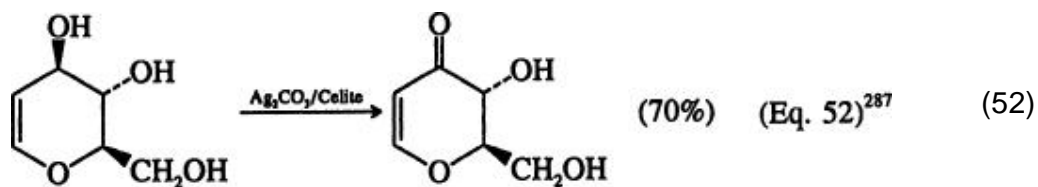
In oxidations of diols with silver carbonate, cyclization of intermediate hydroxy aldehydes to lactols which are further oxidized to lactones occurs (cf. Eq. 44), whereas these substrates are oxidized to dialdehydes by dimethyl sulfoxide. (158)

Manganese dioxide in activated form is a commercially available reagent (Fluka, Aldrich, Alfa Products) that is also readily prepared, and is often used for the oxidation of allylic or benzylic alcohols. (228, 231, 232)

Organic Syntheses reports a procedure for the oxidation of 3-(hydroxyalkyl)pyrroles to 3-acylpyrroles using manganese dioxide. (288)

Manganese dioxide shares with silver oxide and with some of the chromium(VI) methods the greater reactivity toward alcohols activated by their allylic or benzylic nature, and this frequently permits selective oxidation, as in Eq. 52. These oxidants are also subject to steric effects, while the dimethyl sulfoxide oxidations respond in different ways to both conjugative activation and steric crowding. Thus there is some scope for the development of selective oxidations of polyols, and while there has been some progress in such studies, particularly with silver, manganese, and chromium reagents, much more effort will be required before such selective oxidations become routine procedures.

Ruthenium tetroxide, generated in situ from activated ruthenium dioxide and periodate, is effective in the oxidation of secondary alcohols to ketones using two-phase solvent systems and phase-transfer catalysis. (245)

4.3. Comparison with Other Reagents for Oxidation of Alcohols
Oxidations using dimethyl sulfoxide are generally suitable for most primary and secondary alcohols. The mildly acidic conditions of the dicyclohexylcarbodiimide activation precludes the use of this technique in some cases, but the use of oxalyl chloride as the activator avoids this problem and gives higher yields with greater ease of operation in almost all cases. The amine base used in the final step rarely leads to complications. Activation of dimethyl sulfoxide by sulfur trioxide/pyridine is even better for avoiding acid-catalyzed side reactions, and the yields are usually good, although reaction times are long. The reaction temperatures of –60 to –78° used with

oxalyl chloride activations are readily attained, even for reactions on a 0.2–0.36 molar scale. (289, 290) Oxidation of 2.5 mols of yohimbine to yohimbinone in 84% yield is conveniently carried out with dimethyl sulfoxide/acetic anhydride at room temperature for 18 hours, (11) and sulfur trioxide/pyridine is also useful for large-scale reactions, although chromium (VI) is most often used for this purpose.

Some classes of alcohols that have given difficulty with dimethyl sulfoxide/oxalyl chloride activation as discussed above are certain β-phenylethanols and those with the structural units $RCHOHC = CH$ and $RC = CCH_2CHOHR$. These substrates can usually be successfully oxidized with the chromium, manganese, or silver oxidants.

Some alcohols in which activated dimethyl sulfoxide has proven to be a significantly better oxidant than metal derivatives, including pyridinium chlorochromate and silver carbonate, are **60** (180) and **84–97a**. The reasons for the greater effectiveness of the dimethyl sulfoxide oxidant in these reactions are not clear since comparative studies of all the common oxidants have not been made. However, the evidence indicates that dimethyl sulfoxide deserves equal consideration as an oxidant for most substrates. In a comparison of 14 oxidants for 1,1,1-trichloropropanol, the dimethyl sulfoxide reagents were the most effective of the group. (290a)

84[291]   85[292]   86[293]

87[294]   88[286]

89[295] **90**[296]

91[297] **92**[298]

$(CH_3)_2C{=}CHCON(CH_2)_3OH$
93[299]

$C_6H_5CH_2O(CH_2)_2OH$
94[300] **95**[301] **96**[302]

97[303] **97a**[303a]
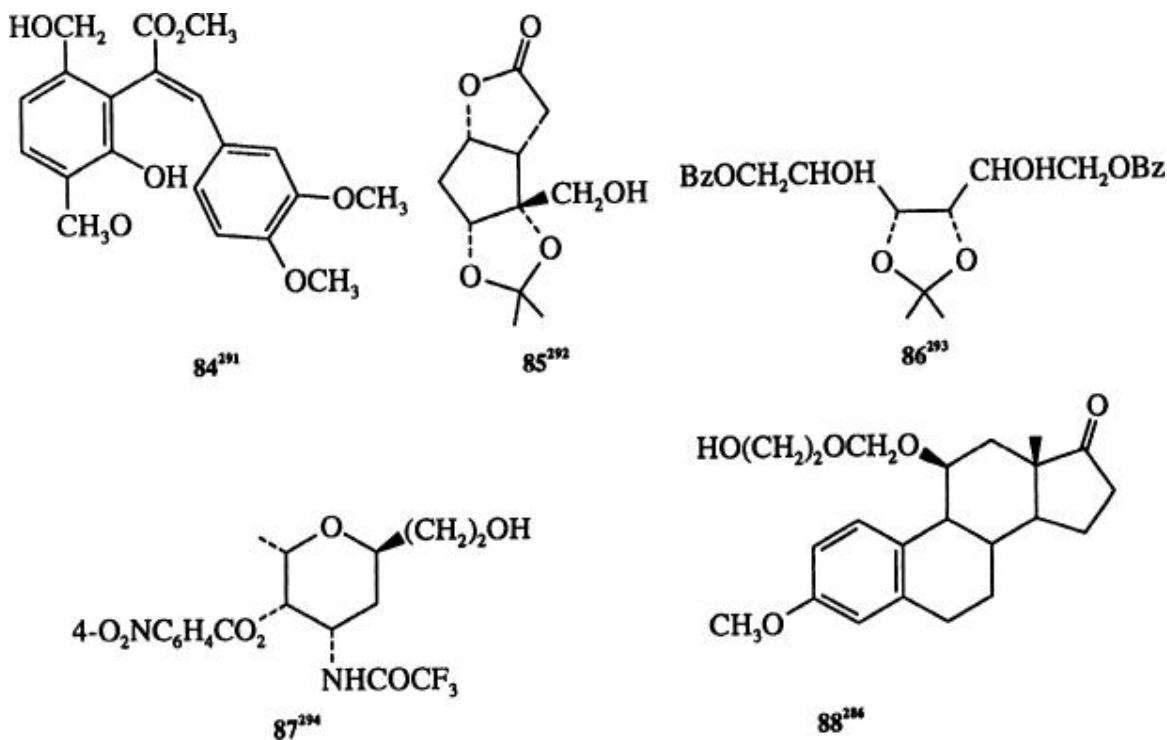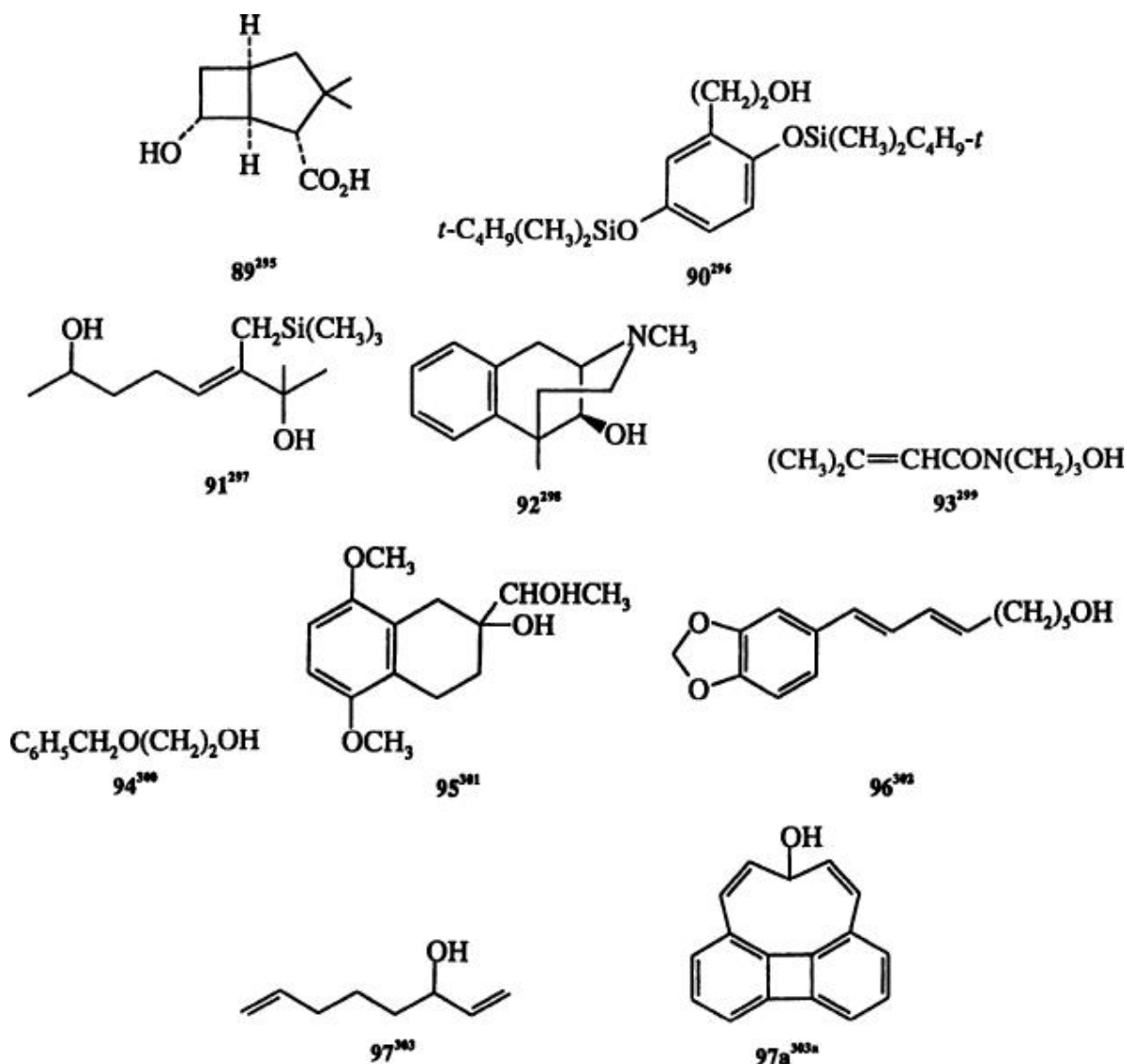
A carbohydrate alcohol with bulky substituents is remarkably resistent to oxidation by various chromium(VI) reagents as well as by dimethyl sulfoxide with phosphorus pentoxide or acetic anhydride, but is oxidized by dimethyl sulfoxide and oxalyl chloride in quantitative yield (Eq. 53). (304) Similarly oxidation of a penicillin fails with chromium(VI) and silver(I) but succeeds with dimethyl sulfoxide and oxalyl chloride (Eq. 54). (305)

A few alcohols have not been oxidized satisfactorily. In alcohol **98**, (306) this failure is attributed to the hydrogen bond, while alcohol **99** undergoes a retroaldol reaction to propiophenone. (127) Alcohol **100** either does not react or undergoes C — C bond cleavage. (285) Other oxidation-resistant alcohols include **101**, (307) **102**, (308) **103**, (309) and **104**. (310) In some of these the

high lability of the substrates or products may cause the lack of success, while in others optimum conditions may yet be successful.

(53)

(100%)

(54)

(100%)

2-ClC$_6$H$_4$

98

C$_6$H$_5$COCH(CH$_3$)CHOHCH=CH$_2$

99

CO$_2$C$_2$H$_5$

100

HOCH$_2$

4-CH$_3$C$_6$H$_4$CO$_2$

101

CH$_2$OH

CO$_2$CH$_3$

102

CH$_2$OH

103

HOCH$_2$ OC$_2$H$_5$

AcO
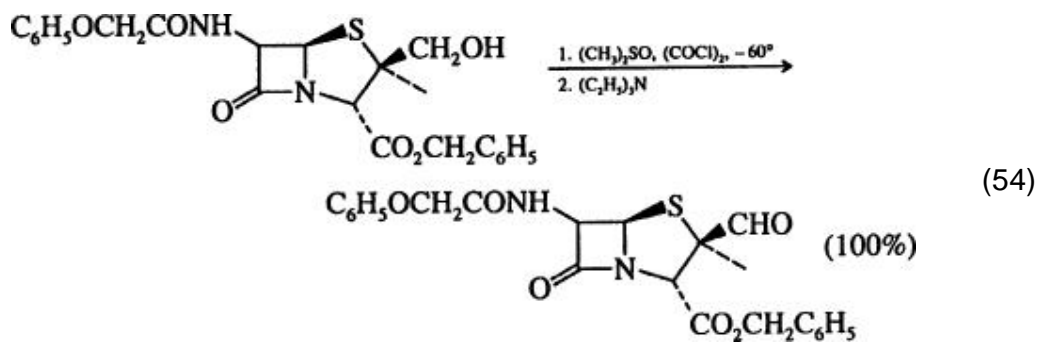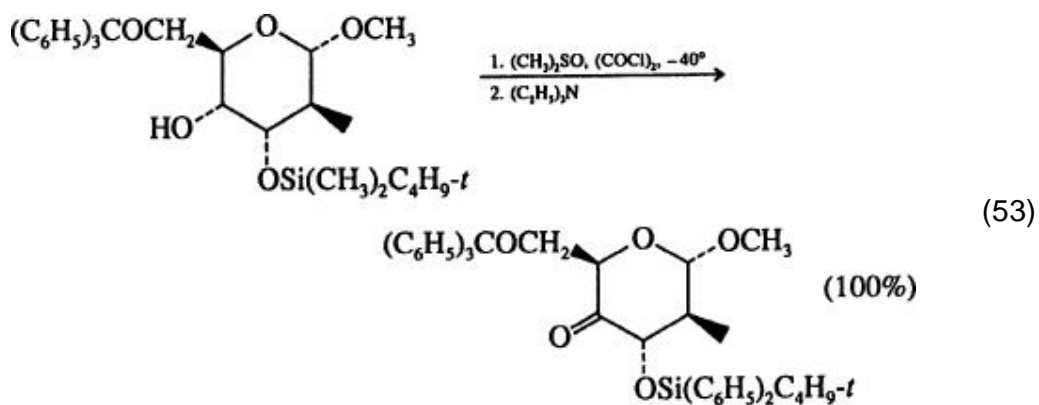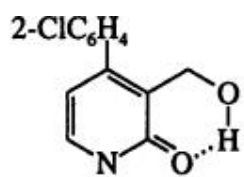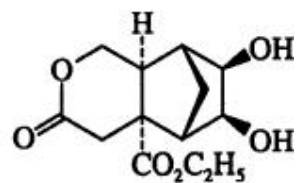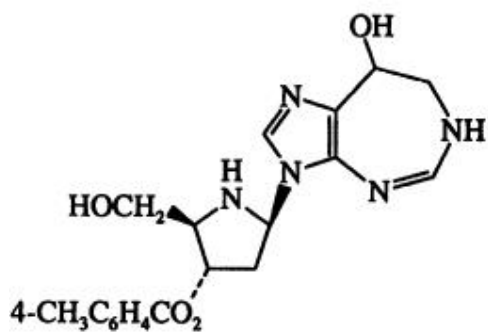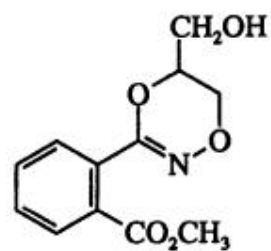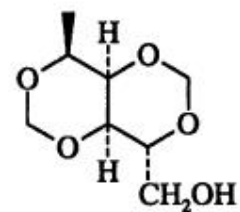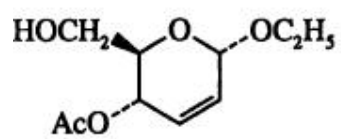
104

5. Experimental Conditions

5.1. Solvent
Many nonhydroxylic solvents are used in these oxidations, including methylene chloride, toluene, dimethyl sulfoxide, hexamethylphosphoramide, tetrahydrofuran, acetonitrile, diethyl ether, acetone, and 9/1 hexane/methylene chloride. (21, 23, 27) Some comparative results are given in Table A. (23) Yields in methylene chloride equal or exceed those in other solvents for procedures using activated dimethyl sulfoxide, and this solvent is recommended. (8) It has the advantages of low freezing point, good solvent power, and easy removal because of its volatility. Reagent grade material can be distilled under reduced pressure and stored over molecular sieves. (6) Methods for drying and purifying dimethyl sulfoxide have been reviewed. 310a,b The dimethyl sulfoxide/oxalyl chloride procedure can be carried out in tetrahydrofuran (311) or diethyl ether (311a) so that sensitive carbonyl products can be captured by Grignard or organolithium reagents without warming or isolation. Toluene gives the best yields in the dimethyl sulfide/*N*-chlorosuccinimide procedure. (23)

5.2. Reagents
Many of the reagents are hygroscopic and should be handled under a nitrogen or argon atmosphere. The use of syringes for transfer of solvents and liquid reagents is recommended.

Most sulfur-based oxidations use dimethyl sulfoxide or dimethyl sulfide. These reagents have the advantages of availability, good solubility in most reaction solvents, and ease of separation from reaction products. However, because of the strong unpleasant odor of dimethyl sulfide, reactions involving it or dimethyl sulfoxide must be carried out with good ventilation; dimethyl sulfide in waste wash solutions can be destroyed with sodium hypochlorite or potassium permanganate.

Dimethyl sulfoxide should be purified by distillation under reduced pressure and stored over molecular sieves such as Linde Type 4A. (23) It is important that dimethyl sulfoxide be kept dry because many activators react with water to form hydrochloric acid or other strong acids that can interfere with the desired reaction. 310a,b

Pyridine and triethylamine can be distilled from calcium hydride and stored over fresh calcium hydride.

Dicyclohexylcarbodiimide should be dry crystalline material; if it is oily it should be distilled (bp 140°/5 mm). (312)

Oxalyl chloride and sulfur trioxide/pyridine complex are available from Aldrich Chemical and Alpha Products and usually can be used directly. Sulfur trioxide/pyridine complex can also be prepared in the laboratory. (313)

N-Chlorosuccinimide can be used as supplied by Aldrich Chemical. Less pure material can be recrystallized from benzene to mp 150–151° (98% pure). (314)

Impure acetic anhydride can be distilled from aluminum chloride or calcium carbide. (315)

5.3. Apparatus

For small-scale reactions involving activation with oxalyl chloride, it is convenient to use a three-necked flask equipped with a magnetic stirring bar and a dry ice–acetone or 2-propanol bath to maintain the temperature between –60 and –78°. In one neck there is a rubber adapter with a low-temperature alcohol thermometer, another neck is equipped with a septum cap which is pierced by the nitrogen inlet, and the third neck has an outlet tube leading to a bubbler. The reagents are added with syringes through the septum cap, with the rate of addition regulated to maintain a constant temperature. For a 0.2-mol scale reaction, a 2-L flask and pressure-equalizing funnels are used. (289)

5.4. Product Isolation

Many of the carbonyl products are quite sensitive so that isolation and storage are not practical. Such products can be trapped by reaction with Wittig or Grignard reagents, (311) organolithiums, (311a) or Mannich reagents. (311b) As noted in the section on carbodiimides, separation of carbonyl products from dicyclohexylurea may require conversion of the product to a derivative from which it is regenerated after separation.

Organic Syntheses describes procedures involving dimethyl sulfoxide/dicyclohexylcarbodiimide, (312) dimethyl sulfoxide/oxalyl chloride, (289) dimethyl sulfide/N-chlorosuccinimide, (314) and dimethyl sulfoxide with a polymeric carbodiimide. (55a)

6. Experimental Procedures

6.1.1.1. Methyl 2,3-O-Isopropylidene- β -D-ribo-pentodialdo-1,4-furanoside [Oxidation with Dimethyl Sulfoxide/Dicyclohexylcarbodiimide] (316)
A solution of 0.98 g (10 mmol) of anhydrous crystalline orthophosphoric acid in 2.0 mL of dimethyl sulfoxide was added to a solution of 4.08 g (20 mmol) of methyl 2,3-*O*-isopropylidene- β -D-ribofuranoside, 0.8 mL (10 mmol) of pyridine, and 12.4 g (60 mmol) of dicyclohexylcarbodiimide in 50 mL of dimethyl sulfoxide. The mixture was kept near 25° for 3 hours by occasional ice cooling, diluted with 100 mL of ethyl acetate, and a solution of 5.04 g (40 mmol) of oxalic acid dihydrate in 10 mL of methanol was added. The mixture was poured into 200 mL of saturated sodium chloride solution and filtered, and the aqueous phase was extracted with 100 mL of ethyl acetate. The combined organic phases were washed successively with 100 mL of dilute sodium bicarbonate, two 100-mL portions of saturated sodium chloride, and 100 mL of ice water. The organic phase was dried with magnesium sulfate and evaporated under reduced pressure, and the residue was dissolved in 25 mL of ethyl acetate and filtered to remove residual *N,N¢*-dicyclohexylurea. The solution was concentrated to a syrup (4.7 g), which was purified by sublimation at 60–70° (0.1 torr) to give the product as a white crystalline solid, 3.23 g (16 mmol, 80%), mp 50–56°. The product contained about 3% of the 5-thiomethylmethyl ether as judged by ^{1}H NMR. Recrystallization from hexane at –18° gave material with mp 60–61°, [α]$_D$ – 214° (*c* 0.1, CHCl$_3$).

6.1.1.2. Cholan-24-al [Oxidation with Dimethyl Sulfoxide/Dicyclohexylcarbodiimide] (312)
Cholan-24-ol (1.033 g, 3 mmol) was dissolved by gentle warming in 10 mL of dry benzene and 10 mL of dry dimethyl sulfoxide was added, followed successively by 0.24 mL (3.0 mmol) of dry pyridine, 0.12 mL (1.5 mmol) of distilled trifluoroacetic acid, and 1.85 g (9 mmol) of dicyclohexylcarbodiimide. The flask was tightly stoppered and left at room temperature for 18 hours. Benzene (30 mL) was then added, and the crystalline dicyclohexylurea was removed by filtration and washed with benzene. The combined filtrates and washings were extracted three times with 50-mL portions of water, dried over sodium sulfate, and evaporated under reduced pressure to give 2.12 g of syrup which partially crystallized. The crude product was dissolved in 1:1 benzene/hexane and chromatographed on 125 g of silica gel with this solvent to give cholan-24-al (0.87 g, 84%), mp 102–104°.

6.1.1.3. (1 β ,3 αα,9 α β)-Decahydro-1,8,8-trimethyl-3a-[(2-trimethylsilyl)ethoxymethoxy]-6H-cyclopentacyclooctan-6-one. [Oxidation with Dimethyl Sulfoxide/Oxalyl Chloride and Diisopropylethylamine] (73)

Dimethyl sulfoxide (0.536 mL, 0.397 g, 5.10 mmol) was added dropwise to a stirred solution of oxalyl chloride (0.213 mL, 0.311 g, 2.45 mmol) in 20 mL of methylene chloride at –78°. The mixture was stirred 15 minutes at –78°, and then a solution of (1β ,3 α α ,9 α β)-decahydro-1,8,8-trimethyl-3a-[(2-trimethylsilyl)ethoxymethoxy]-3aH-cyclopentacyclooctan-6-ol (0.74 g crude, ca. 2.04 mmol) in 5 mL of methylene chloride was added dropwise via a syringe. After 15 minutes of additional stirring at –78°, N,N-diisopropylethylamine (2.83 mL, 2.10 g, 16.3 mmol) was added, and the reaction was allowed to warm to room temperature. After 1 hour, the reaction was poured into 10 mL of saturated aqueous sodium bicarbonate solution. The layers were shaken and separated, and the aqueous layer was extracted with methylene chloride. The combined organic layers were washed with 10 mL of brine, dried, and concentrated. The residue was diluted with 25 mL of hexane, washed with 5 mL of water, dried, and concentrated. Purification by flash chromatography on 25 g of silica gel with 10% ethyl acetate in hexane gave 546 mg (75%) of product: IR (CCl$_4$) 1700 cm^{-1} (C = O); ^{1}H NMR (CDCl$_3$) δ 0.0 (s, 9H), 0.92 (d, J = 6.3 Hz, 3H), 0.93 (s, 3H), 0.99 (s, 3H), 0.9–1.2 (m, 5H), 1.51 (m, 1H), 1.87 (m, 5H), 2.20 (m, 2H), 2.28 (s, 2H), 2.50 (m, 1H), 3.62 (m, 2H), 4.70 (s, 2H); MS (CI, CH$_4$), m/z (rel intensity) 355 (M + 1)$^+$, 279, 207, 189 (100).

6.1.1.4. Ethyl (E)-3-(Trimethylsilyl)methacrylate. [Oxidation with Dimethyl Sulfoxide/Oxalyl Chloride and Capture of a Sensitive Aldehyde as the Wittig Adduct] (311)

To a stirred solution of 131 μL (0.190 mg, 1.50 mmol) of oxalyl chloride in 8.0 mL of methylene chloride at –78° was added 121 μL (0.133 mg, 1.70 mmol) of dimethyl sulfoxide. After 10 minutes, a solution of 104 mg (1.00 mmol) of (trimethylsilyl)methanol in 2 mL of methylene chloride was added over 4 minutes, and after 15 minutes, 0.52 mL (377 mg, 3.7 mmol) of triethylamine was added over 1 minute. After 5 minutes at –78°, a solution of 690 mg (1.9 mmol) of ethyl 2-(triphenylphosphoranylidene)propionate in methylene chloride was added over 3 minutes. The reaction mixture was then allowed to warm to room temperature, diluted with 70 mL of diethyl ether, and then washed with 40 mL of water and 40 mL of brine. The organic phase was dried over magnesium sulfate and then concentrated under reduced pressure. Chromatography of the residue with 3:97 ethyl ether/petroleum ether afforded 101 mg (54%) of product as a colorless oil: R_f 0.33 (silica gel, 5:95 ether/petroleum ether); IR (CHCl)$_3$ 1700 cm^{-1} (C = O); ^{1}H NMR (CDCl)$_3$ δ 0.17 (s, 9H), 1.30 (t, J = 7 Hz, 3H), 2.00 (s, 3H), 4.17 (q, J = 7 Hz, 2H), 6.82 (s, 1H); mass spectrum m/z (relative intensity) 170 (100, M$^+$ − CH$_3$).

6.1.1.5. 2,2-Dimethyl-5-(trimethylsilyl)-4-pentynal [Oxidation with Dimethyl Sulfoxide/Oxalyl Chloride on a 0.36-mol Scale] (290)

A solution of dimethyl sulfoxide (62 mL, 68.3 g, 0.874 mol) in 200 mL of methylene chloride was added dropwise over 2 hours to a solution of oxalyl

chloride (36.6 mL, 53.2 g, 0.420 mol) in 500 mL of methylene chloride cooled to –60°. The mixture was stirred for an additional 30 minutes and a solution of 2,2-dimethyl-5-(trimethylsilyl)-4-pentyn-1-ol (66.3 g, 0.360 mol) in 200 mL of methylene chloride was added dropwise over 2.5 hours. The resulting solution was stirred for an additional 40 minutes, and then triethylamine (251 mL, 182 g, 1.80 mol) was added dropwise over 1 hour, and the solution was stirred for an additional 45 minutes and then allowed to warm to room temperature, and 400 mL of water was added. The aqueous layer was separated and extracted 3 times with 75-mL portions of methylene chloride, and the combined organic layers were washed 3 times with 200-mL portions of 1 N hydrochloric acid and then with water. The separate washes were successively extracted 3 times with 50-mL portions of methylene chloride and all the organic layers were combined and washed with saturated sodium chloride solution and dried over magnesium sulfate. The dried solution was concentrated and passed through a florosil column with 10% ether in hexane and the solvent was removed. The crude product was transferred in a vacuum train at room temperature, and small scale (2–4 g) medium-pressure liquid chromatography on silica gel using 3% ether in hexane afforded pure product in 80% yield; IR (neat, film) 2830, 2730, 2190 (C $=$ C), 1730 (C $=$ O) cm^{-1}; ^{1}H NMR (360 MHz, CDCl$_3$) δ 0.11 (s, 9H), 1.12 (s, 6H), 2.33 (s, 2H), 9.50 (s, 1H). Anal. Calcd. for C$_{10}$H$_{18}$OSi : C, 65.80; H, 9.95. Found: C, 65.50; H, 10.00.

6.1.1.6. 3-(Benzoyloxy)-3-[(benzoyloxy)methyl]cyclohexane-1,2-dione [Oxidation with Dimethyl Sulfoxide/Trifluoroacetic Anhydride] (317)

Trifluoroacetic anhydride (104 μL, 155 mg, 0.74 mmol) was added over 5 minutes to a solution of dimethyl sulfoxide (70 μL, 77 mg, 0.99 mmol) in 1.1 mL of dry methylene chloride at –70° under argon. After 20 minutes of stirring at –70°, 2-(benzoyloxy)-2-[(benzoyloxy)methyl]-6-hydroxycyclohexane (192 mg, 0.5 mmol) was added over 5–10 minutes, and stirring was continued for 30 minutes. Triethylamine (20 μL, 15 mg, 0.1 mmol) was added over 10–15 minutes, the solution was allowed to warm to room temperature, and water was added. The mixture was extracted with ether, and the extract was washed with 5% hydrochloric acid, water, dried over sodium sulfate, and evaporated under reduced pressure. The residue was chromatographed on silica gel (100–200 mesh, 15 g) with 10% ethyl acetate–hexane to give the product, which was crystallized from methanol; yield 125 mg (0.34 mmol, 68%); mp 159–160°, ^{1}H NMR (CDCl$_3$) δ 2.3–3.1 (m, 4H), 4.70 and 4.82 (AB, J_{AB} = 12 Hz, 2H), 5.93 (s, D$_2$O exchangeable, 1H), 6.23 (dd, J = 5.6 and 2.8 Hz, 1H), 7.4–8.1 (m, 10H); FAB mass spectrum, m/z (relative intensity) 389 (10; M$^+$ + Na); 367 (25; M$^+$ + H); 349 (8), 305 (7), 245 (100), 123 (60), 122 (50).

6.1.1.7. 4-tert-Butylcyclohexanone [Oxidation with Dimethyl Sulfide/N-Chlorosuccinimide] (314)

N-Chlorosuccinimide (8.0 g, 0.060 mol) and 200 mL of toluene were cooled to 0° in a 1-L, three-necked, round-bottomed flask equipped with a mechanical

stirrer, a thermometer, a dropping funnel, and an argon-inlet tube. Dimethyl sulfide (6.0 mL, 0.10 mol) was added and the mixture was cooled to –25° using a carbon tetrachloride–dry ice bath. A solution of 4-*tert*-butylcyclohexanol (6.24 g, 0.04 mol, mixture of *E* and *Z*) in 40 mL toluene was added dropwise over 5 minutes, the stirring was continued for 2 hours at –25°, and then a solution of 6.0 g (0.06 mol) of triethylamine in 10 mL of toluene was added dropwise over 3 minutes. The cooling bath was removed, and after 5 minutes 400 mL of dimethyl ether was added. The organic layer was washed with 100 mL of 1% aqueous hydrochloric acid and then twice with two 100-mL portions of water and dried over anhydrous magnesium sulfate. The solvents were evaporated under reduced pressure, and the residue was transferred to a 50-mL, round-bottomed flask and distilled bulb-to-bulb at 120° (25 mm) to yield 5.72 g (93%) of 4-*tert*-butylcyclohexanone, mp 41–45°. Recrystallization from petroleum ether at –20° gave an 88% recovery of material with mp 45–46°; IR 1712 cm^{-1} (C $=$ O); ^{1}H NMR (CDCl$_3$) δ 0.93 (s, 9*H*), 1.3–2.2 (m, 5*H*), and 2.2–2.50 (m, 4*H*).

6.1.1.8. 1,5-Dimethyl-4-methoxycyclohexa-2,4-dienylacetaldehyde [Oxidation with Dimethyl Sulfoxide with Sulfur Trioxide/Pyridine Complex] (318)

To a solution of 450 mg (2.47 mmol) of 2-(1,5-dimethyl-4-methoxycyclohexa-2,4-dienyl)ethanol in 5 mL of anhydrous triethylamine and 5 mL of anhydrous dimethyl sulfoxide was added a solution of 1.90 g (11.9 mmol) of sulfur trioxide–pyridine complex (available from Aldrich Chemical or Alfa Products) in 7 mL of anhydrous dimethyl sulfoxide. The reaction mixture was stirred at room temperature for 2.25 hours and then partitioned between water and diethyl ether. The combined ethereal extracts were washed with water and brine and dried over magnesium sulfate. The solvent was removed to give 3.23 mg (1.79 mmol, 73%) of virtually pure product. Column chromatography on alumina with benzene gave pure material; IR (film) 1700 cm^{-1} (C $=$ O); ^{1}H NMR (CCl$_4$) δ 1.14 (s, 3*H*), 1.66 (br s, 3*H*); 2.12 (m, 2*H*), 2.28 (m, 2*H*), 3.48 (s, 3*H*), 5.58 (d, *J* = 10 Hz, 1*H*), 5.87 (d, *J* = 10 Hz, 1*H*), 9.63 (t, *J* = 3 Hz, 1*H*); mass spectrum, *m/z* 180 (M$^+$).

6.1.1.9. 1,3,4-Tri-O-benzyl-5-O-triphenylmethyl-keto-D-threo-pentulose [Oxidation with Dimethyl Sulfoxide/Acetic Anhydride] (34, 319)

2,3,5-Tri-*O*-benzyl-1-*O*-triphenylmethyl-D-arabinitol (5 g, 7.5 mmol) was dissolved in 30 mL of dimethyl sulfoxide/acetic anhydride (3:2, v/v) and kept at room temperature for 18 hours. Cold water (120 mL) was added, the mixture was stirred for 30 minutes, and the aqueous phase was decanted. The yellowish syrup was washed twice with water and dissolved in hexane, and this solution was washed repeatedly with water, once with 10% aqueous silver nitrate solution, and concentrated under reduced pressure to yield 4.9 g of a syrup. Chromatography on 250 g of silica gel (0.05–0.20 mm, No. 7734 of E.

Merck) with 9:1 v/v benzene/ether gave the product, pure by TLC, as a syrup (4.3 g, 6.5 mmol, 87%); $[\alpha]_D^{21} - 26.2°$ (c 2.1, CHCl₃); IR 1735 cm⁻¹ (C = O).

6.1.1.10. Methyl 4,6-O-Benzylidene-2-O-p-toluenesulfonyl- α -D-ribo-hexopyranosid-3-ulose [Oxidation with Dimethyl Sulfoxide/Phosphorus Pentoxide] (12, 320)

A mixture of 7.2 g (16.5 mmol) of methyl 4,6-*O*-*p*-toluenesulfonyl- α -D-glucopyranoside, 5 g (65 mmol) of dimethyl sulfoxide, 8 g (56 mmol) of phosphorus pentoxide, and 200 mL dimethylformamide was heated 2 hours at 65–70° with stirring. The reaction mixture was poured into ice and water and the solution was kept in a refrigerator overnight. The crystals were collected by filtration and washed with water; yield 6.7 g (15.4 mmol, 93%). The product contained no impurities detectable by TLC on silica gel with benzene–methanol (98:2, v/v). Crystallization from ethanol gave white crystals, mp 162–164°, $[\alpha]_D^{28} + 45°$ (c 1.0, CHCl₃); IR (Nujol) 1775 cm⁻¹ (C = O); ¹H NMR (CDCl₃) δ 3.42 (s, 3*H*, OCH₃), 5.12 (d, *J* = 4.1 Hz, 1*H*, C*H*OTs), 5.26 (d, *J* = 4.1 Hz, 1*H*, C*H*OCH₃).

7. Introduction to the Tabular Survey

The frequent use of dimethyl sulfoxide to oxidize alcohols makes it impossible to compile a complete tabulation. Moreover, while new citations are appearing at a rate of ³100/year, most of them do not involve any advance in methodology. Because many different reagents are used in dimethyl sulfoxide oxidations, it is impractical to locate all literature citations. Many citations in the following tables were found by a search of *Science Citation Index* for the most commonly cited original references. Since this Index begins in 1973, some citations prior to that date will have been missed if they were not cited by other authors. The key articles so searched were references 4, 8, 11, 13, 15, 17, 19, 22-24, 35, and 155.

The *Science Citation Index* was searched through June 1985, and several journals were scanned for selected references through mid-1987. Important methodological references through mid-1989 are reported in the text.

Division of the tables into classes of substrates has been kept to a minimum, with primary alcohols, secondary alcohols, and polyhydroxy compounds being the principal groupings; a separate classification of carbohydrates was made because of the many examples of this class. The decision as to which compounds would be classified as carbohydrates sometimes could not be made on logical grounds. Carbohydrate rings are drawn as vertical views rather than in perspective.

The conditions used in dimethyl sulfoxide oxidations usually parallel those given in the Experimental Procedures; accordingly, only departures from the norm are specified in the tables. The products of dimethyl sulfoxide oxidations are often not isolated, but are used directly in a synthetic sequence; when only the overall yield of such a sequence is reported, the yield of oxidation product is denoted as greater than the overall sequence yield. The tables do indicate when the oxidation product was converted into a derivative for characterization.

Ac	acetyl
Bn	benzyl
Bz	benzoyl
CMC	cyclohexyl-3-[2-(*N*-methylmorpholino)ethyl]carbodiimide *p*-toluenesulfonate
CSCB	1-(4-chlorobenzenesulfonyloxy)-6-chloro-1*H*-benzotriazole
DCC	dicyclohexylcarbodiimide
DEC	diethylcarbodiimide

DIPC   diisopropylcarbodiimide
DIPEA *N,N*-diisopropylethylamine
DMF   dimethylformamide
DMSO dimethyl sulfoxide
ether   diethyl ether
HMPA hexamethylphosphoric triamide
Ms   methanesulfonyl
NCS   *N*-chlorosuccinimide
Py   pyridine
TEA   triethylamine
Tf   trifluoromethanesulfonyl
TFA   trifluoroacetic acid
TFAA   trifluoroacetic anhydride
THP   tetrahydropyranyl
Ts   *p*-toluenesulfonyl

Table I. Oxidation of Primary Alcohols

View PDF

Table II. Oxidation of Primary Carbohydrate Alcohols

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Table III. Oxidation of Secondary Alcohols

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Table IV. Oxidation of Secondary Carbohydrate Alcohols

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Table V. Oxidation of Diols and Polyols

[View PDF](#)

TABLE I. OXIDATION OF PRIMARY ALCOHOLS
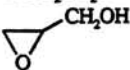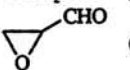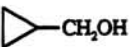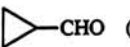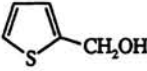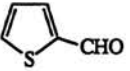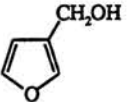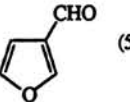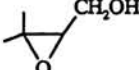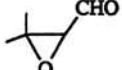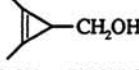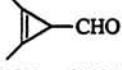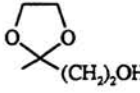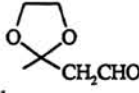
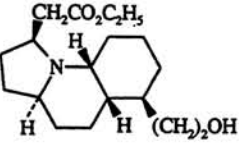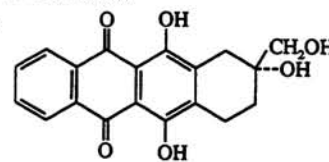| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C$_2$ FCH$_2$CH$_2$OH	DMSO, (COCl)$_2$	FCH$_2$CHO (32)	321
BrCH$_2$CH$_2$OH	(CH$_3$)$_2$S, NCS	BrCH$_2$CHO (—)	322
C$_3$ epoxide-CH$_2$OH	DMSO, (COCl)$_2$	epoxide-CHO (—)	323
C$_4$ NCCH=CHCH$_2$OH	DMSO, (COCl)$_2$	NCCH=CHCHO (66)	324
cyclopropyl-CH$_2$OH	DMSO, (COCl)$_2$	cyclopropyl-CHO (98)	26
Cl(CH$_2$)$_4$OH	DMSO, (COCl)$_2$	Cl(CH$_2$)$_3$CHO (85)	325
1-Butanol	1. COCl$_2$ 2. DMSO	1-Butanal (65)	15
	DMSO, SbCl$_5$, O$_2$, 80°	" (47)	326
i-C$_3$H$_7$CH$_2$OH	DMSO, DCC, Py, TFA	i-C$_3$H$_7$CHO (41)	327
	1. COCl$_2$ 2. DMSO	" (70)	15
	DMSO, SbCl$_5$, O$_2$, 80°	" (41)	326
(CH$_3$)$_3$SiCH$_2$OH	1. DMSO, (COCl)$_2$, CH$_2$Cl$_2$ 2. (C$_6$H$_5$)$_3$P=C(CH$_3$)CO$_2$C$_2$H$_5$	(E)-(CH$_3$)$_3$SiCH=C(CH$_3$)CO$_2$C$_2$H$_5$ (54)	311
	1. DMSO, (COCl)$_2$, ether 2. TEA, −78 to 0° 3. C$_6$H$_5$C≡CLi	(CH$_3$)$_3$SiCHOHC≡CC$_6$H$_5$ (76)	311c
C$_5$ thiophene-2-CH$_2$OH	DMSO, (COCl)$_2$	thiophene-2-CHO (92)	26
furan-3-CH$_2$OH	DMSO, (COCl)$_2$	" (90)	26
	DMSO, TFAA	furan-3-CHO (59)	328

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

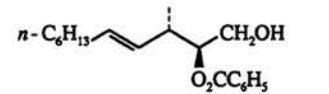| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
$HC\equiv C(CH_2)_3OH$	DMSO, $(COCl)_2$	$HC\equiv C(CH_2)_3COH$ (100)	22
(epoxide with CH₂OH)	DMSO, $(COCl)_2$	(epoxide with CHO) (—)	323
$t\text{-}C_4H_9CH_2OH$	DMSO, TFAA	$t\text{-}C_4H_9CHO$ (81)	25
	1. $COCl_2$	" (57)	15
	2. DMSO		
C₆ 2-(pyridyl)CH₂OH	DMSO, $(COCl)_2$	2-(pyridyl)CHO (70)	26
3-	DMSO, $(COCl)_2$	3- " (100)	26
4-	DMSO, $(COCl)_2$	4- " (100)	26
$(E,E)\text{-}CH_3(CH=CH)_2CH_2OH$ (84)	DMSO, $(COCl)_2$	$(E,E)\text{-}CH_3(CH=CH)_2CHO$ (84)	329
$CH_2=CH$—(cyclopropyl)—CH_2OH	DMSO, $(COCl)_2$	$CH_2=CH$—(cyclopropyl)—CHO (>32)	330
(cyclopropene)—CH_2OH	DMSO, $(COCl)_2$	(cyclopropene)—CHO (82)	331
$(E)\text{-}n\text{-}C_3H_7CH=CHCH_2OH$	DMSO, $(COCl)_2$	$(E)\text{-}n\text{-}C_3H_7CH=CHCHO$ (100)	23, 27
(dioxolane)—$(CH_2)_2OH$	DMSO, $(COCl)_2$	(dioxolane)—CH_2CHO (76)	332
1-Hexanol	1. $COCl_2$	1-Hexanal (68)	15
	2. DMSO		
$(S)\text{-}CH_3CH(OCH_2OCH_3)(CH_2)_2OH$	DMSO, $(COCl)_2$	$(S)\text{-}CH_3CH(OCH_2OCH_3)CH_2CHO$ (100)	333
$(CH_3)_3Si(CH_2)_3OH$	1. $COCl_2$	$(CH_3)_3Si(CH_2)_3CHO$ (70)	334
	2. DMSO		
C₇ $2\text{-}ClC_6H_4CH_2OH$	DMSO, O_2, 190°	$2\text{-}ClC_6H_4CHO$ (78)	69
$4\text{-}ClC_6H_4CH_2OH$	DMSO, O_2, 190°	$4\text{-}ClC_6H_4CHO$ (86)	69
	DMSO, DCC	" (100)	30
	DMSO, $SbCl_5$, O_2	" (10)	326
$2\text{-}O_2NC_6H_4CH_2OH$	DMSO, O_2, 190°	$2\text{-}O_2NC_6H_4CHO$ (27)	69
$3\text{-}O_2NC_6H_4CH_2OH$	DMSO, O_2, 190°	$3\text{-}O_2NC_6H_4CHO$ (63)	69
$4\text{-}O_2NC_6H_4CH_2OH$	DMSO, DCC, H_3PO_4	$4\text{-}O_2NC_6H_4CHO$ (92)	30
	DMSO, O_2, 190°	(77)	69
	DMSO, Ac_2O	" (75)	10
	DMSO, SO_3, Py	" (—)	13
	DMSO, 2-fluoro-1,3-dimethylpyridinium tosylate	" (88)	216
	DMSO, 2-fluoro-1-methylpyridinium tosylate	" (76)	216
	DMSO, $SbCl_5$, O_2	" (43)	326
	$(CH_3)_2Se$, NCS	" (77)	46
	$(CH_3)_2Se$, Ms_2O, HMPA, $-20°$	(88)	335
$C_6H_5CH_2OH$	$(CH_3)_2S$, NCS	C_6H_5CHO (90)	17

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
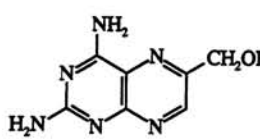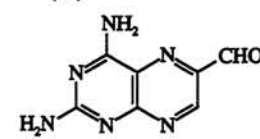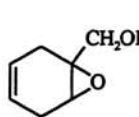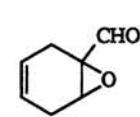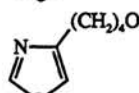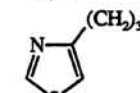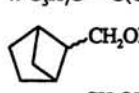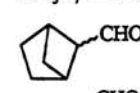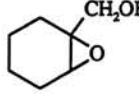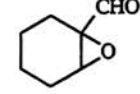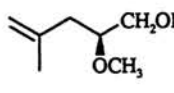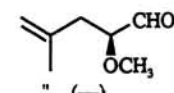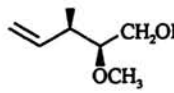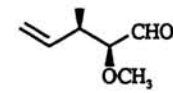
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)$_2$	" (100)	23
	DMSO, TFAA, −50°	" (84)	24
	DMSO, TFAA, −50°, TEA at 25°	" (42)	24
	DMSO, Cl$_2$	" (98)	14
	DMSO, polymer-supported carbodiimide	" (95)	55
	DMSO, AcCl	" (—)	336
	DMSO, H$_2$SO$_4$, 190°, 4 h	" (67)	337
	DMSO, 2-fluoro-1-methylpyridinium tosylate	" (86)	197
	DMSO, ClSO$_2$NCO	" (90)	338
	DMSO, O$_2$, 190°	" (80	68
	DMSO, Hg(OAc)$_2$, 130°	" (86)	339
	Polymer-supported sulfide, Cl$_2$	" (67)	42
	DMSO, SbCl$_5$, O$_2$	" (57)	326
	(CH$_3$)$_2$Se, NCS	" (93)	46
	DMSO, CH$_3$O$_2$CCOCl	" (98)	26
	(*i*-C$_3$H$_7$)$_2$S, NCS	" (98)	39
	(*n*-C$_4$H$_9$)$_2$S, NCS	" (98)	39

| | DMSO, DCC, H$_3$PO$_4$ | (89) | 340 |

| | DMSO, TFAA | (70) | 341 |

| | DMSO, diisopropylcarbodiimide | (44) | 342 |

| *n*-C$_4$H$_9$C≡CCH$_2$OH | DMSO, (COCl)$_2$ | *n*-C$_4$H$_9$C≡CCHO (98) | 22 |
| *n*-C$_3$H$_7$C≡C(CH$_2$)$_2$OH | DMSO, (COCl)$_2$ | *n*-C$_3$H$_7$C≡CCH$_2$CHO (90) | 22 |

| | DMSO, NCS | (85) | 343 |

| | DMSO, (COCl)$_2$ | (—) | 323 |

C$_6$H$_{11}$CH$_2$OH	DMSO, Cl$_2$	C$_6$H$_{11}$CHO (94)	14
	(CH$_3$)$_2$S, NCS	" (93)	17
	(*i*-C$_3$H$_7$)$_2$S, NCS, 0°	" (84)	39
	(*n*-C$_4$H$_9$)$_2$S, NCS, 0°	" (88)	39

| | DMSO, Py, SO$_3$ | (91) | 104, 344 |
| | DMSO, (COCl)$_2$ | " (—) | |

| | DMSO, (COCl)$_2$ | (—) | 345 |

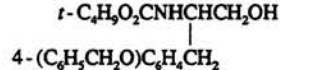TABLE I.   OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
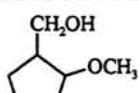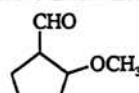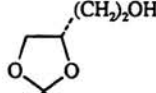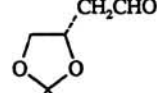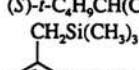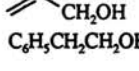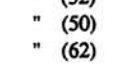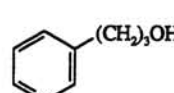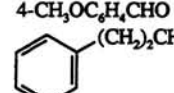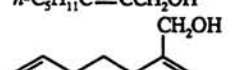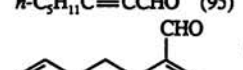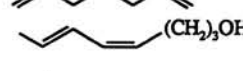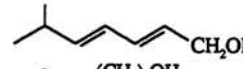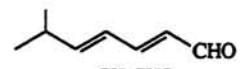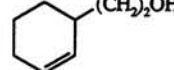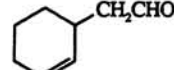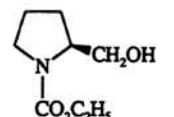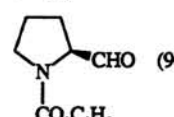
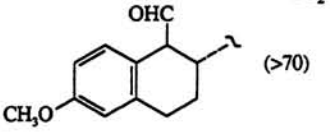| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
CH$_2$OH / OCH$_3$ cyclopentane *cis* and *trans*	1. COCl$_2$ 2. DMSO 3. (C$_2$H$_5$)$_3$N	CHO / OCH$_3$ cyclopentane (67)	346
i-C$_4$H$_9$ / CH$_2$OH epoxide	DMSO, (COCl)$_2$	*i*-C$_4$H$_9$ / CHO epoxide (>47)	347
(CH$_2$)$_2$OH dioxolane	DMSO, (COCl)$_2$, DIPEA	CH$_2$CHO dioxolane (84)	348
n-Heptanol	DMSO, polymer-supported carbodiimide, H$_3$PO$_4$	*n*-Heptanal (97)	55
	(CH$_3$)$_2$Se, NCS	" (82)	46
(*R*)-*n*-C$_3$H$_7$CH(CH$_3$)CH$_2$CH$_2$OH	DMSO, (COCl)$_2$	(*R*)-*n*-C$_3$H$_7$CH(CH$_3$)CH$_2$CHO (80)	349
(*S*)-*t*-C$_4$H$_9$CH(CH$_3$)CH$_2$OH	DMSO, DCC, Py, TFA	(*S*)-*t*-C$_4$H$_9$CH(CH$_3$)CHO (44)	106
CH$_2$Si(CH$_3$)$_3$ / CH$_2$OH	DMSO, (COCl)$_2$	CH$_2$Si(CH$_3$)$_3$ / CHO (>77)	350
C$_8$ C$_6$H$_5$CH$_2$CH$_2$OH	DMSO, (COCl)$_2$	C$_6$H$_5$CH$_2$CHO (23)	23, 26
	DMSO, TFAA, −50°	" (32)	24
	DMSO, TFAA, 25°	" (50)	24
	DMSO, (C$_6$H$_5$O)POCl$_2$	" (62)	64c
4-CH$_3$C$_6$H$_4$CH$_2$OH	DMSO, O$_2$, 190°	4-CH$_3$C$_6$H$_4$CHO (85)	69
	DMSO, SbCl$_5$, O$_2$	" (56)	326
C$_6$H$_5$OCH$_2$CH$_2$OH	DMSO, (COCl)$_2$	C$_6$H$_5$OCH$_2$CHO (83)	26
	DMSO, DCC, Py, TFA	" (20)	351
4-CH$_3$OC$_6$H$_4$CH$_2$OH	DMSO, O$_2$, 190°	4-CH$_3$OC$_6$H$_4$CHO (9) + (4-CH$_3$OC$_6$H$_4$CH$_2$)$_2$O (85)	69
	DMSO, 2-fluoro-1-methylpyridinium tosylate	4-CH$_3$OC$_6$H$_4$CHO (74)	216
(CH$_2$)$_3$OH pyridine	DMSO, (COCl)$_2$	(CH$_2$)$_2$CHO pyridine (88)	26
			300
CF$_3$CONH(CH$_2$)$_6$OH	DMSO, (COCl)$_2$	CF$_3$CONH(CH$_2$)$_5$CHO (—)	352
n-C$_5$H$_{11}$C≡CCH$_2$OH	DMSO, (COCl)$_2$	*n*-C$_5$H$_{11}$C≡CCHO (95)	22
CH$_2$OH	DMSO, (COCl)$_2$	CHO (>41)	353
(CH$_2$)$_3$OH	DMSO, (COCl)$_2$	(CH$_2$)$_2$CHO (54)	354
CH$_2$OH	DMSO, (COCl)$_2$	CHO (93)	355
(CH$_2$)$_2$OH cyclohexene	DMSO, DCC, Py, TFA	CH$_2$CHO cyclohexene (90)	356
(CH$_3$)$_2$C=CHCONH(CH$_2$)$_3$OH	DMSO, (COCl)$_2$	(CH$_3$)$_2$C=CHCONH(CH$_2$)$_2$CHO (84)	299
CH$_2$OH pyrrolidine / CO$_2$C$_2$H$_5$	DMSO, (COCl)$_2$	CHO pyrrolidine / CO$_2$C$_2$H$_5$ (90)	100
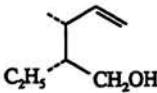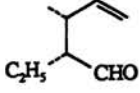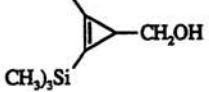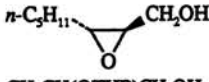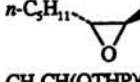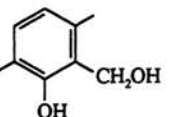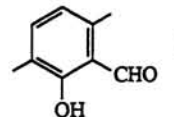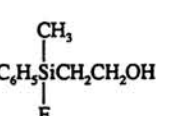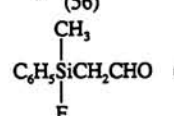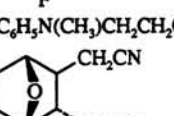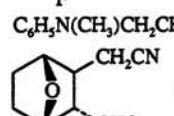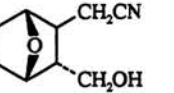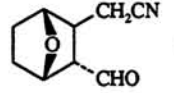
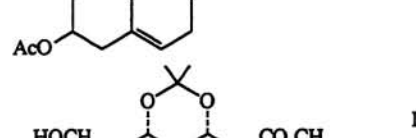TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

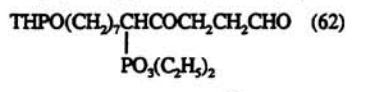| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
[structure: allyl/vinyl with C_2H_5 and CH_2OH]	DMSO, SO_3, Py	[structure with C_2H_5 and CHO] (83)	357
[cyclopropene with CH_2OH, $(CH_3)_3Si$]	DMSO, $(COCl)_2$	[cyclopropene with CHO, $(CH_3)_3Si$] (70)	331
[epoxide n-C_5H_{11} with CH_2OH]	DMSO, $(COCl)_2$	[epoxide n-C_5H_{11} with CHO] (—)	323
$CH_3CH(OTHP)CH_2OH$	DMSO, $(COCl)_2$	$CH_3CH(OTHP)CHO$ (88)	358
t-$C_4H_9O_2CNHCH(CH_3)CH_2OH$	DMSO, SO_3, Py	t-$C_4H_9O_2CNHCH(CH_3)CHO$ (66)	88
	DMSO, TFAA	" (—)	359
1-Octanol	DMSO, $(COCl)_2$	1-Octanal (95)	23
	DMSO, AcCl	" (—)	336
	DMSO, Cl_2	" (95)	14
	DMSO, NCS	" (96)	17
	Polymer-supported sulfide, Cl_2	" (95)	42
	Polymer-supported sulfide, NCS	" (75)	42
		+ 1-octyl chloride (25)	
	DMSO, CH_3O_2CCOCl	1-Octanal (100)	26
(S)-$C_2H_5O(CH_2)_2OCH_2CH(CH_3)CH_2OH$	DMSO, $(COCl)_2$	(S)-$C_2H_5O(CH_2)_2OCH_2CH(CH_3)CHO$ (82)	360
$C_6H_5C\equiv CCH_2OH$	DMSO, Ac_2O	$C_6H_5C\equiv CCHO$	79
$C_6H_5CH\!=\!CHCH_2OH$	DMSO, $(COCl)_2$	$C_6H_5CH\!=\!CHCHO$	23
	DMSO, TFAA	" (83)	24
	DMSO, O_2, 190°	" (60)	69
	DMSO, AcCl	" (—)	336
	DMSO, $ClSO_2NCO$	" (69)	338
	DMSO, 2-fluoro-1,3-dimethylpyridinium tosylate	" (85)	216
	$(CH_3)_2SeO$	" (100)	46
	$(CH_3)_2Se$, NCS	" (70)	46
	(i-$C_3H_7)_2S$, NCS, −78°	" (100)	39
	(n-$C_4H_9)_2S$, NCS, −78°	" (100)	39
(E)-$CH_3CH\!=\!CHCH_2C\equiv C(CH_2)_3OH$	DMSO, $(COCl)_2$	(E)-$CH_3CH\!=\!CHCH_2C\equiv C(CH_2)_2CHO$ (>60)	361
$C_6H_5(CH_2)_3OH$	DMSO, O_2	$C_6H_5(CH_2)_2CHO$ (26)	69
	DMSO, $(COCl)_2$	$C_6H_5(CH_2)_2CHO$ (96)	23
	DMSO, 2-fluoro-1,3-dimethylpyridinium tosylate	" (85)	216
$C_6H_5CH(CH_3)CH_2OH$	DMSO, $(COCl)_2$	$C_6H_5CH(CH_3)CHO$ (38)	26
[aryl with CH_2OH, OH, two CH_3]	$(CH_3)_2SeO$	[aryl with CHO, OH, two CH_3] (98)	47
$C_6H_5CH_2(CH_2)_2OH$	DMSO, $(COCl)_2$	$C_6H_5CH_2OCH_2CHO$ (—)	168
	DMSO, DCC	" (56)	300
[$C_6H_5\overset{CH_3}{\underset{F}{Si}}CH_2CH_2OH$]	$(CH_3)_2S$, NCS	[$C_6H_5\overset{CH_3}{\underset{F}{Si}}CH_2CHO$] (—)	362
$C_6H_5N(CH_3)CH_2CH_2OH$	DMSO, $(COCl)_2$	$C_6H_5N(CH_3)CH_2CHO$ (—)	91
[bicyclic oxa with CH_2CN, CH_2OH]	$(CH_3)_2S$, NCS	[bicyclic oxa with CH_2CN, CHO] (92)	363, 364

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
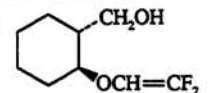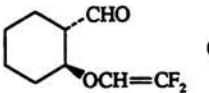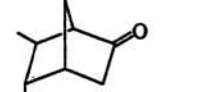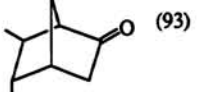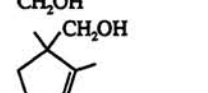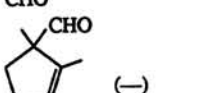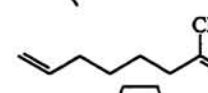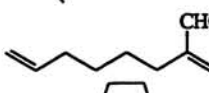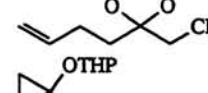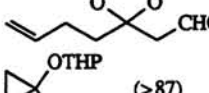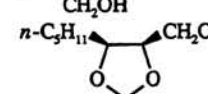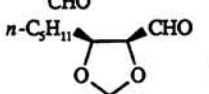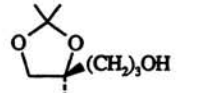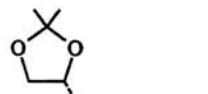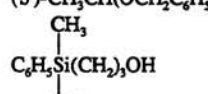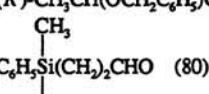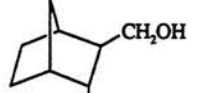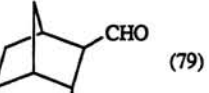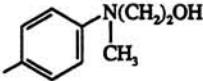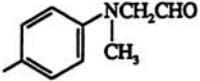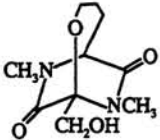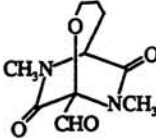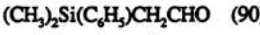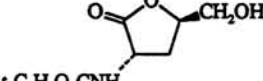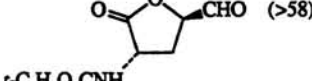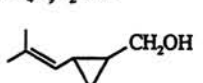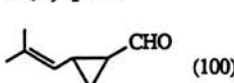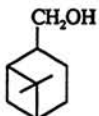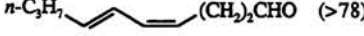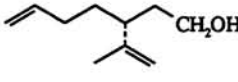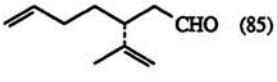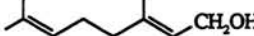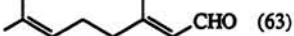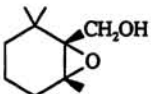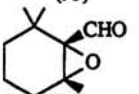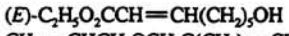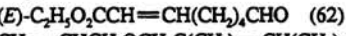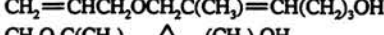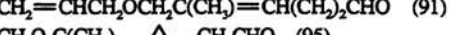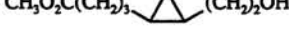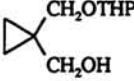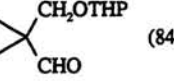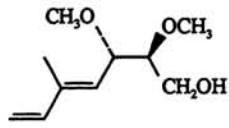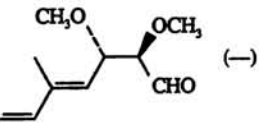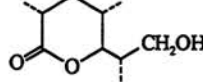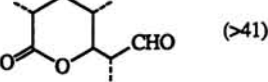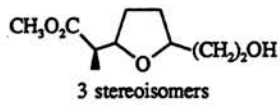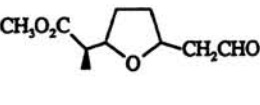
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C₉ (cyclohexane CH₂OH, OCH=CF₂)	DMSO, (COCl)₂	(CHO, OCH=CF₂) (80)	365
(norbornene CH₂OH)	(CH₃)₂S, NCS	CHO (55)	366
(bicyclic CH₂OH, ketone)	DMSO, (COCl)₂	(93) CHO	367, 368
(cyclopentene CH₂OH)	DMSO, SO₃, Py	CHO (—)	369
(dienyl CH₂OH)	DMSO, (COCl)₂	CHO (>41)	353
(dioxolane CH₂OH)	DMSO, (COCl)₂	CHO (87)	370
(cyclopropyl OTHP, CH₂OH)	DMSO, (COCl)₂	CHO (>87)	371
n-C₅H₁₁ (dioxolanone CH₂OH)	DMSO, (COCl)₂	n-C₅H₁₁ CHO (>47)	372
(pyrrolidinone) NCO(CH₂)₄OH	DMSO, (COCl)₂	NCO(CH₂)₃CHO (79)	373
(CH₃)₂C=CH(CH₂)₅OH	DMSO, (COCl)₂	(CH₃)₂C=CH(CH₂)₄CHO (81)	374
THPOCH₂CH(CH₃)CH₂OH	DMSO, DCC, Py, TFA	THPOCH₂CH(CH₃)CHO (>79)	375
(R)-	DMSO, (COCl)₂	(S)- " (—)	376
(dioxolane (CH₂)₃OH)	DMSO, TFAA	(CH₂)₂CHO (68)	344
(dioxolane C(CH₃)₂CH₂OH)	DMSO, (COCl)₂	C(CH₃)₂CHO (>85)	377
HO(CH₂)₃COCH₂PO(OC₂H₅)₂	DMSO, (COCl)₂	OHC(CH₂)₂COCH₂PO(OC₂H₅)₂ (42)	62
C₁₀ (OC)₃CrC₆H₅CH₂OH	DMSO, Ac₂O	(OC)₃CrC₆H₅CHO (57)	378
4-CH₃OC₆H₄C≡CCH₂OH	DMSO, (COCl)₂	4-CH₃OC₆H₄C≡CCHO	79
4-CH₃OC₆H₄(CH₂)₃OH	Polymer-supported sulfide, Cl₂	4-CH₃OC₆H₄(CH₂)₂CHO (94)	42
3,4-(CH₃O)₂C₆H₃(CH₂)₂OH	DMSO, DCC, Py, TFA	3,4-(CH₃O)₂C₆H₃CH₂CHO (66)	379
(S)-CH₃CH(OCH₂C₆H₅)CH₂OH	DMSO, (COCl)₂	(R)-CH₃CH(OCH₂C₆H₅)CHO (88)	107, 380
C₆H₅Si(CH₃)F(H)(CH₂)₃OH	(CH₃)₂S, NCS	C₆H₅Si(CH₃)F(H)(CH₂)₂CHO (80)	362
(norbornane CH₂OH, CH₂CN)	(CH₃)₂S, NCS	CHO, CH₂CN (79)	381

368
369

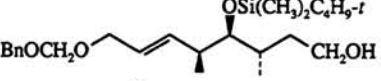TABLE I. Oxidation of Primary Alcohols (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
N(CH₂)₂OH structure (p-tolyl, CH₃)	DMSO, (COCl)₂	NCH₂CHO structure (—)	91
CH₃N, NCH₃, CH₂OH bicyclic structure	DMSO, (COCl)₂	CHO structure (~100)	382
norbornene (CH₂)₂OH	(CH₃)₂S, NCS	norbornene CH₂CHO (64)	383
(CH₃)₂Si(C₆H₄)CH₂CH₂OH	(CH₃)₂S, NCS	(CH₃)₂Si(C₆H₄)CH₂CHO (90)	362
lactone CH₂OH, t-C₄H₉O₂CNH	DMSO, (COCl)₂	lactone CHO (>58)	384
CH₂OH cyclopropane isopropenyl	DMSO, (COCl)₂	CHO (100)	26
CH₂OH pinane structure	DMSO, (COCl)₂	CHO (82)	26
n-C₃H₇ (CH₂)₃OH diene	(CH₃)₂S, NCS	n-C₃H₇ (CH₂)₂CHO (>78)	354
CH₂OH isopropenyl structure	DMSO, (COCl)₂	CHO (85)	385
CH₂OH geranial-type	DMSO, polymer-supported carbodiimide, H₃PO₄	CHO (63)	55
	DMSO, (COCl)₂	" (95)	22
CH₂OH epoxide structure	DMSO, (COCl)₂	CHO (89)	386
(E)-C₂H₅O₂CCH=CH(CH₂)₅OH	DMSO, (COCl)₂	(E)-C₂H₅O₂CCH=CH(CH₂)₄CHO (62)	370
CH₂=CHCH₂OCH₂C(CH₃)=CH(CH₂)₃OH	DMSO, (COCl)₂	CH₂=CHCH₂OCH₂C(CH₃)=CH(CH₂)₂CHO (91)	387
CH₃O₂C(CH₂)₃ cyclopropane (CH₂)₂OH	DMSO, (COCl)₂	CH₃O₂C(CH₂)₃ cyclopropane CH₂CHO (95)	388
CH₂OTHP cyclopropane CH₂OH	DMSO, (COCl)₂	CH₂OTHP cyclopropane CHO (84)	388
CH₃O OCH₃ CH₂OH diene structure	DMSO, (COCl)₂	CH₃O OCH₃ CHO (—)	389
lactone CH₂OH	DMSO, (COCl)₂	lactone CHO (>41)	390
CH₃O₂C tetrahydrofuran (CH₂)₂OH, 3 stereoisomers	DMSO, (COCl)₂	CH₃O₂C tetrahydrofuran CH₂CHO (90–95%)	391

TABLE I. Oxidation of Primary Alcohols (*Continued*)

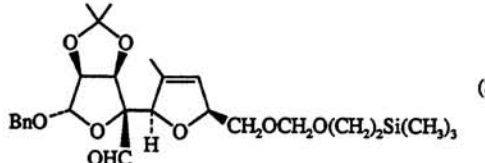| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
[bicyclic pyrrolizidine structure with (CH₂)₂OH]	DMSO, (COCl)₂	[bicyclic pyrrolizidine structure with CH₂CHO] (>28)	392
(CH₃)₂C=CH(CH₂)₂CH(CH₃)(CH₂)₂OH	1. COCl₂ 2. DMSO	(CH₃)₂C=CH(CH₂)₂CH(CH₃)CH₂CHO (46)	15
	DMSO, (COCl)₂	" (85)	22, 393
[pyran ring with CH₂OH side chain]	DMSO, (COCl)₂	[pyran ring with CHO side chain] (94)	394, 395, 396
t-C₄H₉O₂CNHCHCH₂OH, C₃H₇-i	DMSO, SO₃, Py	t-C₄H₉O₂CNHCHCHO (86), C₃H₇-i	88
t-C₄H₉O₂CNHCHCH₂OH, (CH₂)₂SCH₃	DMSO, SO₃, Py	t-C₄H₉O₂CNHCHCHO (90), (CH₂)₂SCH₃	88
n-Decanol	DMSO, (COCl)₂	n-Decanal (97)	23
	DMSO, TFAA	" (37)	24
	(i-C₃H₇)₂S, NCS, 0°	" (90)	39
	(n-C₄H₉)₂S, NCS, 0°	" (89)	39
	(CH₃)₂Se, NCS	" (68)	46
[branched chain CH₂OH]	(CH₃)₂S, NCS	[branched chain CHO] (85)	397
[cyclopropane with OSi(CH₃)₂C₄H₉-t and CH₂OH]	DMSO, (COCl)₂	[cyclopropane with OSi(CH₃)₂C₄H₉-t and CHO] (>94)	398
C₁₁ [8-bromonaphthalene-1-CH₂OH]	(CH₃)₂S, NCS	[8-bromonaphthalene-1-CHO] (89)	399
[8-iodonaphthalene-1-CH₂OH]	(CH₃)₂S, NCS	[8-iodonaphthalene-1-CHO] (62)	400
[naphthalene-2-CH₂OH]	(CH₃)₂SeO	[naphthalene-2-CHO] (100)	47
[pyrimidine with OCH₃, CH₃O, C≡CCH₂OH, CO₂CH₃]	DMSO, (COCl)₂	[pyrimidine with OCH₃, CH₃O, C≡CHO, CO₂CH₃] (71)	83
[dioxane ring with C₆H₅ and CH₂OH]	DMSO, SO₃, Py	[dioxane ring with C₆H₅ and CHO] (—)	401
[bicyclic lactone with CH₂OH, OAc, H]	DMSO, (COCl)₂	[bicyclic lactone with CHO, OAc, H] (81)	113
4-CH₃OC₆H₄(CH₂)₄OH	DMSO, (COCl)₂	4-CH₃OC₆H₄(CH₃)₃CHO (—)	402
(S)-C₆H₅CH₂OCH₂CH(CH₃)CH₂OH	DMSO, (COCl)₂	(R)-C₆H₅CH₂OCH₂CH(CH₃)CHO (95)	403, 404
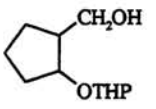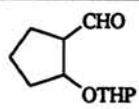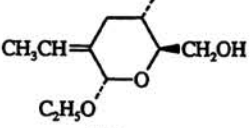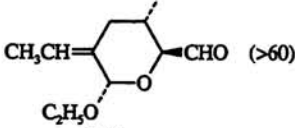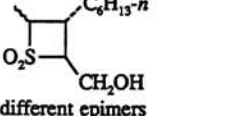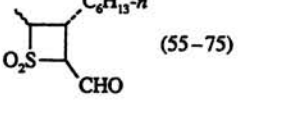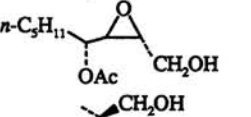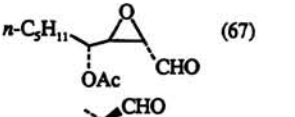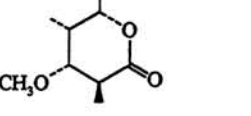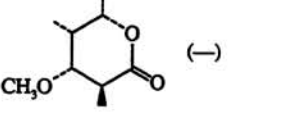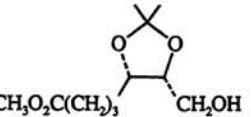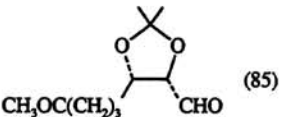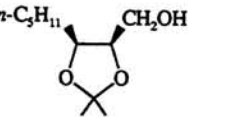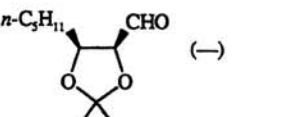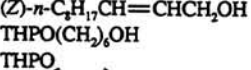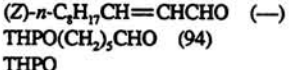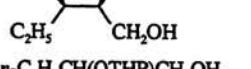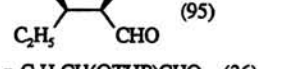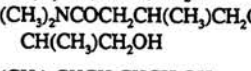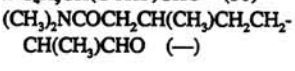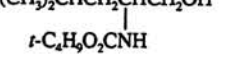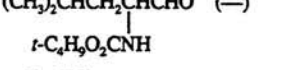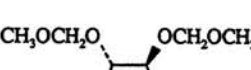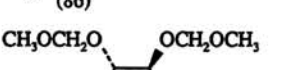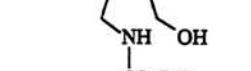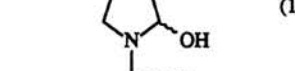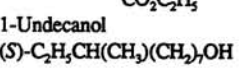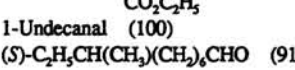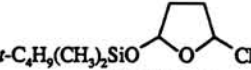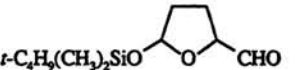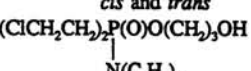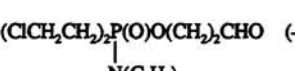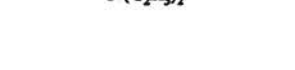
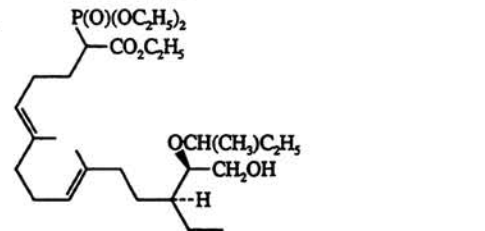TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	$(CH_3)_2SeO$	(97)	47
	DMSO, DCC	(80)	259, 405
	DMSO, DCC, Cl_2CHCO_2H	(82)	292
	DMSO, $(COCl)_2$	Z (99) E (95)	396 406
$C_6H_5Si(CH_2)_4OH$	$(CH_3)_2S$, NCS	$C_6H_5Si(CH_2)_3CHO$ (—)	362
	DMSO, $(COCl)_2$	(99)	23
	DMSO, Ms_2O, HMPA, $-20°$ DMSO, TFAA	'' (67) '' (86)	335 25
	DMSO, $(COCl)_2$	(99)	182
	DMSO, SO_3, Py	(72)	318
	DMSO, $(COCl)_2$	(95)	388
	DMSO, SO_3, Py	(85)	407
	DMSO, $(COCl)_2$	(—)	408
	DMSO, $(COCl)_2$	(95)	98
	DMSO, DCC, TFA	'' (40)	98

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

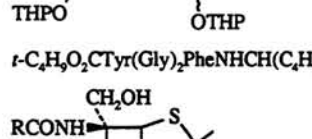| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
(cyclopentane with CH₂OH and OTHP) CH₂OH / OTHP	DMSO, CMC, TFA, Py	(cyclopentane with CHO and OTHP) CHO / OTHP (80)	346
CH₃CH= ...CH₂OH (pyran, C₂H₅O)	DMSO, (COCl)₂	CH₃CH= ...CHO (pyran, C₂H₅O) (>60)	409
O₂S (thietane, C₆H₁₃-n) CH₂OH different epimers	DMSO, DCC, Py, TFA	O₂S (thietane, C₆H₁₃-n) CHO (55–75)	410
n-C₅H₁₁ (epoxide) CH₂OH / OAc	DMSO, (COCl)₂	n-C₅H₁₁ (epoxide) CHO / OAc (67)	411
(pyranone, CH₃O, CH₃) CH₂OH	DMSO, (COCl)₂	(pyranone, CH₃O, CH₃) CHO (—)	412, 413
CH₃O₂C(CH₂)₃ (dioxolane) CH₂OH	DMSO, (COCl)₂	CH₃OC(CH₂)₃ (dioxolane) CHO (85)	414
n-C₅H₁₁ (dioxolane) CH₂OH	DMSO, (COCl)₂	n-C₅H₁₁ (dioxolane) CHO (—)	415
(Z)-n-C₈H₁₇CH=CHCH₂OH	DMSO, (COCl)₂	(Z)-n-C₈H₁₇CH=CHCHO (—)	416
THPO(CH₂)₆OH	DMSO, (COCl)₂	THPO(CH₂)₅CHO (94)	374, 417
THPO (C₂H₅) CH₂OH	DMSO, (COCl)₂	THPO (C₂H₅) CHO (95)	390
n-C₄H₉CH(OTHP)CH₂OH	(CH₃)₂S, NCS	n-C₄H₉CH(OTHP)CHO (36)	418
(CH₃)₂NCOCH₂CH(CH₃)CH₂CH₂-CH(CH₃)CH₂OH	DMSO, SO₃, Py	(CH₃)₂NCOCH₂CH(CH₃)CH₂CH₂-CH(CH₃)CHO (—)	419
(CH₃)₂CHCH₂CHCH₂OH / t-C₄H₉O₂CNH	DMSO, (COCl)₂	(CH₃)₂CHCH₂CHCHO (—) / t-C₄H₉O₂CNH	420
	DMSO, SO₃, Py	'' (86)	88
CH₃OCH₂O, OCH₂OCH₃ (pyrrolidine) NH OH / CO₂C₂H₅		CH₃OCH₂O, OCH₂OCH₃ (pyrrolidine) N OH / CO₂C₂H₅ (100)	421
1-Undecanol	DMSO, (COCl)₂	1-Undecanal (100)	22
(S)-C₂H₅CH(CH₃)(CH₂)₇OH	DMSO, (COCl)₂	(S)-C₂H₅CH(CH₃)(CH₂)₆CHO (91)	393
t-C₄H₉(CH₃)₂SiO (furan) CH₂OH cis and trans	DMSO, (COCl)₂	t-C₄H₉(CH₃)₂SiO (furan) CHO cis (90–100) trans (70–81)	422
(ClCH₂CH₂)₂P(O)O(CH₂)₃OH / N(C₂H₅)₂	(CH₃)₂S, NCS	(ClCH₂CH₂)₂P(O)O(CH₂)₂CHO (—) / N(C₂H₅)₂	423

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
OSi(CH₃)₂C₄H₉-*t* structure, CH₂OH	DMSO, (COCl)₂	OSi(CH₃)₂C₄H₉-*t* structure, CHO (>85)	361, 424, 425
(*n*-C₃H₇)₃SiCH₂CH₂OH	(CH₃)₂S, NCS	(*n*-C₃H₇)₃SiCH₂CHO (60)	426
C₁₂ pyrrolidinone CH₂OH, CH₂SC₆H₅	DMSO, TFAA	CHO structure (>72)	427
C₆H₅CH₂OCH₂ structure, CH₂OH	DMSO, (COCl)₂	C₆H₅CH₂OCH₂ structure, CHO (>90)	168
C₆H₅ isoxazolidine CH₂OH	DMSO, (COCl)₂	C₆H₅ structure, CHO (>68)	428
C₆H₅CH₂O structure, CH₂OH	DMSO, (COCl)₂	C₆H₅CH₂O structure, CHO (>70)	376
(*S*)-4-CH₃C₆H₄CH(CH₂)₃OH, CH₃	DMSO, (COCl)₂	(*S*)-4-CH₃C₆H₄CH(CH₂)₂CHO (85), CH₃	429
oxazole cyclohexane CH₂OH	DMSO, (COCl)₂	oxazole structure CHO (98)	86, 430
CH₂OH bicyclic structure H	DMSO, (COCl)₂	CHO bicyclic structure H (90)	116
adamantane (CH₂)₂OH	DMSO, DCC, Py, TFA	adamantane CH₂CHO (98)	431
dithiolane structure CH₂OH	DMSO, DCC, H₃PO₄	dithiolane structure CHO (80)	117
(CH₃)₂Si(C₆H₅)(CH₂)₄OH	(CH₃)₂S, NCS	(CH₃)₂Si(C₆H₅)(CH₂)₃CHO (90)	362
AcO structure CH₂OH	DMSO, (COCl)₂	AcO structure CHO (81)	119
OTHP cyclopropane =CHCH₂OH	DMSO, (COCl)₂	OTHP =CHCHO (93)	432
(*E,E*)-CH₃OCH₂OCH₂(CH=CH)₂(CH₂)₅OH	DMSO, (COCl)₂	(*E,E*)-CH₃OCH₂OCH₂(CH=CH)₂(CH₂)₄CHO (80)	417
I structure (CH₂)₃OH, OCH(CH₃)OC₂H₅	DMSO, (COCl)₂	I structure (CH₂)₂CHO (90), OCH(CH₃)OC₂H₅	433
(*Z*)-C₂H₅CH=CH(CH₂)₈OH	1. COCl₂ 2. DMSO 3. TEA	(*Z*)-C₂H₅CH=CH(CH₂)₇CHO (19)	434

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

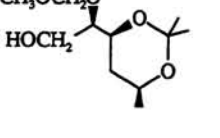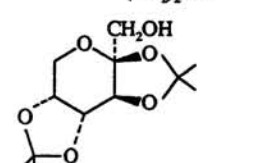| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, DCC, Py, TFA	(95)	435
$Br(CH_2)_{12}OH$	DMSO, $(COCl)_2$	$Br(CH_2)_{11}CHO$ (89)	436, 437
1-Dodecanol	DMSO, $(COCl)_2$, $-60°$	1-Dodecanal (100)	22
	" $-10°$	" (98)	22
	DMSO, 2-fluoro-1,3-dimethylpyridinium tosylate	" (85)	216
	$(CH_3)_2SeO$	" (80)	47
	$(i\text{-}C_3H_7)_2S$, NCS, $0°$	" (88)	39
	$(n\text{-}C_4H_9)_2S$, NCS, $0°$	" (91)	39
$C_2H_5CH(CH_3)(CH_2)_3CH(CH_3)(CH_2)_3OH$	DMSO, $(COCl)_2$	$C_2H_5CH(CH_3)(CH_2)_3CH(CH_3)(CH_2)_2CHO$ (—)	438
$(ClCH_2CH_2)_2NP(O)O(CH_2)_4OH$ $N(C_2H_5)_2$	$(CH_3)_2S$, NCl	$(ClCH_2CH_2)_2P(O)O(CH_2)_3CHO$ (—) $N(C_2H_5)_2$	423
	DMSO, $(COCl)_2$	(>73)	439
	DMSO, $(COCl)_2$	(67)	389
C_{13}	DMSO, DCC, Py, TFA	(67)	440
	DMSO, Ac_2O	(26) + methylthiomethyl ether (45)	378
	DMSO, DCC, Py, TFA	(85)	441
	DMSO, SO_3, Py	(96)	88
$CH_2{=}C(C_6H_5)(CH_2)_5OH$	DMSO, $(COCl)_2$	$CH_2{=}C(C_6H_5)(CH_2)_4CHO$ (92)	370
	DMSO, $(COCl)_2$	(>62)	442
	DMSO, $(COCl)_2$	(44)	443
$4\text{-}CH_3OC_6H_5CH_2O$ CH_2OH	DMSO, $(COCl)_2$	$4\text{-}CH_3OC_6H_4CH_2O$ CHO (>71)	425
	DMSO, $(COCl)_2$	(99)	390
	DMSO, $(COCl)_2$	(82)	444

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
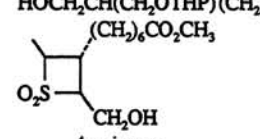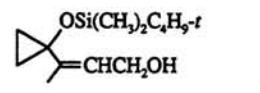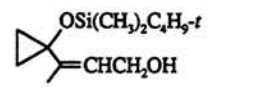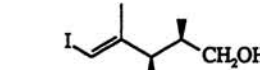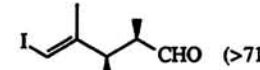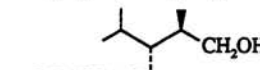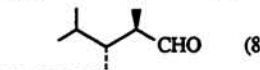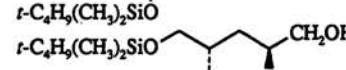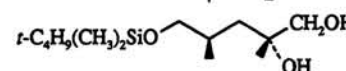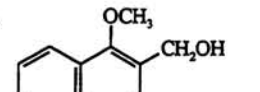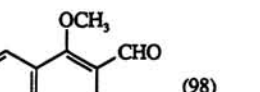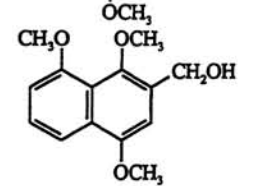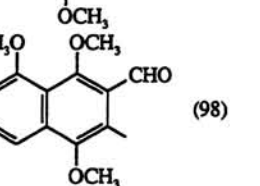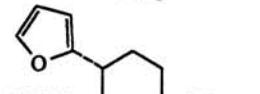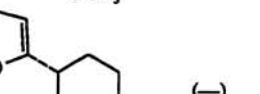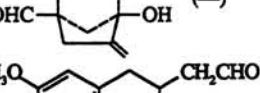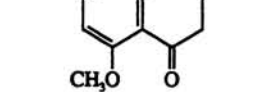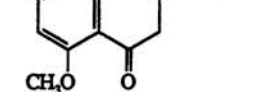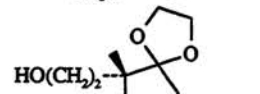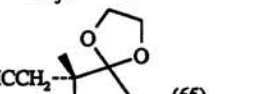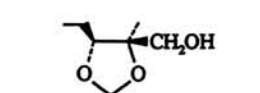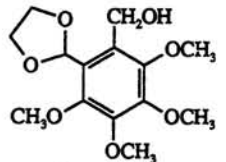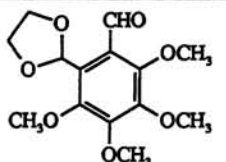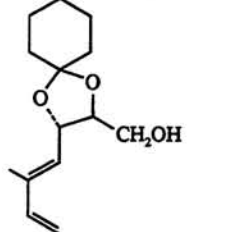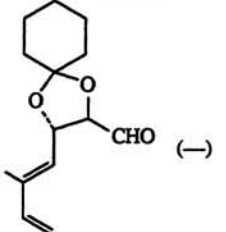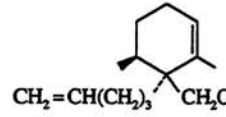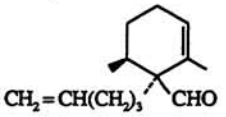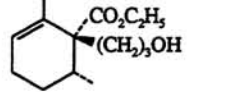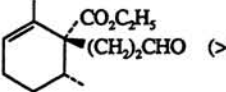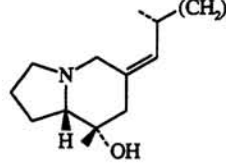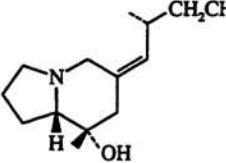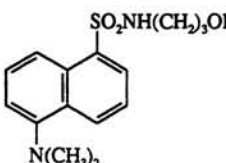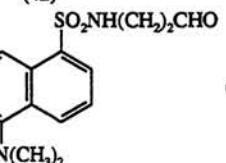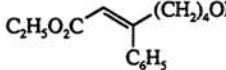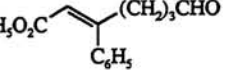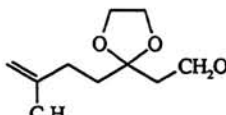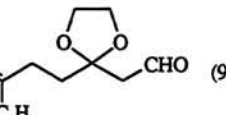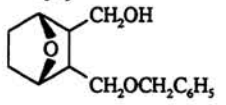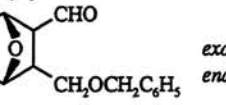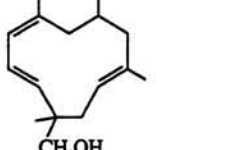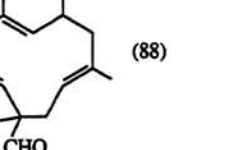
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
HOCH$_2$CH(CH$_2$OTHP)(CH$_2$)$_3$CO$_2$CH$_3$ (CH$_2$)$_6$CO$_2$CH$_3$	DMSO, (COCl)$_2$	OHCCH$_2$CH(CH$_2$OTHP)(CH$_2$)$_3$CO$_2$CH$_3$ (90) (CH$_2$)$_6$CO$_2$CH$_3$	388, 445
[β-sultam structure] O$_2$S–CH$_2$OH, 4 epimers	DMSO, DCC, Py, TFA	[β-sultam structure] O$_2$S–CHO (65–76)	410
[cyclopropane] OSi(CH$_3$)$_2$C$_4$H$_9$-*t* =CHCH$_2$OH	DMSO, (COCl)$_2$	[cyclopropane] OSi(CH$_3$)$_2$C$_4$H$_9$-*t* =CHCHO (93)	432
(*R*)-C$_2$H$_5$O$_2$C(CH$_2$)$_6$CH(CH$_3$)CH$_2$CH$_2$OH	DMSO, (COCl)$_2$	(*R*)-C$_2$H$_5$O$_2$C(CH$_2$)$_6$CH(CH$_3$)CH$_2$CHO (87)	446
[vinyl iodide structure] I ... CH$_2$OH, *t*-C$_4$H$_9$(CH$_3$)$_2$SiO	DMSO, (COCl)$_2$	[vinyl iodide structure] I ... CHO (>71), *t*-C$_4$H$_9$(CH$_3$)$_2$SiO	447
n-C$_9$H$_{19}$CH(C$_2$H$_5$)CH$_2$OH	DMSO, (COCl)$_2$	*n*-C$_9$H$_{19}$CH(C$_2$H$_5$)CHO (97)	448
n-C$_9$H$_{19}$CH(CH$_3$)CH$_2$CH$_2$OH	DMSO, (COCl)$_2$	*n*-C$_9$H$_{19}$CH(CH$_3$)CH$_2$CHO (90)	448
n-C$_{10}$H$_{21}$CH(SeCH$_3$)CH$_2$OH	(CH$_3$)$_2$S, NCS	*n*-C$_{10}$H$_{21}$CH(SeCH$_3$)CHO (53)	449
[structure] CH$_2$OH, *t*-C$_4$H$_9$(CH$_3$)$_2$SiO	DMSO, (COCl)$_2$	[structure] CHO (84), *t*-C$_4$H$_9$(CH$_3$)$_2$SiO	450
t-C$_4$H$_9$(CH$_3$)$_2$SiO [structure] CH$_2$OH	DMSO, (COCl)$_2$	*t*-C$_4$H$_9$(CH$_3$)$_2$SiO [structure] CHO (—)	451
t-C$_4$H$_9$(CH$_3$)$_2$SiO [structure] CH$_2$OH, OH	(CH$_3$)$_2$S, NCS	*t*-C$_4$H$_9$(CH$_3$)$_2$SiO [structure] CHO (95), OH	452
C$_{14}$ [naphthalene] OCH$_3$, CH$_2$OH, OCH$_3$, CH$_3$	(CH$_3$)$_2$SeO	[naphthalene] OCH$_3$, CHO, OCH$_3$, CH$_3$ (98)	47
[naphthalene] CH$_3$O, OCH$_3$, CH$_2$OH, OCH$_3$	(CH$_3$)$_2$SeO	[naphthalene] CH$_3$O, OCH$_3$, CHO, OCH$_3$ (98)	47
[furan-cyclohexane] HOCH$_2$ ... OH	DMSO, (COCl)$_2$	[furan-cyclohexane] OHC ... OH (—)	453
[tetralone] CH$_3$O, (CH$_2$)$_2$OH, CH$_3$O, O	DMSO, DCC, TFA, Py	[tetralone] CH$_3$O, CH$_2$CHO, CH$_3$O, O (66)	454
HO(CH$_2$)$_2$ [dioxolane-furan structure]	DMSO, SO$_3$, Py	OHCCH$_2$ [dioxolane-furan structure] (65) + methylthiomethyl ether (17)	455
[dioxolane] CH$_2$OH, 4-CH$_3$OC$_6$H$_4$	DMSO, (COCl)$_2$	[dioxolane] CHO (—), 4-CH$_3$OC$_6$H$_4$	456

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

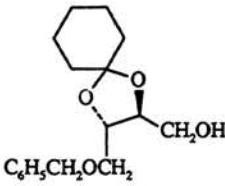| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	$(CH_3)_2SeO$	(92)	47
	DMSO, $(COCl)_2$	(—)	389
$CH_2=CH(CH_2)_3$	DMSO, $(COCl)_2$	(95)	457
	DMSO, $(COCl)_2$	(>68)	458
	DMSO, $(COCl)_2$	(88)	459
(Z)-n-C$_4$H$_9$CH=CH(CH$_2$)$_8$OH	1. COCl$_2$ 2. DMSO 3. (C$_2$H$_5$)$_3$N	(Z)-n-C$_4$H$_9$CH=CH(CH$_2$)$_7$CHO (21)	434
1-Tetradecanol	DMSO, $(COCl)_2$, $-60°$ DMSO, $(COCl)_2$, $-10°$ $(CH_3)_2SeO$ DMSO, TFAA DMSO, TFAA, DIPEA DMSO, SO$_3$, Py	1-Tetradecanal (23) " (96) " (75) " (72) " (85) " (42)	22 22 47 22 22 22
C$_{15}$	DMSO, Ac$_2$O	(—)	460
	DMSO, $(COCl)_2$	(62)	370
	DMSO, $(COCl)_2$	(90)	370
	DMSO, DCC	*exo,exo* (~100) *endo,endo* (—)	461 461
	$(CH_3)_2S$, NCS	(88)	462

TABLE I.   OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
$C_6H_5CH_2OCH_2O$ ... CH_2OH	DMSO, $(COCl)_2$	$C_6H_5CH_2OCH_2O$ ... CHO (>90)	390
$CH_3O_2C(CH_2)_3$ ... OAc CH_2OH	DMSO, $(COCl)_2$	$CH_3O_2C(CH_2)_3$ ... OAc CHO (85)	463
$C_6H_5CH_2OCH_2$ ... OCH_2OCH_3 CH_3OCH_2O ... CH_2OH	DMSO, $(COCl)_2$	$C_6H_5CH_2OCH_2$ ... OCH_2OCH_3 CH_3OCH_2O ... CHO (82)	464
(dithiane/dioxolane structure) O_2CCH_2Cl CH_2OH	DMSO, TFAA	(dithiane/dioxolane structure) O_2CCH_2Cl CHO (>67)	465
... CH_2OH	DMSO, $(COCl)_2$, −10°	... CHO (92)	22
(epoxide structure) CH_2OH	DMSO, Ac_2O	(epoxide structure) CHO (—)	466
$(CH_2=CHCH_2)_2NCH(CH_2)_3OH$ $CO_2C_4H_9$-t	DMSO, $(COCl)_2$	$(CH_2=CHCH_2)_2NCH(CH_2)_2CHO$ (97) $CO_2C_4H_9$-t	467
$CH_2OSi(CH_3)_2C_4H_9$-t CH_2OH (epoxide)	DMSO, $(COCl)_2$	$CH_2OSi(CH_3)_2C_4H_9$-t CHO (epoxide) (—)	468
$THPO(CH_2)_{10}OH$	DMSO, $(COCl)_2$	$THPO(CH_2)_9CHO$ (—)	469
1-Pentadecanol	DMSO, $(COCl)_2$, −10°	1-Pentadecanal (99)	22
	DMSO, TFAA	" (66)	22
$(n\text{-}C_4H_9)_3Sn(CH_2)_3OH$	$(CH_3)_2S$, NCS	$(n\text{-}C_4H_9)_3SnCH_2CH_2CHO$ (81)	470
C$_{16}$ (anthracene) CHO / CH_2OH	DMSO, SO_3, Py	(anthracene) CHO / CHO (95)	471
(naphthalene) OCH_3 CH_2OH / CH_3O dioxolane	$(CH_3)_2SeO$	(naphthalene) OCH_3 CHO / CH_3O dioxolane (93)	47
(naphthalene)—$CHCH_2OH$ C_4H_9-t α and β	DMSO, DCC, Py, TFA	(naphthalene)—CHCHO α (71) C_4H_9-t β (97)	472
(naphthalene)—$CHC(CH_2)_2CH_2OH$ CH_3	DMSO, DCC, Py, TFA	(naphthalene)—$CHC(CH_2)_2CHO$ CH_3 (98)	472
(methylenedioxyphenyl)—CH=CH—CH=CH—$(CH_2)_5OH$	DMSO, DCC, Py, TFA	(methylenedioxyphenyl)—CH=CH—CH=CH—$(CH_2)_4CHO$ (83)	473
...CON—...CH_2OH $CH_2C_6H_5$	DMSO, $(COCl)_2$	...CON—...CHO (>75) $CH_2C_6H_5$	474

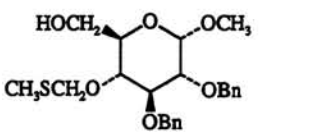TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
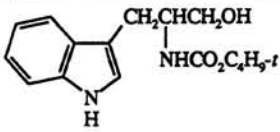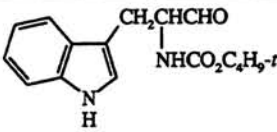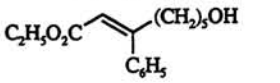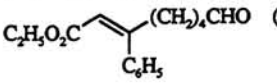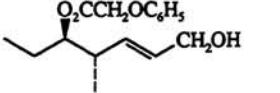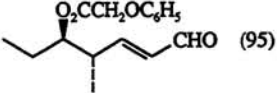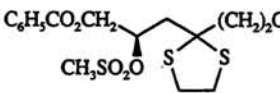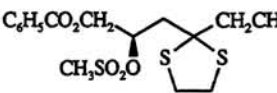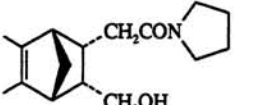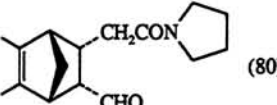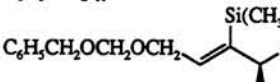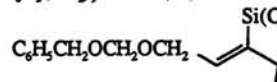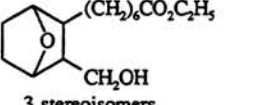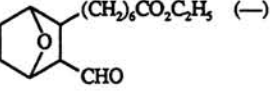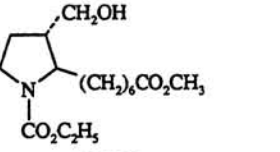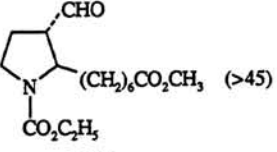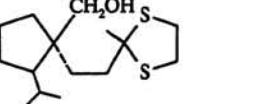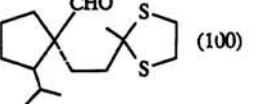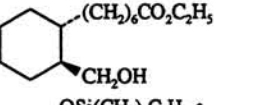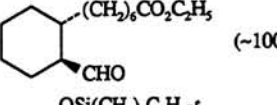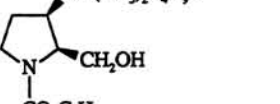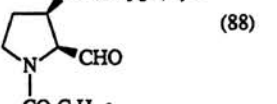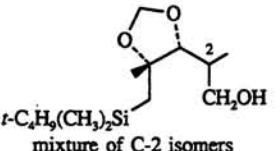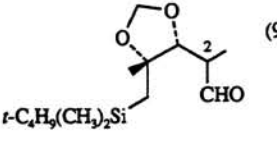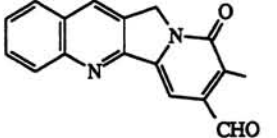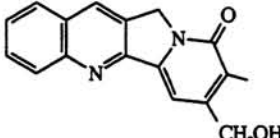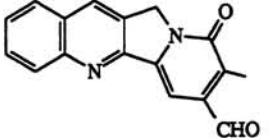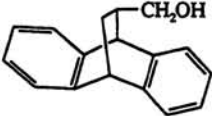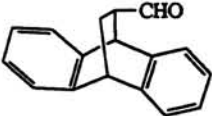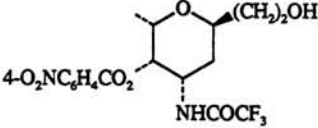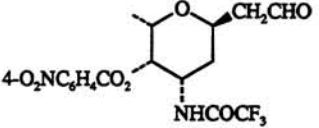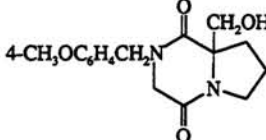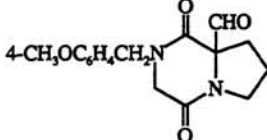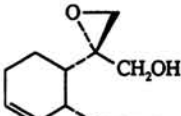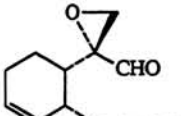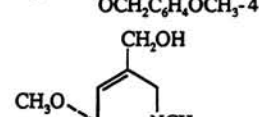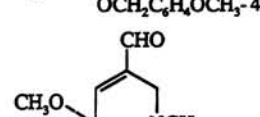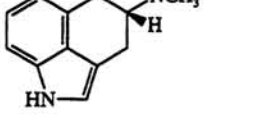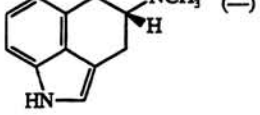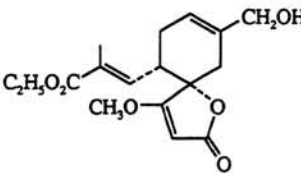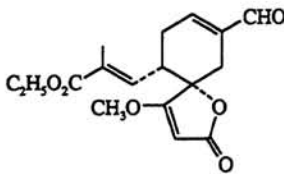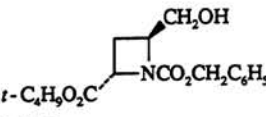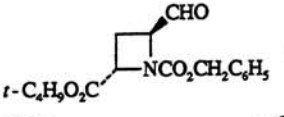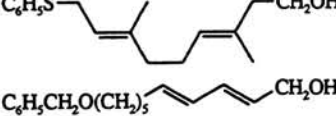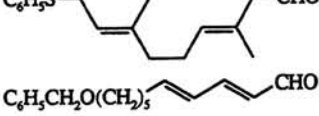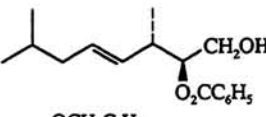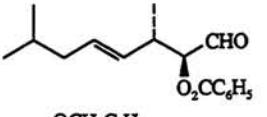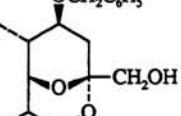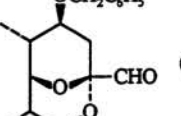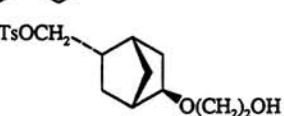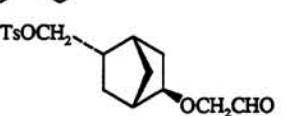
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.

DMSO, SO₃, Py → product (85), ref 88

(E,E)-C₆H₅CH₂O(CH₂)₄(CH═CH)₂CH₂OH | DMSO, (COCl)₂ | (E,E)-C₆H₅CH₂O(CH₂)₄(CH═CH)₂CHO (>57) | 475

(CH₃)₂S, NCS | (47) | 370

DMSO, (COCl)₂ | (95) | 111, 476

DMSO, (COCl)₂ | (85) | 477

DMSO, CMC, H₃PO₄ | (80) | 478

C₆H₅(CH₂)₁₀OH | DMSO, (COCl)₂ | C₆H₅(CH₂)₉CHO (—) | 469

DMSO, (COCl)₂ | (>72) | 111

DMSO, DCC | (—) | 461

3 stereoisomers

DMSO, DCC, Py, TFA | (>45) | 479

DMSO, SO₃, Py | (100) | 480

DMSO, DCC, Py | (~100) | 481

DMSO, TFAA | (88) | 482

1-Hexadecanol | DMSO, (COCl)₂, −35° | 1-Hexadecanal (80) | 22

DMSO, (COCl)₂ | (95) | 483

mixture of C-2 isomers

DMSO, Ac₂O | (70) | 484

388

389

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
[structure: CH₂OH-substituted dibenzobicyclic]	DMSO, (COCl)₂	[structure: CHO product] (—)	485
[structure: pyran with (CH₂)₂OH, 4-O₂NC₆H₄CO₂, NHCOCF₃]	DMSO, (COCl)₂	[structure] CH₂CHO, 4-O₂NC₆H₄CO₂, NHCOCF₃ (73)	294
C₆H₅CH₂O₂CNHCH(CH₂C₆H₅)CH₂OH	DMSO, SO₃, Py	C₆H₅CH₂O₂CNHCH(CH₂C₆H₅)CHO (85)	88
[structure: 4-CH₃OC₆H₄CH₂N diketopiperazine with CH₂OH]	DMSO, (COCl)₂	[structure: 4-CH₃OC₆H₄CH₂N with CHO] (82)	486
[structure: cyclohexene with epoxide CH₂OH, OCH₂C₆H₄OCH₃-4]	DMSO, (COCl)₂	[structure with CHO] (>45)	487
[structure: CH₃O, NCH₃, HN indole, CH₂OH]	DMSO, DCC, TFA	[structure with CHO] (—)	488
[structure: C₂H₅O₂C, CH₃O, cyclohexene furanone with CH₂OH]	DMSO, (COCl)₂	[structure with CHO] (60)	489
[structure: azetidine t-C₄H₉O₂C, NCO₂CH₂C₆H₅, CH₂OH]	DMSO, DCC, Py, TFA	[structure with CHO] (75)	490
C₆H₅S—[chain]—CH₂OH	DMSO, (COCl)₂	C₆H₅S—[chain]—CHO (72)	119
C₆H₅CH₂O(CH₂)₅[diene]CH₂OH	DMSO, (COCl)₂	C₆H₅CH₂O(CH₂)₅[diene]CHO (>75)	491
[structure with CH₂OH, O₂CC₆H₅]	DMSO, (COCl)₂	[structure with CHO, O₂CC₆H₅] (98)	492
[structure: OCH₂C₆H₅ pyran with CH₂OH]	DMSO, (COCl)₂	[structure with CHO] (99)	493
[structure: TsOCH₂ bicyclic O(CH₂)₂OH]	DMSO, (COCl)₂	[structure: TsOCH₂ OCH₂CHO] (>63)	494

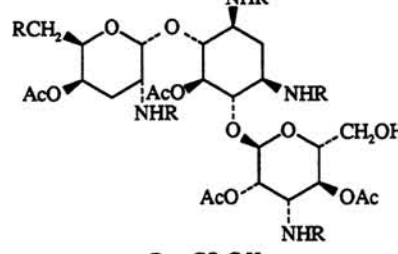TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
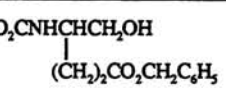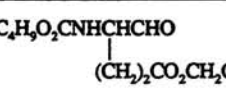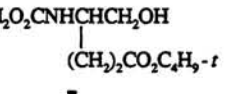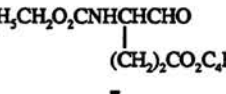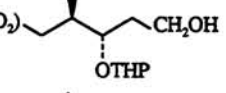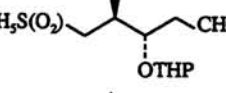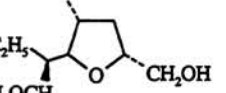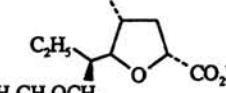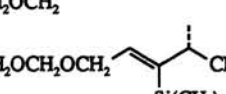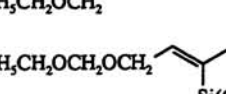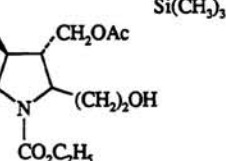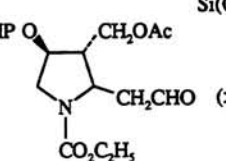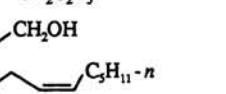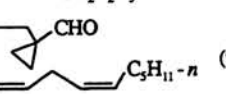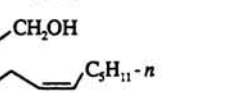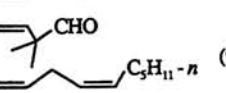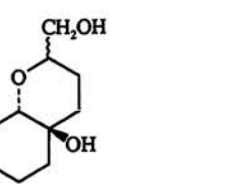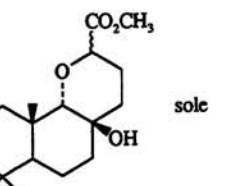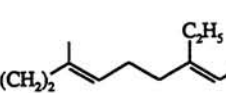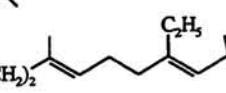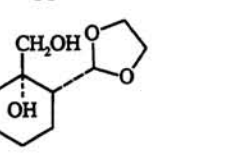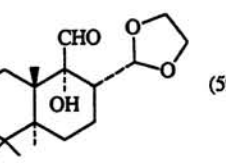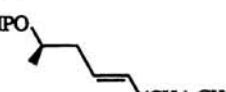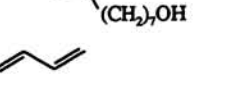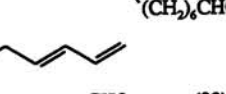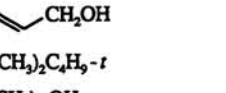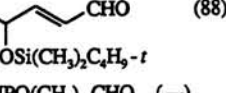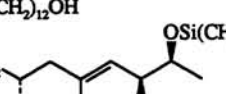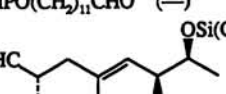
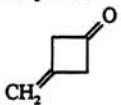| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
t-C₄H₉O₂CNHCHCH₂OH (CH₂)₂CO₂CH₂C₆H₅	DMSO, SO₃, Py	t-C₄H₉O₂CNHCHCHO (88) (CH₂)₂CO₂CH₂C₆H₅	88
C₆H₅CH₂O₂CNHCHCH₂OH (CH₂)₂CO₂C₄H₉-t	DMSO, SO₃, Py	C₆H₅CH₂O₂CNHCHCHO (79) (CH₂)₂CO₂C₄H₉-t	90
C₆H₅S(O₂)⟋⟍CH₂OH OTHP	DMSO, (COCl)₂	C₆H₅S(O₂)⟋⟍CHO (>83) OTHP	401
[structure with C₂H₅, C₆H₅CH₂OCH₂, CH₂OH]	1. DMSO, (COCl)₂ 2. Ag₂O	[structure with C₂H₅, C₆H₅CH₂OCH₂, CO₂H] (95)	495
C₆H₅CH₂OCH₂OCH₂⟋⟍CH₂OH Si(CH₃)₃	DMSO, (COCl)₂	C₆H₅CH₂OCH₂OCH₂⟋⟍CHO (>64) Si(CH₃)₃	118
THPO, CH₂OAc [pyrrolidine] (CH₂)₂OH CO₂C₂H₅	DMSO, CMC, Py, TFA	THPO, CH₂OAc [pyrrolidine] CH₂CHO (>10) CO₂C₂H₅	496
CH₂OH [cyclopropane ring] C₅H₁₁-n	DMSO, SO₃, Py	CHO [cyclopropane ring] C₅H₁₁-n (90)	497
CH₂OH [ring] C₅H₁₁-n	DMSO, (COCl)₂	CHO [ring] C₅H₁₁-n (94)	498
CH₂OH [decalin/pyran structure] OH	1. DMSO, TFAA 2. CH₂N₂	CO₂CH₃ [decalin/pyran structure] OH sole	186
CH₃O₂C(CH₂)₂ [chain] C₂H₅ (CH₂)₂OH	DMSO, (COCl)₂	CH₃O₂C(CH₂)₂ [chain] C₂H₅ CH₂CHO (89)	412, 413
CH₂OH [decalin with dioxolane] OH	DMSO, (CCl₃CO)₂O	CHO [decalin with dioxolane] OH (59)	499
THPO, [chain] (CH₂)₇OH	(CH₃)₂S, NCS	THPO, [chain] (CH₂)₆CHO (75)	500
CH₂OH [chain with diene] OSi(CH₃)₂C₄H₉-t	DMSO, (COCl)₂	CHO [chain with diene] OSi(CH₃)₂C₄H₉-t (88)	475, 501
THPO(CH₂)₁₂OH	DMSO, (COCl)₂	THPO(CH₂)₁₁CHO (—)	469
HOCH₂ [chain] OSi(CH₃)₂C₄H₉-t	DMSO, (COCl)₂	OHC [chain] OSi(CH₃)₂C₄H₉-t (81)	424

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
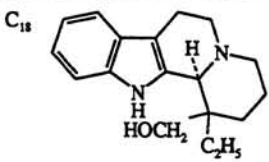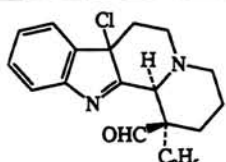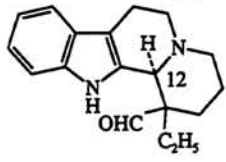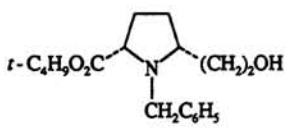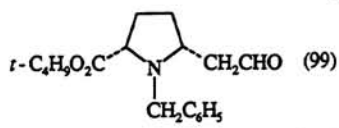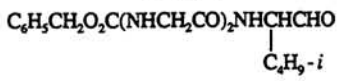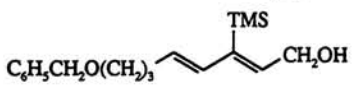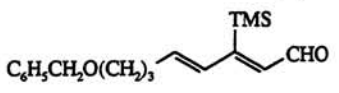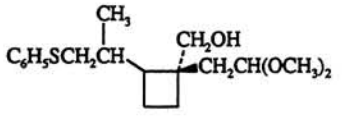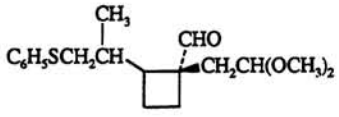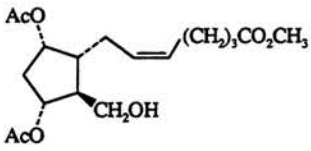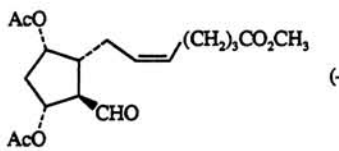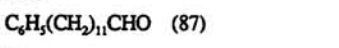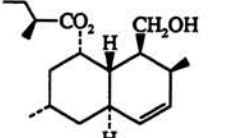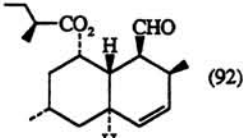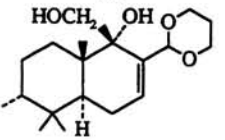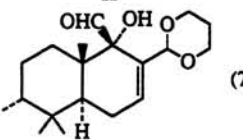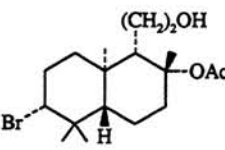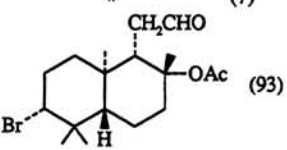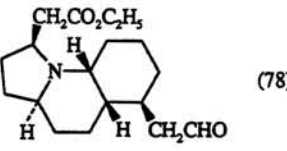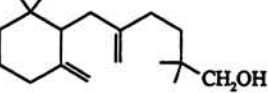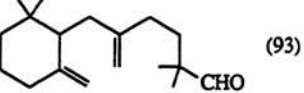
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{18}$ β-CH$_2$OH	DMSO, (COCl)$_2$	(80)	169
	DMSO, SO$_3$, Py	β-CHO (80)	169
α-CH$_2$OH	DMSO, DCC, H$_3$PO$_4$	" (38)	502
	DMSO, SO$_3$, Py	" α-CHO (50)	169
	DMSO, (COCl)$_2$	" (83)	170, 503
	DMSO, DCC, H$_3$PO$_4$	" " (88)	170, 503
t-C$_4$H$_9$O$_2$C (CH$_2$)$_2$OH CH$_2$C$_6$H$_5$	DMSO, (COCl)$_2$	t-C$_4$H$_9$O$_2$C CH$_2$CHO (99) CH$_2$C$_6$H$_5$	92
C$_6$H$_5$CH$_2$O$_2$C(NHCH$_2$CO)$_2$NHCHCH$_2$OH C$_4$H$_9$-i	DMSO, DCC	C$_6$H$_5$CH$_2$O$_2$C(NHCH$_2$CO)$_2$NHCHCHO C$_4$H$_9$-i (—)	504
TMS C$_6$H$_5$CH$_2$O(CH$_2$)$_3$ CH$_2$OH	DMSO, (COCl)$_2$	TMS C$_6$H$_5$CH$_2$O(CH$_2$)$_3$ CHO (92)	505
CH$_3$ C$_6$H$_5$SCH$_2$CH CH$_2$OH CH$_2$CH(OCH$_3$)$_2$	DMSO, SO$_3$, Py	CH$_3$ C$_6$H$_5$SCH$_2$CH CHO CH$_2$CH(OCH$_3$)$_2$ (>92)	506
AcO (CH$_2$)$_3$CO$_2$CH$_3$ CH$_2$OH AcO	DMSO, DCC	AcO (CH$_2$)$_3$CO$_2$CH$_3$ CHO AcO (—)	507
C$_6$H$_5$(CH$_2$)$_{12}$OH	DMSO, (COCl)$_2$	C$_6$H$_5$(CH$_2$)$_{11}$CHO (87)	469
CH$_2$OH	DMSO, (COCl)$_2$	CHO (92)	508
HOCH$_2$ OH	DMSO, DCC, Py, TFA	OHC OH (73)	499, 509
	DMSO, (CCl$_3$CO)$_2$O	" (7)	499
(CH$_2$)$_2$OH OAc Br	DMSO, (COCl)$_2$	CH$_2$CHO OAc (93) Br	510
CH$_2$CO$_2$C$_2$H$_5$ (CH$_2$)$_2$OH	DMSO, (COCl)$_2$	CH$_2$CO$_2$C$_2$H$_5$ CH$_2$CHO (78)	511
CH$_2$OH	DMSO, (COCl)$_2$	CHO (93)	512, 513

TABLE I. Oxidation of Primary Alcohols (*Continued*)

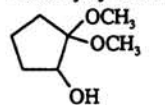| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
(both α and β CH₂OH)	DMSO, CMC, Py, TFA	(90)	514
(Z,Z)-Octadeca-9, 12-dien-1-ol	DMSO, (COCl)₂, –10°	(Z,Z)-Octadec-9, 12-dien-1-al (98)	8
(Z)-Octadec-10-en-1-ol	DMSO, (COCl)₂, –60°	(Z)-Octadec-10-en-1-al (98)	8
(E)-	DMSO, (COCl)₂, –60°	(E)- " (98)	8
1-Octadecanol	DMSO, (COCl)₂, –10°	1-Octadecanal (86)	8
C₁₉	(CH₃)₂S, NCS	(—)	515
	DMSO, (COCl)₂	(>46)	94
C₆H₅CH₂O₂CCH(NHCbz)CH₂CH₂OH	DMSO, DCC, H₃PO₄, Py	C₆H₅CH₂O₂CCH(NHCbz)CH₂CHO (—)	516
(C₆H₅)₂C=CHC(CH₃)(C₂H₅)CH₂OH	DMSO, DCC, Py, TFA	(C₆H₅)₂C=CHC(CH₃)(C₂H₅)CHO (95)	517
	DMSO, SO₃, Py	(73)	518
	(CH₃)₂S, NCS	(—)	120
	DMSO, (COCl)₂	(88)	519
	DMSO, DCC, Py, TFA	(82)	30
	DMSO, (COCl)₂	(—)	492
	1. DMSO, DCC, H₃PO₄ 2. Ag₂O	(20)	520

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
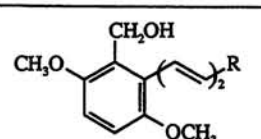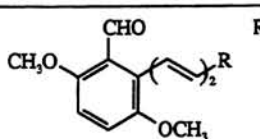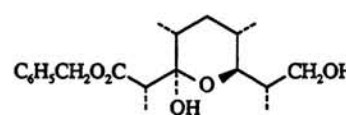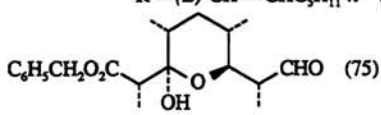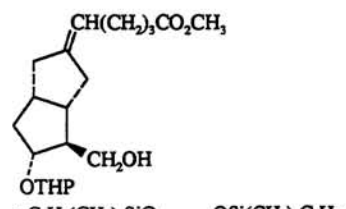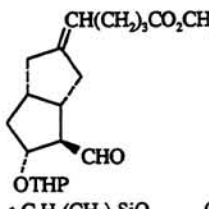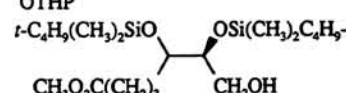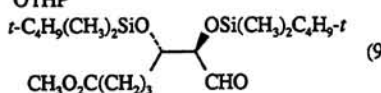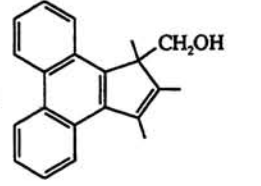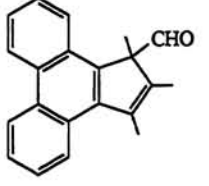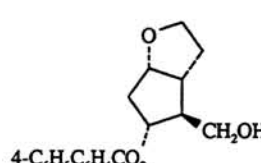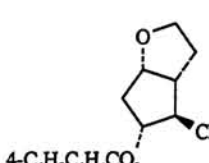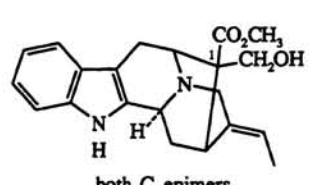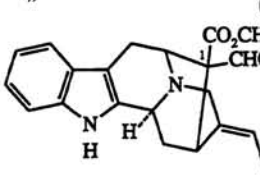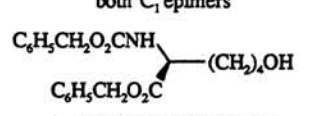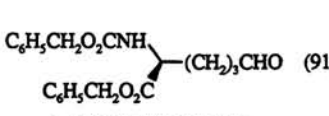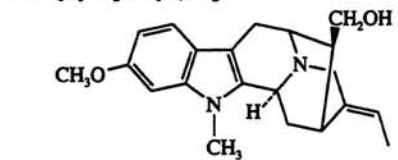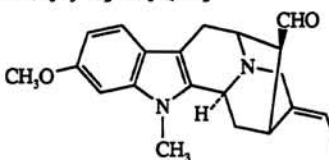
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
NHCO$_2$C$_4$H$_9$-t HO ... HN O$_2$SC$_6$H$_4$OCH$_3$-4 CO$_2$CH$_3$	DMSO, DCC	NHCO$_2$C$_4$H$_9$-t HO ... N CO$_2$CH$_3$ O$_2$SC$_6$H$_4$OCH$_3$-4 (—)	95
t-C$_4$H$_9$O$_2$CNHCHCH$_2$OH (CH$_2$)$_4$NHCO$_2$CH$_2$C$_6$H$_5$	DMSO, SO$_3$, Py	t-C$_4$H$_9$O$_2$CNHCHCHO (CH$_2$)$_4$NHCO$_2$CH$_2$C$_6$H$_5$ (77)	88
(CH$_2$)$_3$OH C$_2$H$_5$	DMSO, TFAA, DIPEA	(CH$_2$)$_2$CHO C$_2$H$_5$ (80)	74
n-C$_6$H$_{13}$ (CH$_2$)$_6$OH O$^-$	DMSO, (COCl)$_2$	n-C$_6$H$_{13}$ (CH$_2$)$_5$CHO O$^-$ (—)	174
C$_{20}$ CH$_2$OH	DMSO, (COCl)$_2$	CHO (95)	521
HOCH$_2$ CO$_2$CH$_3$ OH OCH$_3$ OCH$_3$ OCH$_3$	DMSO, (COCl)$_2$	CHO CO$_2$CH$_3$ OH OCH$_3$ OCH$_3$ OCH$_3$ R=H (78) R=CH$_3$SCH$_2$ (14)	291
OCH$_2$C$_6$H$_5$ CH$_2$CH$_2$OH OCH$_2$C$_6$H$_5$	DMSO, DCC, H$_3$PO$_4$	OCH$_2$C$_6$H$_5$ CH$_2$CHO OCH$_2$C$_6$H$_5$ (91)	522
THPO H (CH$_2$)$_4$CO$_2$CH$_3$ H CH$_2$OH	DMSO, SO$_3$, Py	THPO H (CH$_2$)$_4$CO$_2$CH$_3$ H CHO (>41)	523
NCH$_3$ H CH$_2$OH CH$_3$O O α, α-isomer at 1, 2	DMSO, TFAA	NCH$_3$ H CHO CH$_3$O O α, α-isomer (72)	524
"	DMSO, TFAA	" α, α-isomer (—)	525
C$_6$H$_5$CONH S S CH$_2$OH O$_2$CCH$_2$Cl	DMSO, TFAA	C$_6$H$_5$CONH S S CHO O$_2$CCH$_2$Cl (—)	465
NH 8 N H CH$_2$OH CH$_2$CH(OCH$_3$)$_2$ α - 8H	DMSO, TFAA	NH 8 N H CHO CH$_2$CH(OCH$_3$)$_2$ α - 8H (78)	526
	DMSO, DCC, Py, TFA	(85)	526
C$_6$H$_5$CH$_2$O OAc CH$_2$OH C$_2$H$_5$ O O	DMSO, (COCl)$_2$	C$_6$H$_5$CH$_2$O OAc CHO C$_2$H$_5$ O O (>50)	527

TABLE I. Oxidation of Primary Alcohols (*Continued*)

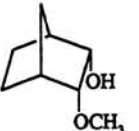| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)₂	R = C₇H₁₅-n (65)	528
		R = (E)-CH=CHC₅H₁₁-n (59)	528
C₆H₅CH₂O₂C ... CH₂OH	DMSO, Py, SO₃	C₆H₅CH₂O₂C ... CHO (75)	72
CH(CH₂)₃CO₂CH₃ ... CH₂OH OTHP	DMSO, SO₃, Py	CH(CH₂)₃CO₂CH₃ (98) ... CHO OTHP	529
t-C₄H₉(CH₃)₂SiO ... OSi(CH₃)₂C₄H₉-t CH₃O₂C(CH₂)₃ CH₂OH	DMSO, (COCl)₂	t-C₄H₉(CH₃)₂SiO ... OSi(CH₃)₂C₄H₉-t (96) CH₃O₂C(CH₂)₃ CHO	530
C₂₁ CH₂OH	DMSO, DCC, Py, TFA	CHO (33)	52
CH₂OH 4-C₆H₅C₆H₄CO₂	C₆H₅SCH₃, Cl₂	CHO (>90) 4-C₆H₅C₆H₄CO₂	18
	(CH₃)₂S, NCS	" (—)	18
	DMSO, polymer-supported carbodiimide	" (90)	55
	Polymer-supported sulfide, Cl₂	" (100)	42
CO₂CH₃ CH₂OH both C₁ epimers	(CH₃)₂S, NCS	CO₂CH₃ CHO (—)	120
C₆H₅CH₂O₂CNH ... (CH₂)₄OH C₆H₅CH₂O₂C	DMSO, (COCl)₂	C₆H₅CH₂O₂CNH ... (CH₂)₃CHO (91) C₆H₅CH₂O₂C	531
t-C₄H₉O₂CNHCHCH₂OH ... 4-(C₆H₅CH₂O)C₆H₄CH₂	DMSO, SO₃, Py	t-C₄H₉O₂CNHCHCHO ... (81) 4-(C₆H₅CH₂O)C₆H₄CH₂	88
CH₂OH CH₃O CH₃	(CH₃)₂S, NCS	CHO CH₃O (76) CH₃	532

400

401

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
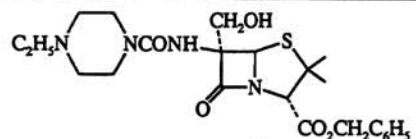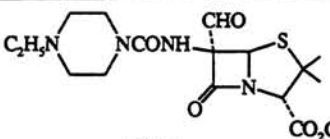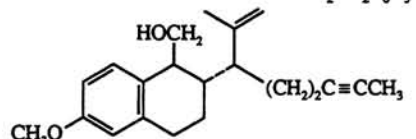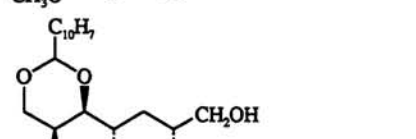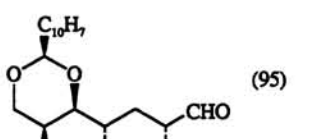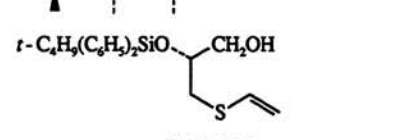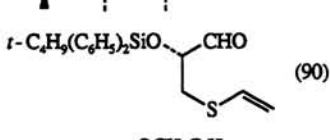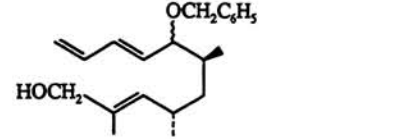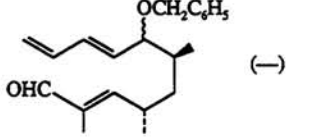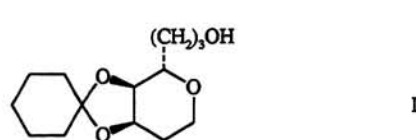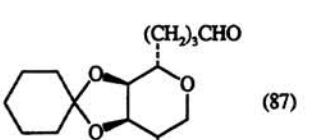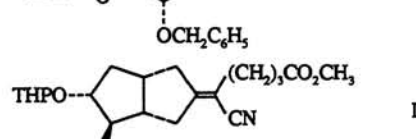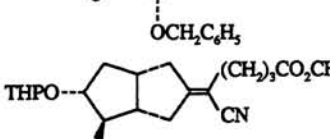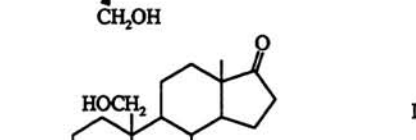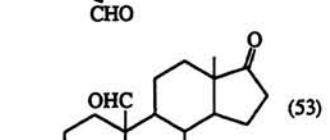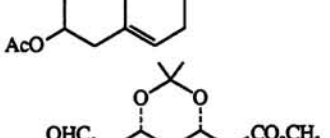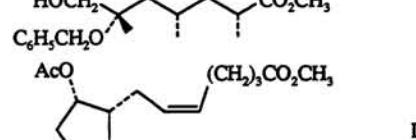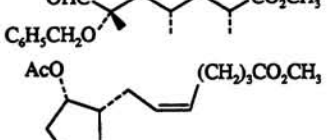
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, SO₃, Py	(——)	164
	DMSO, (COCl)₂	(>70)	533
	DMSO, (COCl)₂	(95)	72
	DMSO, (COCl)₂	(90)	534
	DMSO, (COCl)₂	(—)	451
	DMSO, (COCl)₂	(87)	444
	DMSO, SO₃, Py.	(>82)	535
	DMSO, DCC, Py, TFA	(53)	30
	DMSO, (COCl)₂	(87)	536
	DMSO, SO₃, Py	(90)	537

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
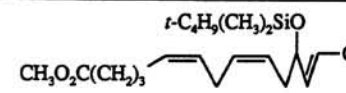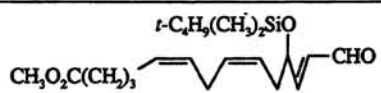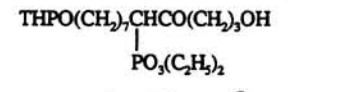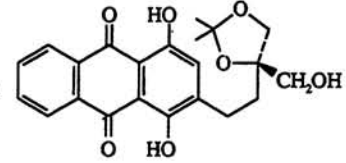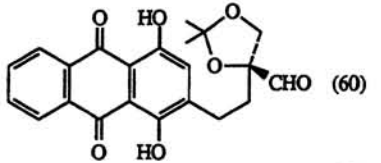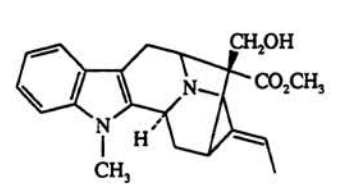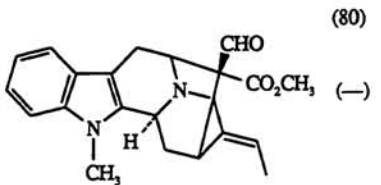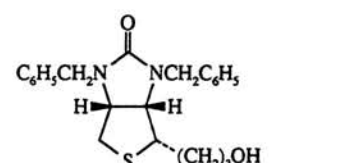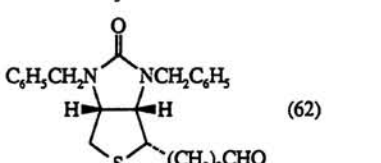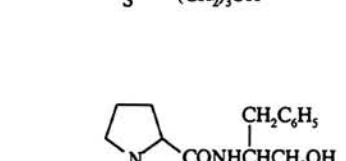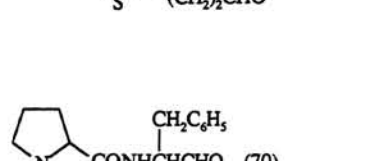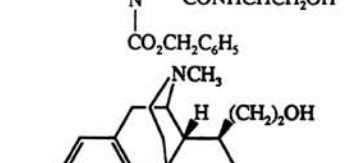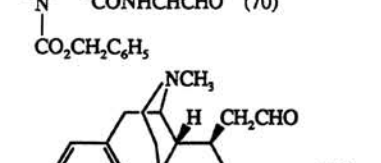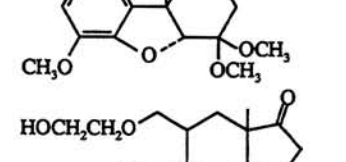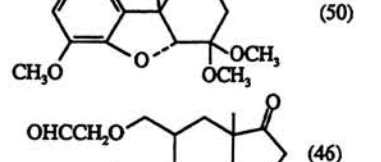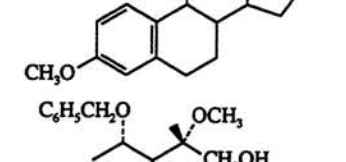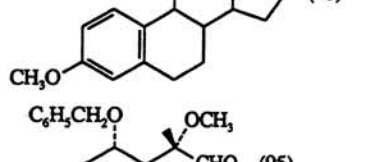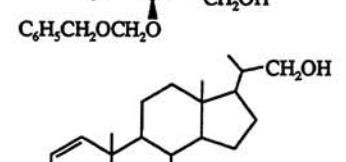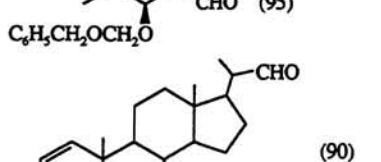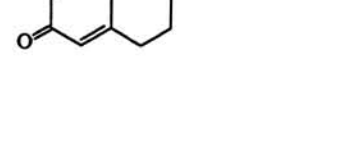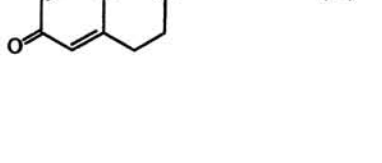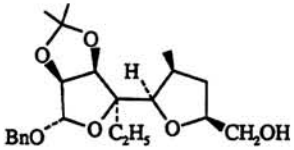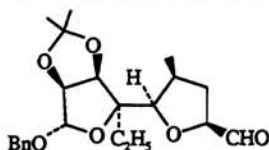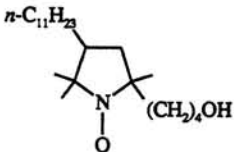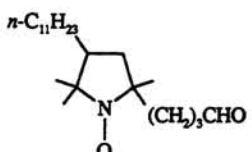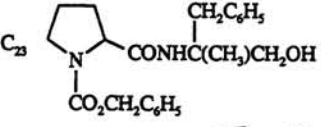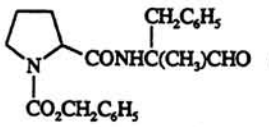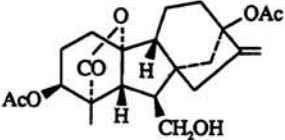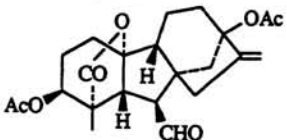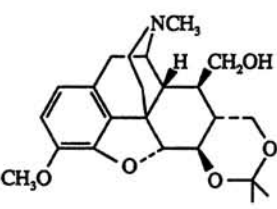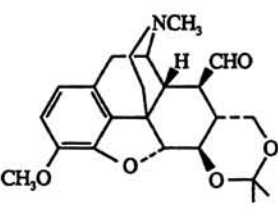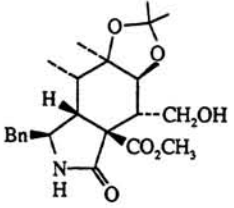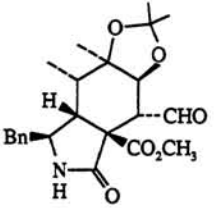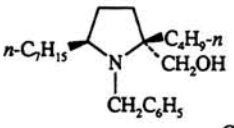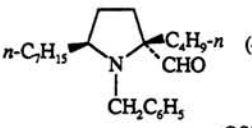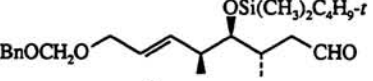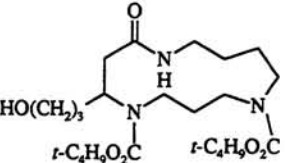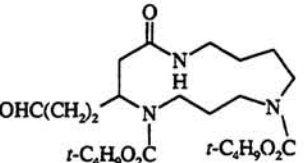
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.

DMSO, (COCl)₂ — (—) 538

THPO(CH₂)₇CHCO(CH₂)₃OH | DMSO, (COCl)₂ | THPO(CH₂)₇CHCOCH₂CH₂CHO (62) | 62
PO₃(C₂H₅)₂ — PO₃(C₂H₅)₂

C₂₂

(CH₃)₂S, NCS — (60) 539

DMSO, DCC, TFA, Py — (80) 540

(CH₃)₂S, NCS — (—) 120

DMSO, DCC, Py, TFA — (62) 541, 542

DMSO, (COCl)₂ — (70) 96

DMSO, TFAA — (50) 524

(CH₃)₂S, NCS — (46) 286

DMSO, (COCl)₂ — (95) 543

(CH₃)₂S, NCS — (90) 544

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)$_2$	(85)	483
	DMSO, (COCl)$_2$	(—)	174
C$_{23}$	DMSO, (COCl)$_2$	(67)	96
	(CH$_3$)$_2$S, NCS	(71) + RCH$_2$OCH$_2$SCH$_3$ (12)	545
	DMSO, TFAA	(90)	524
	DMSO, (COCl)$_2$	(91)	546
n-C$_7$H$_{15}$	DMSO, (COCl)$_2$	n-C$_7$H$_{15}$ (—)	547
BnOCH$_2$O CH$_2$OH	DMSO, (COCl)$_2$	BnOCH$_2$O CHO (96)	111
	DMSO, DCC, TFA, Py	(82)	548

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C_{24}	$(CH_3)_2S$, NCS	(78)	173
	DMSO, TFAA	(82)	549
	DMSO, DCC, Py, TFA	(84)	30, 312
	DMSO, $(COCl)_2$	(—)	174
C_{25}	DMSO, DCC, TFA, Py	(88)	93
	DMSO, $(COCl)_2$	(97)	550
	DMSO, DCC	(>58)	551
C_{26} $RNH(CH_2)_3N(CH_2)_3OH$	DMSO, $(COCl)_2$	$RNH(CH_2)_3N(CH_2)_2CHO$ (—)	552
	DMSO, $(COCl)_2$	(93)	553

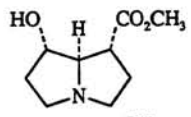TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, TFAA	(80)	554
3,4-(CH₃O)₂C₆H₃CH₂O	DMSO, (COCl)₂	(>60)	555
	DMSO, (COCl)₂	(81)	556
	1. DMSO, (COCl)₂ 2. H₃O⁺	(84)	111, 476
	DMSO, DCC	(>48)	551
3 stereoisomers at C₁, C₃	DMSO, CMC, Py, TFA	(90–95)	514
C₂₇	DMSO, (COCl)₂	(95)	557
	DMSO, (COCl)₂	(94)	97
	DMSO, SO₃, Py	(100)	89
	DMSO, (COCl)₂	(>74)	556

TABLE I.   OXIDATION OF PRIMARY ALCOHOLS (*Continued*)
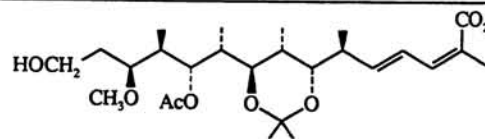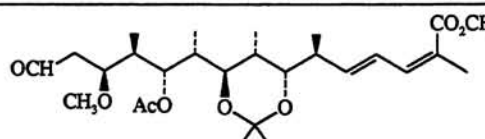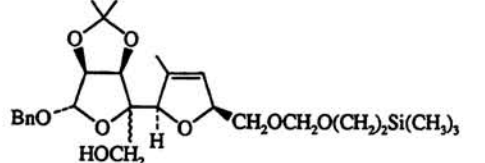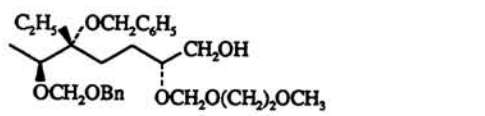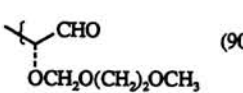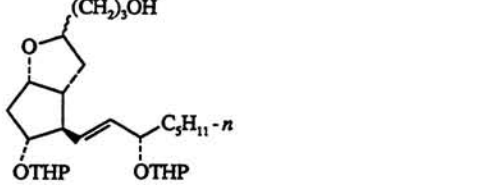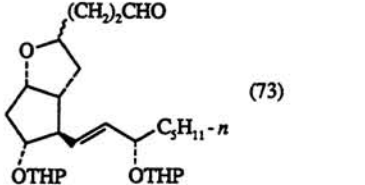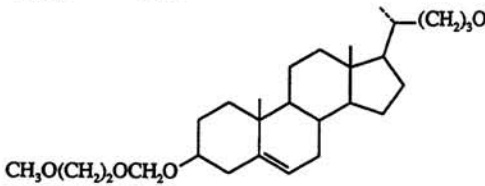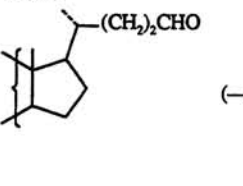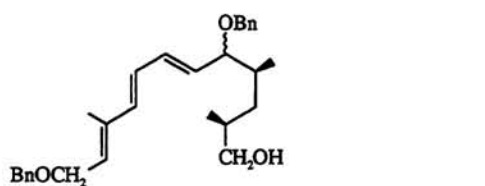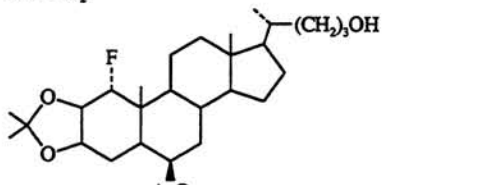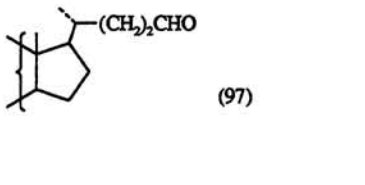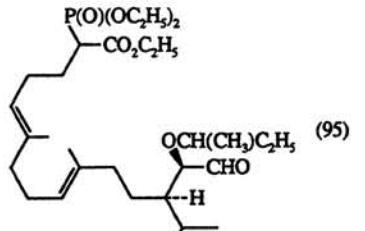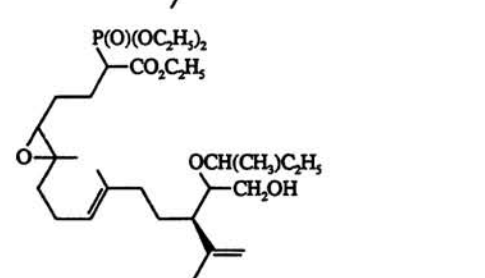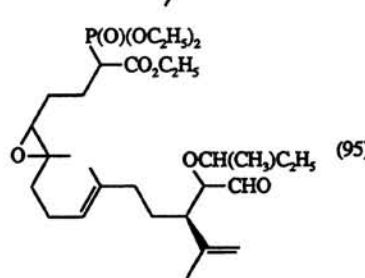
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)$_2$		(—)	558
	DMSO, (COCl)$_2$, THF		(88)	57
C$_{28}$	DMSO, (COCl)$_2$		(90)	559
	DMSO, DCC		(73)	560
	DMSO, (COCl)$_2$		(—)	561
C$_{29}$	DMSO, (COCl)$_2$		(>58)	168
	DMSO, (COCl)$_2$		(97)	562
C$_{30}$	DMSO, (COCl)$_2$		(95)	563
	DMSO, (COCl)$_2$		(95)	564

412

413

TABLE I. OXIDATION OF PRIMARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
[structure: penicillin with CH₂OH, BnO₂CCHCONH, thiophene]	DMSO, DCC, Py, TFA	[structure: penicillin with CHO] (—)	164
C₃₁ [structure: BnO, CH₃O aromatic with CH₂CH₂OH, CH₂N...C₆H₄OBn-4]	DMSO, DCC, Py, TFA	[structure with CH₂CHO] (82)	93
[structure: penicillin RCONH, CH₂OH, CO₂CH₂C₆H₅; R = C₆H₅CHNHCON(piperazinedione)NC₂H₅]	DMSO, SO₃, Py	[structure: RCONH, CHO] (—)	164
[structure: t-C₄H₉(C₆H₅)₂SiO, C₆H₅CH₂OCH₂O, CH₂OH]	DMSO, SO₃, Py	[structure: t-C₄H₉(C₆H₅)₂SiO, C₆H₅CH₂OCH₂O, CHO] (95)	565
C₃₂ [structure: TsN(Bn), BnO, OBn, CH₂OH]	DMSO, (COCl)₂	[structure: TsN(Bn), BnO, OBn, CHO] (67)	566
[structure: BnOCH₂, OBn, CH₂OH polyene]	DMSO, (COCl)₂	[structure: OBn, CHO] (>67)	168
t-C₄H₉O₂CTyr(Gly)₂PheNHCHCH₂OH, (CH₂)₂SCH₃	DMSO, SO₃, Py	*t*-C₄H₉O₂CTyr(Gly)₂PheCHCHO (72), (CH₂)₂SCH₃	88
[structure: cyclopentane with CH₂OH, CH₂CO(CH₂)₄CO₂CH₃, THPO, OTHP, C₅H₁₁-*n*]	DMSO, SO₃, Py	[structure: cyclopentane with CHO] (>25)	567
C₃₃ *t*-C₄H₉O₂CTyr(Gly)₂PheNHCH(C₄H₉-*i*)CH₂OH	DMSO, SO₃, Py	*t*-C₄H₉O₂CTyr(Gly)₂PheNHCH(C₄H₉-*i*)CHO (61)	88
C₃₅ [structure: penicillin RCONH, CH₂OH, CO₂Bn; R = 3,4-(AcO)₂C₆H₃CHNHCON(piperazinedione)N-C₂H₅]	DMSO, SO₃, Py	[structure: RCONH, CHO, CO₂Bn] (—)	164
[structure: BnO, CH₃OCH₂O, OCH₂OCH₃, CH₂OH, OH, CH₃NCO₂CH₃, BnO aromatic]	DMSO, SO₃, Py	[structure: OCH₂OCH₃, CHO] (88)	568

TABLE I. Oxidation of Primary Alcohols (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.

C_{37} t-$C_4H_9(C_6H_5)_2SiOCH_2$—

DMSO, (COCl)₂   (—)   569

C_{39}

DMSO, SO₃, Py   (—)   164

R = 4-BnO₂CC₆H₄CHNHCON

RCONH—SC(CH₃)₂CH₂OH

DMSO, Ac₂O   R = C₆H₅CH₂   (64)   165

"   R = C₆H₅OCH₂   (40)   165

C_{40} RO   (CH₂)₃CO₂CH₃

DMSO, DCC   (—)   507

R = 4-C₆H₅C₆H₄CO

DMSO, (COCl)₂   (81)   569

HOCH₂—

DMSO, SO₃, Py   (>52)   569

TABLE II. OXIDATION OF PRIMARY CARBOHYDRATE ALCOHOLS
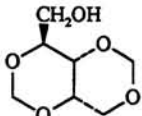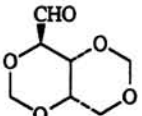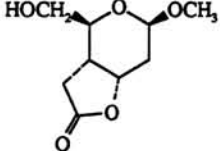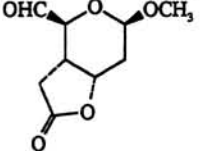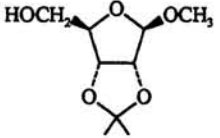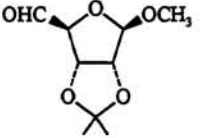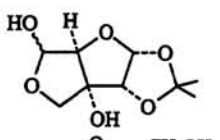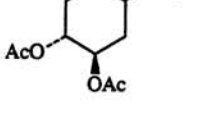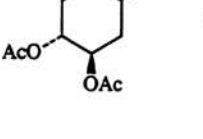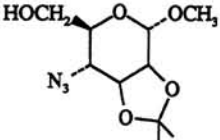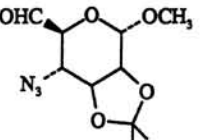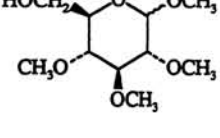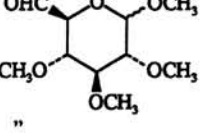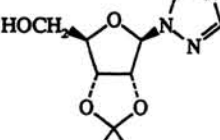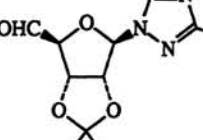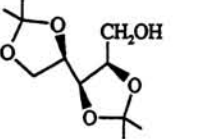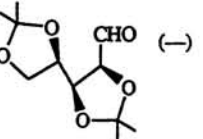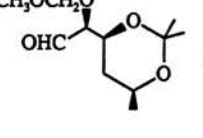
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C_7	DMSO, DCC, $CHCl_2CO_2H$	(41)	570
	$(CH_3)_2S$, NCS	" (20)	570
C_9	DMSO, DCC	(54)	571
	DMSO, DCC, H_3PO_4	(80)	316
	DMSO, $(COCl)_2$	" (42) + α–CHO (43)	108
	DMSO, Ac_2O	(63)	572
C_{10}	DMSO, DCC, H_3PO_3	(45)	573
	DMSO, SO_3, Py	(>56)	574
	DMSO, DCC, Py, TFA	(30)	207
	DMSO, P_2O_5, DMF	" (30)	207
C_{11}	DMSO, DCC, Py, TFA	(70)[a]	575
	DMSO, $(COCl)_2$	(—)	126
	DMSO, $(COCl)_2$	(90)	576

TABLE II. OXIDATION OF PRIMARY CARBOHYDRATE ALCOHOLS (*Continued*)
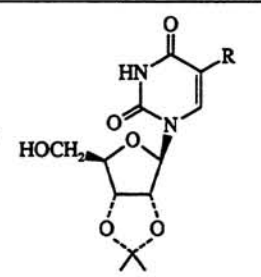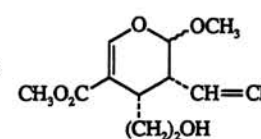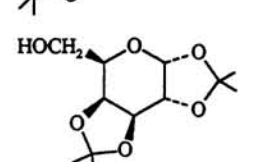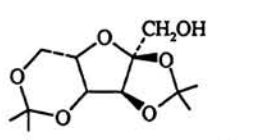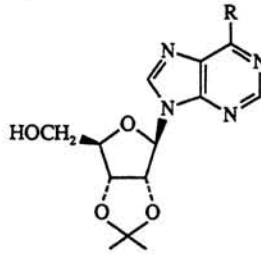
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.

C₁₁

R = H
R = CH₃

	DMSO, DIPC, CHCl₂CO₂H	(60)ᵃ	577
	DMSO, Ac₂O	(—)	578
	DMSO, DCC, CHCl₂CO₂H	(87)	148

C₁₂

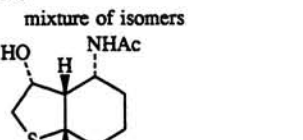| | DMSO, DCC, Py, TFA | (90) | 579 |

| | DMSO, DCC, Py, HCl | (84) | 580 |

| | DMSO, (COCl)₂ | (80) | 26 |

	DMSO, DCC, H₃PO₄	" (80)	581
	DMSO, Py, TFA	" (46)	581
	DMSO, SO₃, Py	" (75)	145, 582
	DMSO, DCC, Py, HCl	" (83)	583
	DMSO, Ac₂O	" (trace)	584
		+ methylthiomethyl ether (major)	

| | DMSO, Ac₂O, 25°, 2 d | (40) | 585 |

C₁₃

R = Cl
R = NH₂

	DMSO, DCC, H₃PO₄	I (32)ᵇ	586
	DMSO, H₃PO₄, (C₆H₅)₂C=C=NC₆H₄CH₃-4	I (60)ᶜ	587
	DMSO, DCC, Py, TFA	I (85)	
	1. DMSO, DCC, Cl₂CHCO₂H		588, 589
	2. H₂O, CH₃CO₂H, 100°	(80)	590

TABLE II. OXIDATION OF PRIMARY CARBOHYDRATE ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, DCC, Py, TFA	(72)	591
	DMSO, DCC, Py, TFA	(85)	592
α-2-OAc	DMSO, Py, SO₃	(75)	145
	DMSO, Py, SO₃	" (α-2-OAc) (82)	145
	DMSO, DCC, Py, TFA	" (33)	593
C₁₄	DMSO, DCC, H₃PO₄	(—)	586
	DMSO, (COCl)₂	(63)	594
	DMSO, (COCl)₂	(65)	595
	DMSO, DCC	(—)	596
	DMSO, (COCl)₂	(98)	597
	DMSO, (COCl)₂	(87)	598
	DMSO, (COCl)₂	(85)	599
	DMSO, Py, SO₃	(83)	145
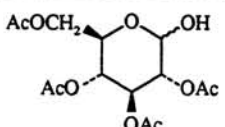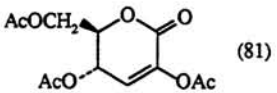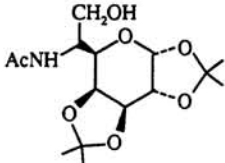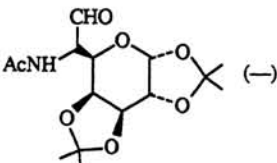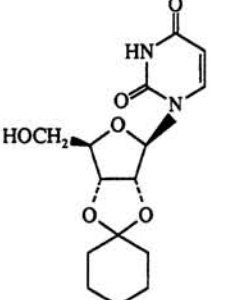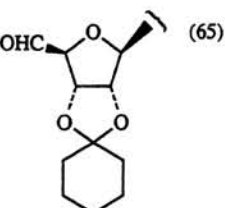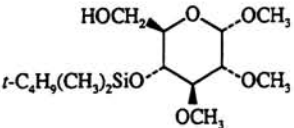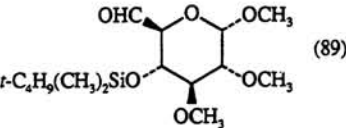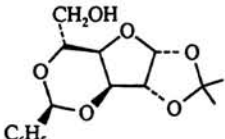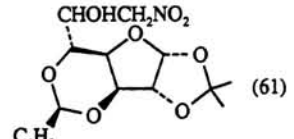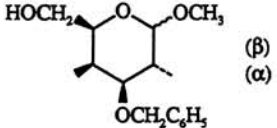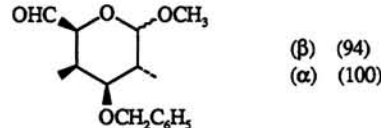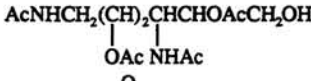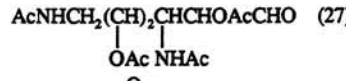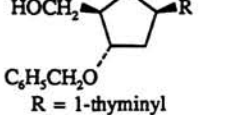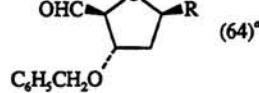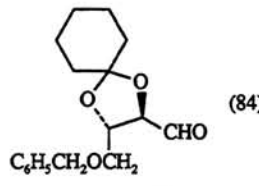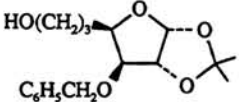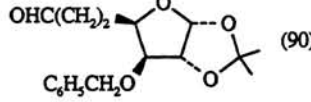
TABLE II.   OXIDATION OF PRIMARY CARBOHYDRATE ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
AcOCH$_2$ / AcO / OAc / OAc / OH	DMSO, Py, SO$_3$	AcOCH$_2$ / AcO / OAc (81)	145
C$_{15}$ CH$_2$OH / AcNH (acetonide structure)	DMSO, CMC	CHO / AcNH (—)	600
HOCH$_2$ (uridine cyclohexylidene structure)	1. DMSO, DIPC, CHCl$_2$CO$_2$H 2. (C$_6$H$_5$NHCH$_2$)$_2$ 3. p-TsOH, H$_2$O	OHC (65)	316
HOCH$_2$ / O / OCH$_3$ / t-C$_4$H$_9$(CH$_3$)$_2$SiO / OCH$_3$ / OCH$_3$	DMSO, (COCl)$_2$	OHC / O / OCH$_3$ / t-C$_4$H$_9$(CH$_3$)$_2$SiO / OCH$_3$ / OCH$_3$ (89)	601
C$_{16}$ CH$_2$OH (benzylidene acetonide structure) / C$_6$H$_5$	1. DMSO, DCC, CHCl$_2$CO$_2$H, Py 2. CH$_3$NO$_2$, CH$_3$ONa	CHOHCH$_2$NO$_2$ (structure) / C$_6$H$_5$ (61)	602
HOCH$_2$ / O / OCH$_3$ (β) (α) / OCH$_2$C$_6$H$_5$	DMSO, (COCl)$_2$ "	OHC / O / OCH$_3$ (β) (94) (α) (100) / OCH$_2$C$_6$H$_5$	603 604
AcNHCH$_2$(CH)$_2$CHCHOAcCH$_2$OH / OAc NHAc	DMSO, DCC, H$_3$PO$_4$	AcNHCH$_2$(CH)$_2$CHCHOAcCHO (27) / OAc NHAc	605
C$_{17}$ HOCH$_2$ / O / R / C$_6$H$_5$CH$_2$O / R = 1-thyminyl	DMSO, DCC, TFA, Py	OHC / O / R / C$_6$H$_5$CH$_2$O (64)^a	606, 607
(cyclohexylidene dioxolane) CH$_2$OH / C$_6$H$_5$CH$_2$OCH$_2$	DMSO, (COCl)$_2$	(cyclohexylidene dioxolane) CHO / C$_6$H$_5$CH$_2$OCH$_2$ (84)	389
HO(CH$_2$)$_3$ / O / O / C$_6$H$_5$CH$_2$O	DMSO, (COCl)$_2$	OHC(CH$_2$)$_2$ / O / O / C$_6$H$_5$CH$_2$O (90)	608

TABLE II. OXIDATION OF PRIMARY CARBOHYDRATE ALCOHOLS (*Continued*)
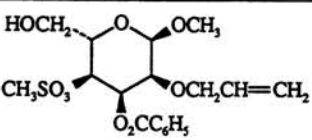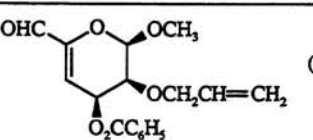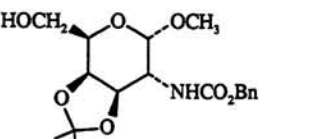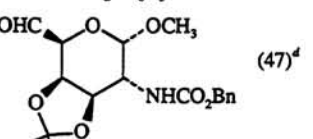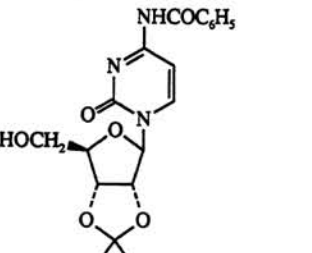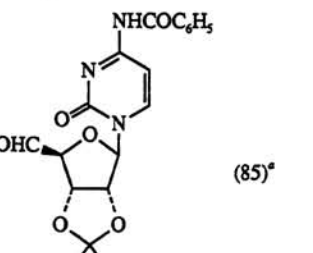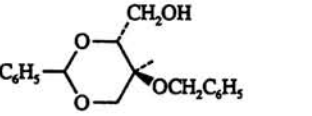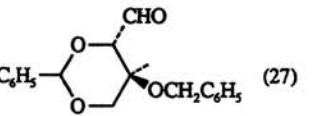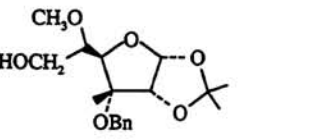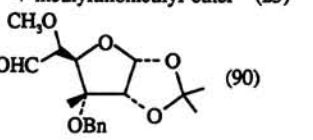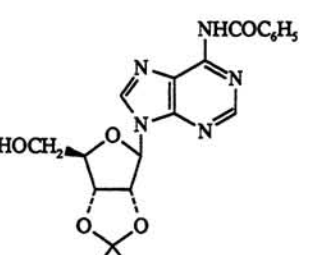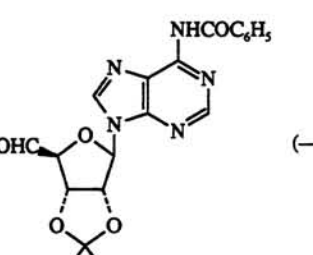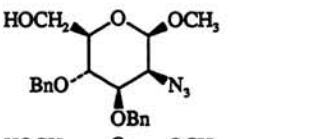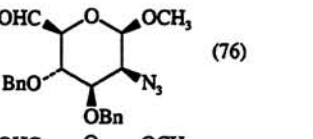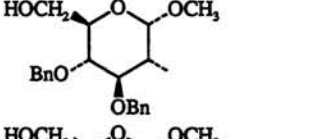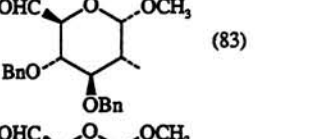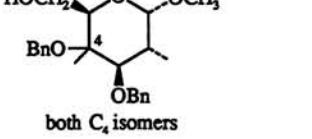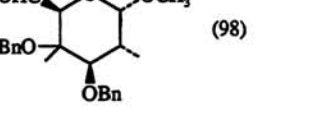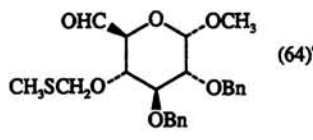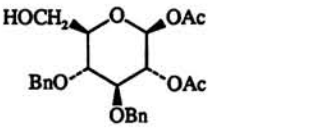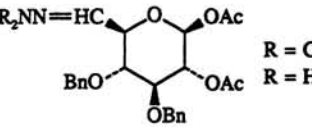
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₈	DMSO, (COCl)₂	(94)	153
	DMSO, DCC, Py, H₃PO₄	(47)[d]	609, 610
C₁₉	DMSO, DCC, TFA, Py	(85)[e]	607
	DMSO, DCC, H₃PO₄, Py	(27) + methylthiomethyl ether (25)	293
	DMSO, (COCl)₂	(90)	611
C₂₀	DMSO, DCC	(—)	607, 612
C₂₁	DMSO, Ac₂O	(76)	613
C₂₂	DMSO, (COCl)₂	(83)	579
C₂₃ both C₄ isomers	DMSO, (COCl)₂	(98)	603, 614–617
	DMSO, DCC, Py, TFA	(64)[e]	618
C₂₄	1. (CH₃)₂S, NCS 2. R₂NNH₂	R = CH₃ (66) R = H (47)	619, 620

TABLE II. OXIDATION OF PRIMARY CARBOHYDRATE ALCOHOLS (*Continued*)
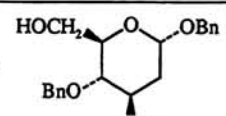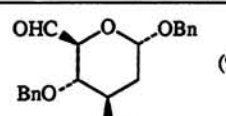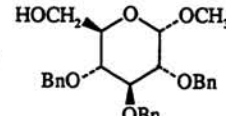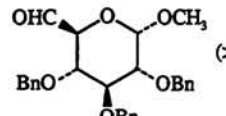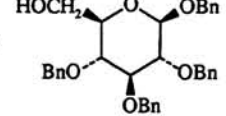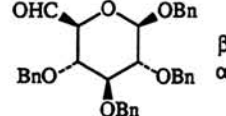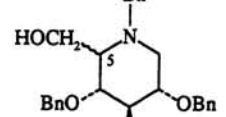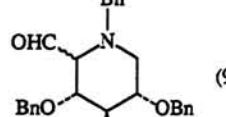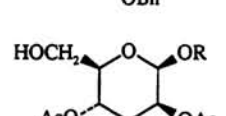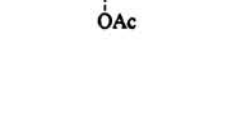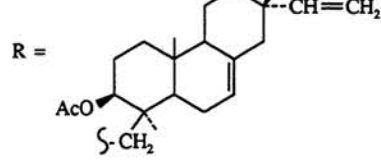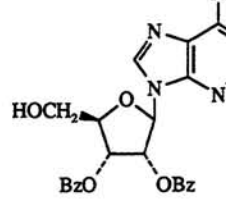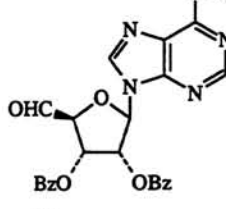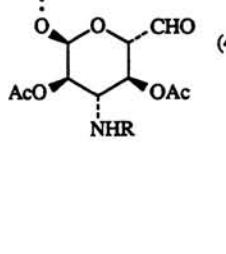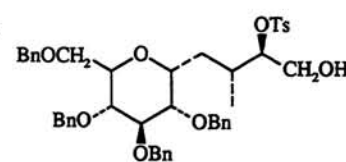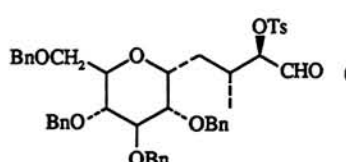
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C_{27}	DMSO, DCC, H_3PO_4, Py	(93)	621
C_{28}	DMSO, $(COCl)_2$	(>70)	622
C_{34}	DMSO, DCC, H_3PO_4, Py	β (80) / α (37)	623 / 624
(C-5 β)	DMSO, $(COCl)_2$	(90)	625
(C-5 α)	DMSO, $(COCl)_2$	" (—)	626
	DMSO, SO_3, Py	(46)	150
$R =$			
C_{38}	DMSO, DCC, $CH_3PO_3H_2$	$(57)^a$	149
$C_{4?}$	DMSO, DCC	(45)	151
$R = CO_2C_2H_5$			
C_{46}	DMSO, $(COCl)_2$	(>80)	628

428

429

TABLE II. OXIDATION OF PRIMARY CARBOHYDRATE ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{68}$	DMSO, DCC, Py, TFA	(85)	141
	DMSO, P$_2$O$_5$	" (40)	141
	DMSO, Ac$_2$O	(70)	141
		+ methylthiomethyl ether (13)	

^{a} The product was isolated as the 1,3-diphenylimidazolidine derivative.

^{b} The product was isolated as the 2,4-dinitrophenylhydrazone.

^{c} The product was isolated as the phenylhydrazone.

^{d} The product was isolated as the nitromethane adduct.

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
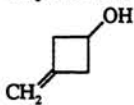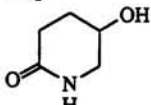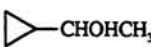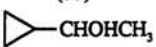
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C$_3$ Cyclopropanol	DMSO, TFAA, DIPEA	Cyclopropanone (78)[a]	8
C$_4$ Cyclobutanol	DMSO, TFAA	Cyclobutanone (95)	27
2-Butanol	1. COCl$_2$ 2. DMSO	2-Butanone (78)	15
	DMSO, Hg(OAc)$_2$, 130°	" (41)	339
	DMSO, SbCl$_5$, O$_2$, 80°	" (51)	326
C$_5$ CH$_3$CHOHCH=CHCN	DMSO, (COCl)$_2$	CH$_3$COCH=CHCN (89)	324
[cyclobutanol structure with CH$_2$ and OH]	DMSO, DCC, quinaldine, TFA	[cyclobutanone structure with CH$_2$] (20)	629
[5-hydroxy-2-piperidinone structure]	1. DMSO, DCC, Py, TFA 2. HCl, H$_2$O	HO$_2$C(CH$_2$)$_2$COCH$_2$NH$_2$·HCl (89)	630
Cyclopentanol	DMSO, (COCl)$_2$	Cyclopentanone (99)	23
	DMSO, TFAA	" (85)	27
	DMSO, ClSO$_2$NCO	" (81)	338
	(CH$_3$)$_2$Se, NCS	" (77)	46
[cyclopropyl]-CHOHCH$_3$	DMSO, TFAA	[cyclopropyl]-CHOHCH$_3$ (63)	27
	DMSO, ClSO$_2$NCO	" (70)	338
CH$_3$CHOHCH$_2$CH=CH$_2$	DMSO, TFAA, −25°	CH$_3$COCH$_2$CH=CH$_2$ (50)	27
C$_6$ (CH$_3$)$_2$C=CHCHOHCCl$_3$	DMSO, DCC, Py, TFA	(CH$_3$)$_2$C=CHCOCCl$_3$ (82)	631
CH$_3$COCH$_2$CHOHCH=CH$_2$	DMSO, (COCl)$_2$	CH$_3$COCH$_2$COCH=CH$_2$ (20)	127
2-Cyclohexenol	DMSO, (COCl)$_2$	2-Cyclohexenone (87)	26
	DMSO, Tf$_2$O	" (46)	45
	DMSO, TFAA	" (82)	24
	DMSO, ClSO$_2$NCO	" (71)	338
(E)-2-Bromocyclohexanol	DMSO, DCC, Py, TFA	2-Bromocyclohexanone (40)	327

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
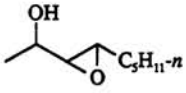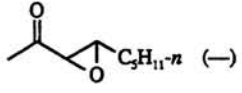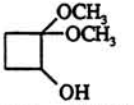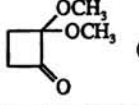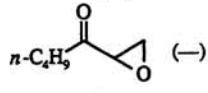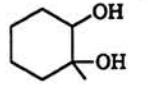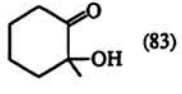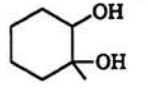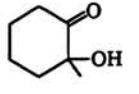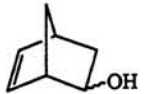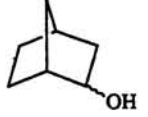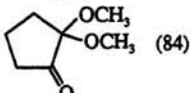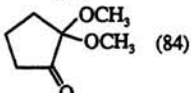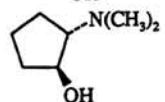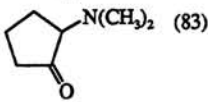
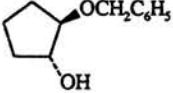| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
Cyclohexanol	DMSO, (COCl)$_2$	Cyclohexanone (95)	23
	DMSO, ClSO$_2$NCO	" (85)	338
	DMSO, TFAA	" (65)	24
	(CH$_3$)$_2$Se, NCS	" (72)	46
	DMSO, Hg(OAc), 130°	" (70)	339
	DMSO, polymer-supported carbodiimide	" (85)	55
	DMSO, AcCl	" (—)	336
(E)-2-Methylcyclopentanol	DMSO, TFAA	2-Methylcyclopentanone (83)	27
[OH, epoxide, C_5H_{11}-n structure]	DMSO, (COCl)$_2$	[ketone, epoxide, C_5H_{11}-n structure] (—)	323
[cyclobutane with OCH$_3$, OCH$_3$, OH]	DMSO, TFAA	[cyclobutanone with OCH$_3$, OCH$_3$] (83)	632
CH$_2$=CHCHOHSi(CH$_3$)$_3$	DMSO, (COCl)$_2$	CH$_2$=CHCOSi(CH$_3$)$_3$ (64)	633
i-C$_3$H$_7$CHOHCH$_3$	C$_6$H$_5$SCH$_3$, electrochemical	i-C$_3$H$_7$CH$_2$COCH$_3$ (89)	20
t-C$_4$H$_9$CHOHCH$_3$	DMSO, (COCl)$_2$	t-C$_4$H$_9$COCH$_3$ (100)	23
	DMSO, TFAA	" (84)	25
	DMSO, Ac$_2$O	" (5)	634
2-Hexanol	(CH$_3$)$_2$Se, NCS	2-Hexanone (60)	46
[n-C$_4$H$_9$, CHOH, epoxide structure]	DMSO, (COCl)$_2$	[n-C$_4$H$_9$, CO, epoxide structure] (—)	323
[cyclohexane with OH, OH, CH$_3$]	C$_6$H$_5$SCH$_3$, Cl$_2$	[cyclohexanone with OH] (83)	19
[bicyclic CH$_2$OH structure]	DMSO, DCC, H$_3$PO$_4$	[bicyclic C=O structure] (81)	635
[bicyclic alkene OH structure]	DMSO, (COCl)$_2$	[bicyclic alkene ketone structure] (>90)	38
	DMSO, DCC	" (—)	636
	DMSO, (COCl)$_2$	" (97)	23
[bicyclic OH structure]	DMSO, TFAA	[bicyclic ketone structure] (96)	25
	DMSO, ClSO$_2$NCO	" (86)	338
(▷)$_2$CHOH	DMSO, BF$_3$, ether, 170°	▷—CH$_2$CH=CHCHO E (39)	138
CH$_3$CH=CHCHOH—◁	DMSO, BF$_3$, ether, 170°	C$_2$H$_5$(CH=CH)$_2$CHO E,E (25)	138
Cycloheptanol	DMSO, (COCl)$_2$, −60°	Cycloheptanone (>90)	38
2-Methylcyclohexanol E,Z	DMSO, (COCl)$_2$, −60°	2-Methylcyclohexanone (100)	23
	DMSO, TFAA	" (84)	25
2-Methylcyclohexanol	C$_6$H$_5$SCH$_3$, electrochemical	" (85)	20, 21
[cyclopentane with OCH$_3$, OCH$_3$, OH]	DMSO, TFAA	[cyclopentanone with OCH$_3$, OCH$_3$] (84)	637
[cyclopentane with N(CH$_3$)$_2$, OH]	DMSO, (COCl)$_2$	[cyclopentanone with N(CH$_3$)$_2$] (83)	638

C$_7$

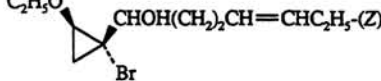TABLE III. Oxidation of Secondary Alcohols (*Continued*)
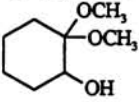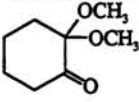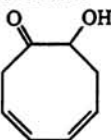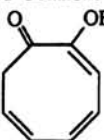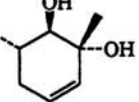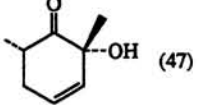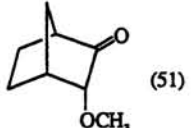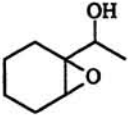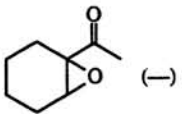
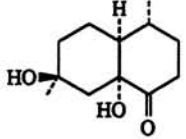| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
2-Heptanol	$(i\text{-}C_3H_7)_2S$, NCS, $-78°$	2-Heptanone (88)	39
	$(n\text{-}C_4H_9)_2S$, NCS, $-78°$	" (90)	39
3-Heptanol	$(i\text{-}C_3H_7)_2S$, NCS, $-78°$	3-Heptanone (88)	39
	$(n\text{-}C_4H_9)_2S$, NCS, $-78°$	" (92)	39
	$(CH_3)_2Se$, NCS	" (58)	46
$(i\text{-}C_3H_7)_2CHOH$	DMSO, TFAA	$(i\text{-}C_3H_7)_2C{=}O$ (100)	25
$CH_2{=}C(CH_3)CHOHSi(CH_3)_3$	DMSO, $(COCl)_2$	$CH_2{=}C(CH_3)COSi(CH_3)_3$ (79)	633
C₈ $C_2H_5O_2CCH_2CHOHCO_2C_2H_5$	DMSO, 2-fluoro-1,3-dimethylpyridinium tosylate	$C_2H_5O_2CCH_2COCO_2C_2H_5$ (76)	216
$n\text{-}C_5H_{11}CHOHCH{=}CH_2$	DMSO, TFAA	$n\text{-}C_5H_{11}COCH{=}CH_2$ (98)	27
2,6-Dimethylcyclohexanol (mixture of isomers)	DMSO, TFAA	2,6-Dimethylcyclohexanone (100)	25
Cyclooctanol	DMSO, $ClSO_2NCO$	Cyclooctanone (79)	339
$C_2H_5COCH(CH_3)CHOHC_2H_5$	DMSO, $(COCl)_2$	$C_2H_5COCH(CH_3)COC_2H_5$ (85)	127
$C_2H_5O_2CCH(CH_3)CHOHC_2H_5$	DMSO, $(COCl)_2$	$C_2H_5O_2CCH(CH_3)COC_2H_5$ (91)	127
	DMSO, TFAA	(90)	637
2-Octanol	DMSO, $(COCl)_2$	2-Octanone (98)	23
	$(CH_3)_2S$, NCS	" (91)	17
	DMSO, TFAA	" (67)	24
	$C_6H_5SCH_3$, electrochemical	" (99)	20
3-Octanol	DMSO, $(COCl)_2$	3-Octanone (>90)	38
	DMSO, $ClSO_2NCO$	(55)	223
	DMSO, TFAA	(—)	639
$CH_2{=}CH(CH_2)_3CHOHCH{=}CH_2$	DMSO, $(COCl)_2$	$CH_2{=}CH(CH_2)_3COCH{=}CH_2$ (—)	303
	DMSO, SO_3, Py	(51)	166
	DMSO, $(COCl)_2$	(47)	640
	DMSO, Py, SO_3	(51)	641
$C_6H_5CHOHCF_3$	DMSO, $(COCl)_2$	$C_6H_5COCF_3$ (>90)	38
$C_6H_5CHOHCH_3$	DMSO, $(COCl)_2$	$C_6H_5COCH_3$ (99)	23
	DMSO, TFAA	" (97)	24
	$(i\text{-}C_3H_7)_2S$, NCS	" (85)	39
	DMSO, $(COCl)_2$	(—)	323

TABLE III. Oxidation of Secondary Alcohols (*Continued*)
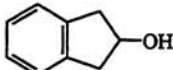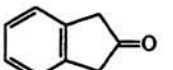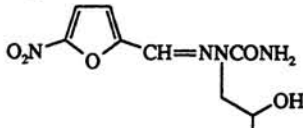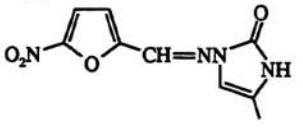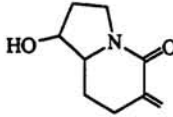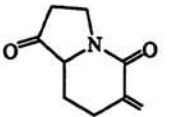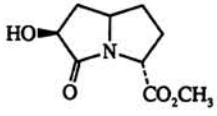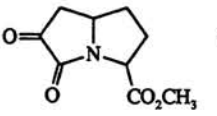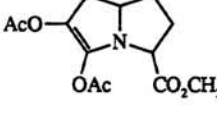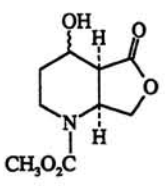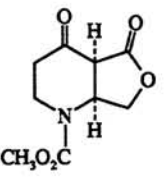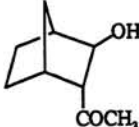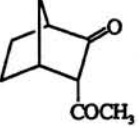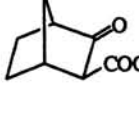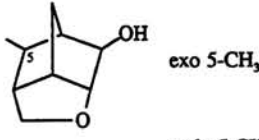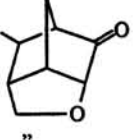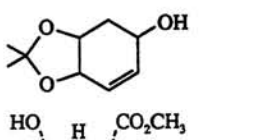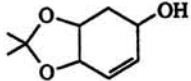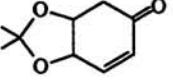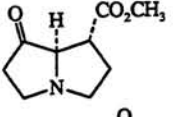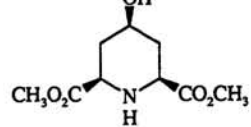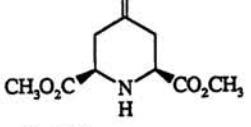
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C$_9$ 4-CF$_3$C$_6$H$_4$CHOHCH$_3$	DMSO, (COCl)$_2$	4-CF$_3$C$_6$H$_4$COCH$_3$ (>90)	38
(2-indanol)	DMSO, (COCl)$_2$	*(2-indanone)* (96)	26
O$_2$N—furan—CH=NNCONH$_2$ (with OH side chain)	DMSO, Ac$_2$O	O$_2$N—furan—CH=N—N *(cyclic urea with CH$_3$)* (77)	163
4-CH$_3$C$_6$H$_4$CHOHCH$_3$	DMSO, (COCl)$_2$	4-CH$_3$C$_6$H$_4$COCH$_3$ (>90)	38
C$_6$H$_5$CH$_2$CHOHCH$_3$	DMSO, O$_2$, 190°	C$_6$H$_5$CH$_2$COCH$_3$ (25) + C$_6$H$_5$CH=CHCH$_3$ (36)	69
C$_6$H$_5$CHOHC$_2$H$_5$	DMSO, CBSB, Py	C$_6$H$_5$COC$_2$H$_5$ (—)	642
C$_6$H$_5$SeCH$_2$CHOHCH$_3$	(CH$_3$)$_2$S, NCS	C$_6$H$_5$SeCH$_2$COCH$_3$ (61)	643
(HO-indolizidinone, methylene)	DMSO, DCC, H$_3$PO$_4$	*(diketo-indolizidinone, methylene)* (85)	644
	DMSO, Ac$_2$O	” (57)	644
(HO-pyrrolizidinone, CO$_2$CH$_3$)	DMSO, DCC, CHCl$_2$CO$_2$H	*(diketo-pyrrolizidine, CO$_2$CH$_3$)* (60)	66
	DMSO, Ac$_2$O	*(AcO, OAc-pyrrolizidine, CO$_2$CH$_3$)* (76)	66
(OH-furo-pyridine, CH$_3$O$_2$C)	DMSO, TFAA	*(keto-furo-pyridine, CH$_3$O$_2$C)* (>30)	612, 645
(bicyclic OH, COCH$_3$)	DMSO, TFAA	*(bicyclic ketone, COCH$_3$)* (80) + *(epimer, COCH$_3$)* (10)	646
(oxabicyclic OH) exo 5-CH$_3$	DMSO, (COCl)$_2$	*(oxabicyclic ketone)* exo 5-CH$_3$ (87)	367, 368
endo 5-CH$_3$	DMSO, (COCl)$_2$	” endo 5-CH$_3$ (79)	367, 647
(dioxolane-cyclohexenol)	DMSO, (COCl)$_2$	*(dioxolane-cyclohexenone)* (55)	26
(HO-pyrrolizidine, CO$_2$CH$_3$)	DMSO, TFAA	*(keto-pyrrolizidine, CO$_2$CH$_3$)* (74)	648
(OH-piperidine, CH$_3$O$_2$C, CO$_2$CH$_3$)	DMSO, DIPC, polymer-supported	*(keto-piperidine, CH$_3$O$_2$C, CO$_2$CH$_3$)* (90)	52
	DMSO, DCC	” (47)	52

TABLE III. Oxidation of Secondary Alcohols (*Continued*)
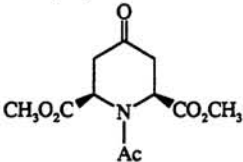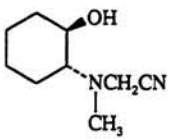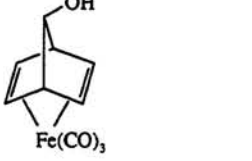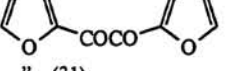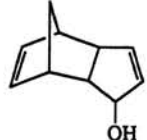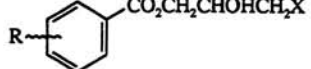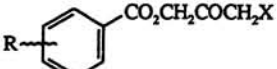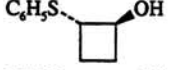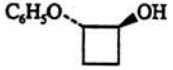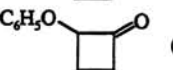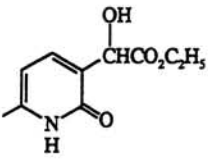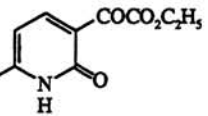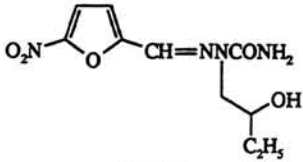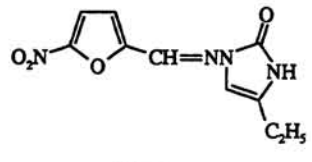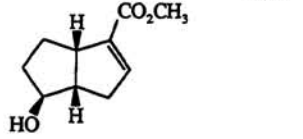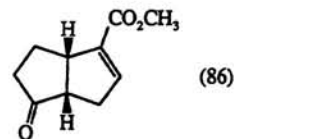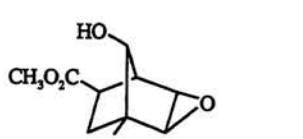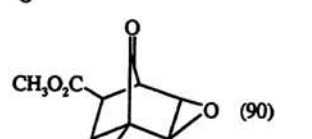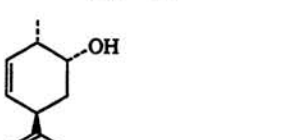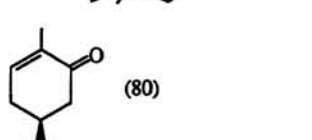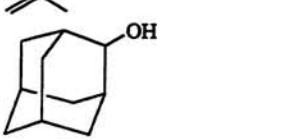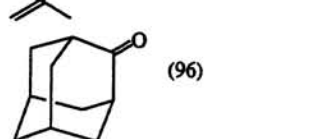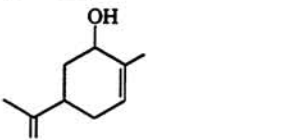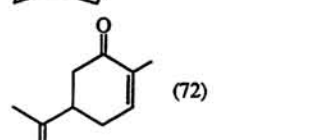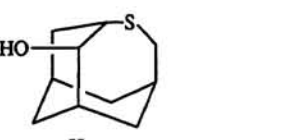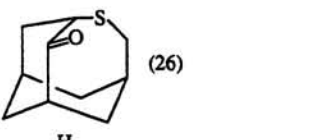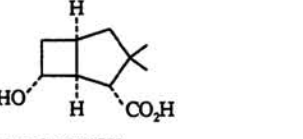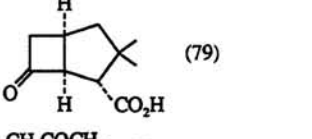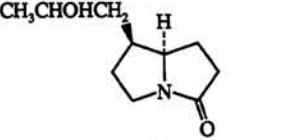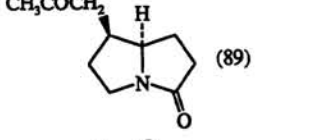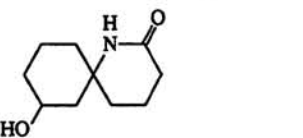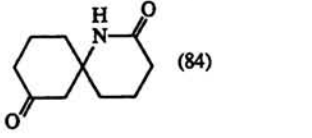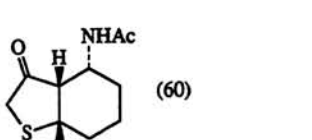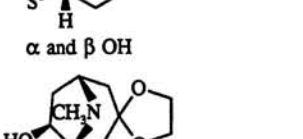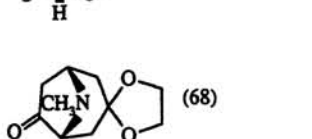
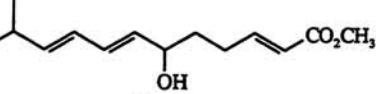| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, DIPC	" (60)	52
	DMSO, DEC	" (53)	52
	DMSO, P₂O₅	" (20)	52
	DMSO, CMC	" (19)	52
	DMSO, Ac₂O	(15)	52
	DMSO, (COCl)₂	(88)	649
(*t*-C₄H₉)₂CHOH	DMSO, (COCl)₂	(*t*-C₄H₉)₂C=O (>90)	38
	DMSO, Py, SO₃	(70)	650
	DMSO, (COCl)₂	(68)	26
	DMSO, Ac₂O	" (31)	651
C₆H₅CHOHCH=CHCN	DMSO, (COCl)₂	C₆H₅COCH=CHCN (98)	292
	DMSO, ClSO₂NCO	(70)	338
C₆H₅CH=CHCHOHCH₃	(*i*-C₃H₇)₂S, NCS	C₆H₅CH=CHCOCH₃ (75)	39
	(*n*-C₄H₉)₂S, NCS	" (80)	39
R = H, X = H, F, Cl, Br R = 4-O₂N, X = F, Cl R = 3,5-(O₂N)₂, X = Cl	DMSO, DCC, Py, TFA	(—)	652
C₆H₅CHOHCO₂C₂H₅	(CH₃)₂Se, NCS	C₆H₅COCO₂C₂H₅ (94)	46
	DMSO, 2-fluoro- 1,3-dimethylpyridinium tosylate	" (88)	216
	DMSO, Ac₂O	(78)	653
	DMSO, Ac₂O	(68)	653
C₆H₅CHOHCO₂C₂H₅	DMSO, 2-fluoro-1,3-dimethyl- pyridinium tosylate	C₆H₅COCO₂C₂H₅ (88)	216
	(CH₃)₂Se, NCS	" (94)	46
	DMSO, Ac₂O	(66)	654

TABLE III. Oxidation of Secondary Alcohols (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac₂O	(76)	163
	DMSO, (COCl)₂	(86)	655
	DMSO, TFAA	(90)	656
	(CH₃)₂S, NCS, TEA	(80)	115
	DMSO, TFAA	(96)	27
	DMSO, (COCl)₂	(72)	26
	DMSO, (COCl)₂	(26)	657
	DMSO, SO₃, Py	(79)	295
	DMSO, (COCl)₂	(89)	658
mixture of isomers	DMSO, (COCl)₂	(84)	659
α and β OH	DMSO, DCC, TFA, Py	(60)	660
	DMSO, DCC, H₃PO₄	(68)	661
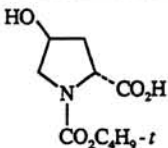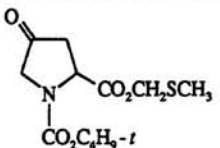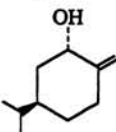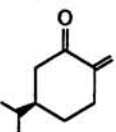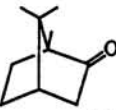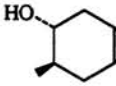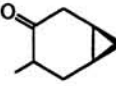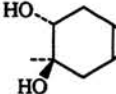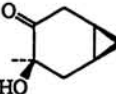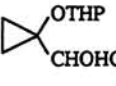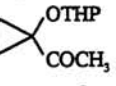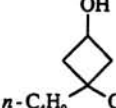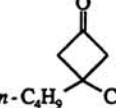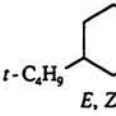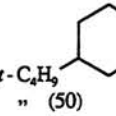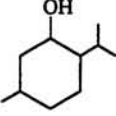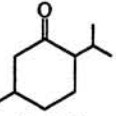
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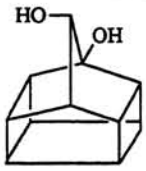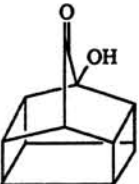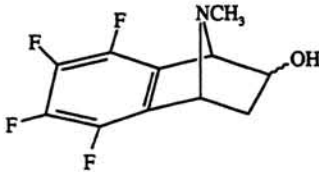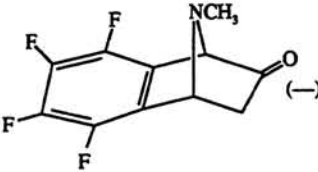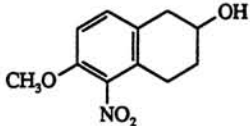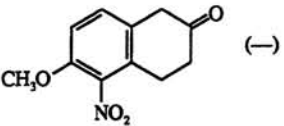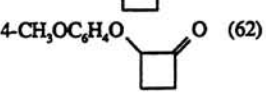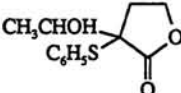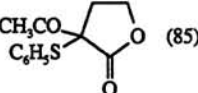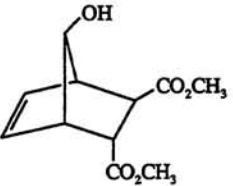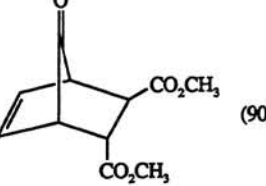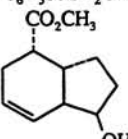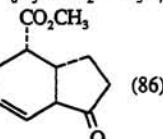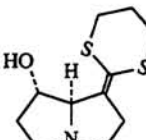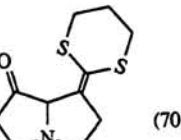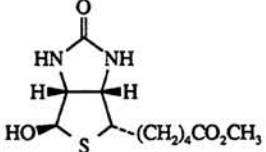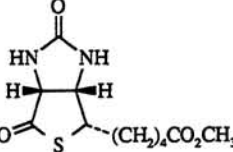
TABLE III. OXIDATION OF SECONDARY ALCOHOLS

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
(4-hydroxy-N-CO₂C₄H₉-t-pyrrolidine-2-CO₂H)	DMSO, DCC, Py, TFA	(4-oxo-N-CO₂C₄H₉-t-pyrrolidine-2-CO₂CH₂SCH₃) (93)	662
$(CH_3)_2C=C=CHCHOHC_4H_9$-t and i-$C_3H_7C\equiv CCHOHC_4H_9$-$t$	DMSO, (COCl)₂	$(CH_3)_2C=C=CHCOC_4H_9$-t (78) and i-$C_3H_7C\equiv CCOC_4H_9$-t	81
(2-hydroxy-4-isopropyl-1-methylenecyclohexane)	DMSO, (COCl)₂	(4-isopropyl-2-methylenecyclohexanone) (93)	663
(N-methyl azabicyclic alcohol, OH)	DMSO, SOCl₂	(ketone) (99)	23
	DMSO, TFAA	" (98)	25
	C₆H₅SCH₃, electrochemical	" (68)	20
(dimethyl azabicyclic alcohol, OH)	DMSO, (COCl)₂	" (99)	23
	DMSO, TFAA, −65°	" (93)	25
(hydroxy dimethylcyclopropane-fused cyclohexane)	DMSO, (COCl)₂	(ketone) (87)	664
(dihydroxy dimethylcyclopropane-fused cyclohexane)	DMSO, (COCl)₂	(hydroxy ketone) (97)	664
(1-OTHP-cyclopropyl)CHOHCH₃	DMSO, (COCl)₂	(1-OTHP-cyclopropyl)COCH₃ (96)	432
(3-hydroxy-1-(n-C₄H₉)-cyclobutane-1-CO₂CH₃)	(CH₃)₂S, Cl₂	(3-oxo-1-(n-C₄H₉)-cyclobutane-1-CO₂CH₃) (~100)	665
(4-t-C₄H₉-cyclohexanol, E, Z)	DMSO, Cl₂	(4-t-C₄H₉-cyclohexanone) (97)	14
	DMSO, Tf₂O	" (50)	45
	DMSO, TFAA	" (88)	27
	(CH₃)₂SeO	" (97)	47
	(CH₃)₂S, NCS	" (97)	17
	(n-C₄H₉)₂S, NCS, −78°	" (89)	39
	(i-C₃H₇)₂S, NCS, −78°	" (83)	39
(menthol)	1. COCl₂, 2. DMSO	(menthone) (26)	15
	C₆H₅SCH₃, electrochemical	" (92)	20
	n-C₈H₁₇SCH₃, electrochemical	" (69)	21
n-$C_6H_{13}CHOHCH_2COCH_3$	DMSO, (COCl)₂	n-$C_6H_{13}COCH_2COCH_3$ (69)	127
	DMSO, TFAA	" (50) $+ n$-$C_6H_{13}CH=CHCOCH_3$ (33)	127
$(C_2H_5O)_2P(O)CH_2CO(CH_2)_2CHOHCH_3$	DMSO, (COCl)₂	$(C_2H_5O)_2P(O)CH_2CO(CH_2)_2COCH_3$ (48)	62

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

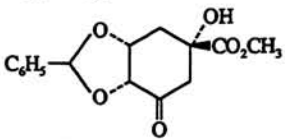| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{11}$	(CH$_3$)$_2$S, Cl$_2$	(84)	666
	DMSO, SO$_3$, (CH$_3$)$_3$N	(—)	667
C$_6$H$_5$C≡CCHOHC$_2$H$_5$	DMSO, TFAA DMSO, (COCl)$_2$	C$_6$H$_5$C≡CCOC$_2$H$_5$ (92) (90)	17 8
	DMSO, TFAA	(—)	668
4-O$_2$NC$_6$H$_4$N⟨⟩OH	DMSO, DCC, Py, TFA	4-O$_2$NC$_6$H$_4$N⟨⟩O (79)	669
4-CH$_3$C$_6$H$_4$S⟨⟩OH	DMSO, (COCl)$_2$	4-CH$_3$C$_6$H$_4$S⟨⟩O (49)	653
4-CH$_3$OC$_6$H$_4$O⟨⟩OH	DMSO, Ac$_2$O	4-CH$_3$OC$_6$H$_4$O⟨⟩O (62)	653
	DMSO, (COCl)$_2$	(85)	670
	DMSO, TFAA	(90)	671
C$_6$H$_5$CHOHC$_4$H$_9$-t	DMSO, TFAA DMSO, Ac$_2$O DMSO, air, reflux	C$_6$H$_5$COC$_4$H$_9$-t (97) " (98) " (47)	25 634 634
C$_6$H$_5$CH$_2$CHOHC$_3$H$_7$-n	C$_6$H$_5$SCH$_3$, electrochemical	C$_6$H$_5$CH$_2$COC$_3$H$_7$-n (70)	20
C$_6$H$_5$SeCH$_2$CHOHC$_3$H$_7$-i	(CH$_3$)$_2$S, NCS	C$_6$H$_5$SeCH$_2$COC$_3$H$_7$-i (60)	643
	DMSO, TFAA	(86)	121
	DMSO, TFAA	(70)	648
	DMSO, TFAA	(59)	672

TABLE III. Oxidation of Secondary Alcohols (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	$C_6H_5SCH_3$, Cl_2	(80)	19
	DMSO, Cl_2	" (72)	19
	DMSO, $(COCl)_2$	(80)	673
	DMSO, $(COCl)_2$	(80)	673
	DMSO, $(COCl)_2$	(—)	432
	DMSO, SO_3, Py	(~90)	674
	DMSO, DCC, H_3PO_4	(71)	675, 676
	DMSO, $(COCl)_2$	(—)	389
also α, α-$(OH)_2$ at C_1, C_2	DMSO, $(COCl)_2$	(35)	677
	DMSO, $(COCl)_2$	(95)	678
	DMSO, $(COCl)_2$	(96)	432
	DMSO, Ac_2O	(76)	378
	DMSO, $(COCl)_2$	(64)	26
$4\text{-}NCC_6H_4N$—OH	DMSO, DCC, Py, TFA	$4\text{-}NCC_6H_4N$=O (58)	669
$4\text{-}OHCC_6H_4N$—OH	DMSO, DCC, Py, TFA	$4\text{-}OHCC_6H_4N$=O (61)	669

446

447

TABLE III. Oxidation of Secondary Alcohols (*Continued*)
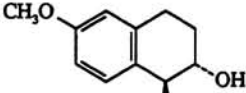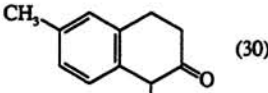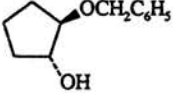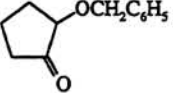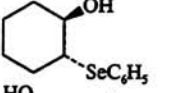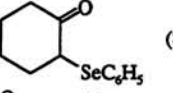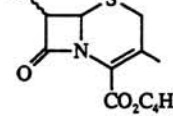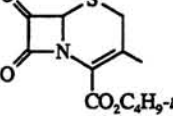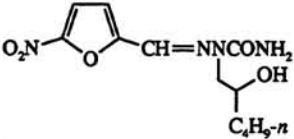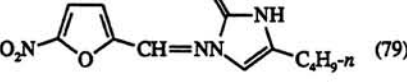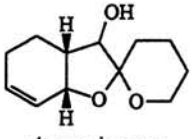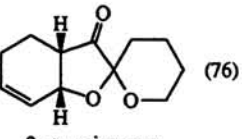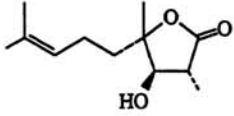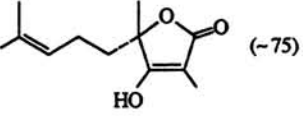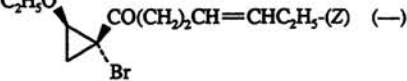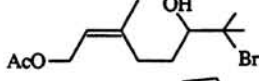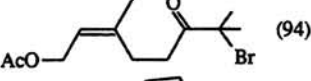
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₂ 4-Phenylcyclohexanol	DMSO, polymer-supported carbodiimide	4-Phenylcyclohexanone (67)	55
	Polymer-supported sulfide, Cl₂	" (90)	42
	(i-C₃H₇)₂S, NCS, −78°	" (95)	39
	(n-C₄H₉)₂S, NCS, −78°	" (88)	39
	(CH₃)₂S, NCS	(30)	679
	DMSO, DCC, Py, TFA	" (80)	641
	DMSO, (COCl)₂	(94)	680
	NCS, DBU	(81)	46
	DMSO, DCC, Cl₂CHCO₂H	(70)	315
	DMSO, Ac₂O	(79)	163
C₆H₅CH₂CHOHC₄H₉-n	n-C₈H₁₇SCH₃, electrochemical	C₆H₅CH₂COC₄H₉-n (49)	21
C₆H₅SeCH₂CHOHC₄H₉-n	(CH₃)₂S, NCS	C₆H₅SeCH₂COC₄H₉-n (74)	643
(CH₃)₂(C₆H₅)SiCHOHC(CH₃)=CH₂	DMSO, (COCl)₂	(CH₃)₂(C₆H₅)SiCOC(CH₃)=CH₂ (83)	681
CH₂=C(TMS)CHOHC₆H₅	(CH₃)₂Se, NCS	CH₂=C(TMS)COC₆H₅ (100)	46
4 stereoisomers	DMSO, SO₃, Py	(76) 2 stereoisomers	682
	DMSO, TFAA	(~75)	673
	DMSO, TFAA	(—)	683
	(CH₃)₂S, NCS	(94)	684
mixture of isomers	DMSO, TFAA	(62)	685
	DMSO, DCC, TFA, Py	(2)	686

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
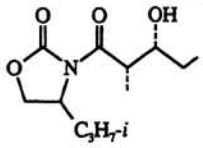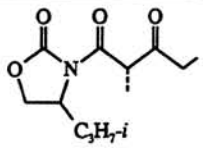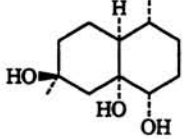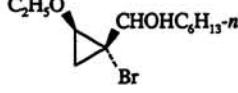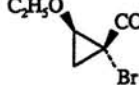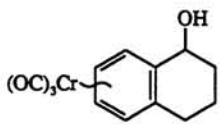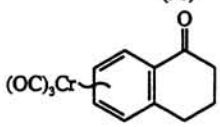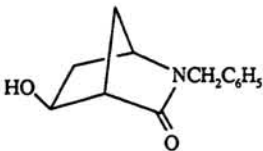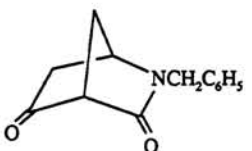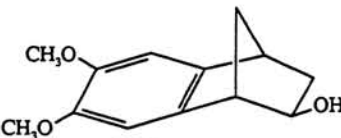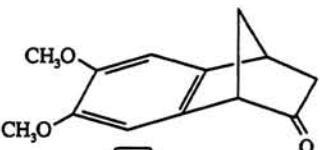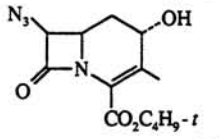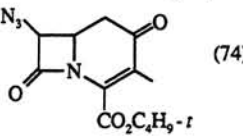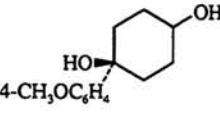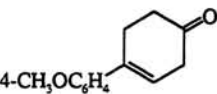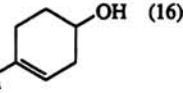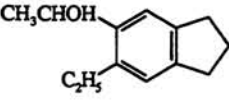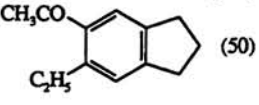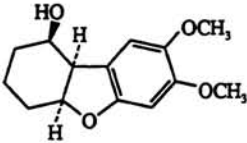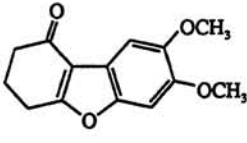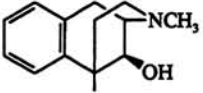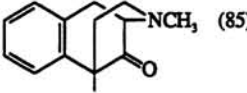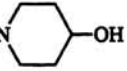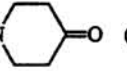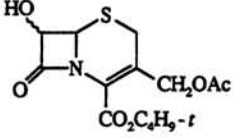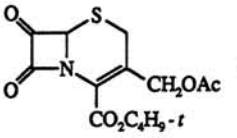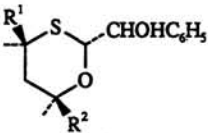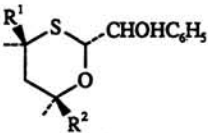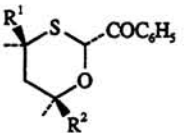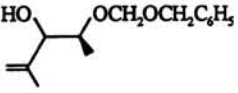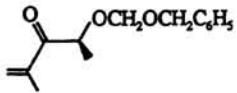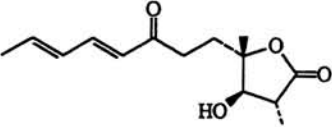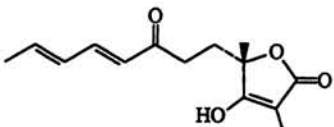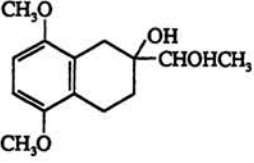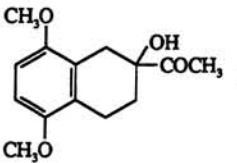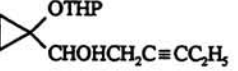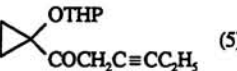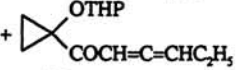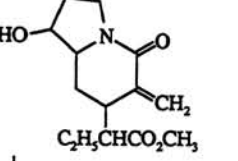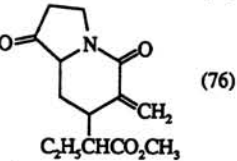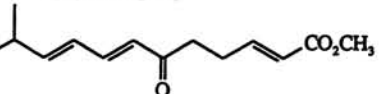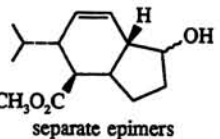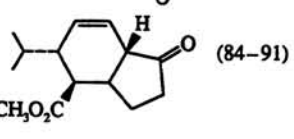
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, SO₃, Py	(~90)	674
	DMSO, (COCl)₂	(>70)	687
	DMSO, TFAA	(74)	683
Cyclododecanol	DMSO, TFAA C₆H₅SCH₃, electrochemical DMSO, (COCl)₂ (CD₃)₂S, NCS	Cyclodecanone (72) ” (75) ” (97) ” (90)	24 20 23 32
C₁₃	DMSO, Ac₂O	(77)	378
Benzhydrol	DMSO, (COCl)₂ DMSO, TFAA DMSO, Cl₂ DMSO, CSCB, Py	Benzophenone (98) ” (98) ” (98) ” (46)	23 24 14 642
[(OC)₃CrC₆H₅](CH₂)₂CHOHCH₃	DMSO, Ac₂O	[(OC)₃CrC₆H₅](CH₂)₂COCH₃ (29)	378
	DMSO, DCC, H₃PO₄	(—)	688
	DMSO, (COCl)₂	(83)	689
4-AcC₆H₄N—OH	DMSO, DCC, Py, TFA	4-AcC₆H₄N=O (68)	669

C₆H₅CH₂O₂CNHCHCHOHCH₃
    CO₂CH₃
	DMSO, DCC, H₃PO₄	C₆H₅CH₂O₂CNHCHCOCH₃ (80)
		    CO₂CH₃
			87

	(CH₃)₂S, NCS	(74)	690
	DMSO, DCC, TFA, Py	(59) + (16)	76
	DMSO, Ac₂O	(50)	691

450

451

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

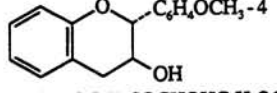| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)$_2$	(38) + (30) *a*	182
	DMSO, (COCl)$_2$	(94)	692
	(CH$_3$)$_2$S, NCS	(100)	693
	1. DMSO, (COCl)$_2$ 2. K$_2$CO$_3$	 R = C$_6$H$_5$ (94) R = C$_6$H$_{11}$ (81) R = C$_6$H$_{13}$ (87)	694, 695
	(CH$_3$)$_2$S, NCS, toluene, 0°	(76)	696
	DMSO, TFAA	(83)	697
	DMSO, (COCl)$_2$	(70)	698
	DMSO, (COCl)$_2$	(100)	698
(C$_2$H$_5$O)$_2$P(O)CH$_2$CO(CH$_2$)$_2$CHOHC$_4$H$_9$-n	DMSO, (COCl)$_2$	(C$_2$H$_5$O)$_2$P(O)CH$_2$CO(CH$_2$)$_2$COC$_4$H$_9$-n (51)	62
n-C$_{10}$H$_{21}$CHOHCH$_2$SeCH$_3$	(CH$_3$)$_2$S, NCS	n-C$_{10}$H$_{21}$COCH$_2$SeCH$_3$ (50)	449
(E)-n-C$_7$H$_{15}$CH=CHCHOHSi(CH$_3$)$_3$	(CH$_3$)$_2$S, NCS	(E)-n-C$_7$H$_{15}$CH=CHCOSi(CH$_3$)$_3$ (>64)	633
	DMSO, Py, SO$_3$	(50)	699
	DMSO, (COCl)$_2$	(57)	700
	DMSO, (COCl)$_2$	(82)	361, 701
C$_{14}$ C$_6$H$_5$COCHOHC$_6$H$_5$	DMSO, (COCl)$_2$ DMSO, Ac$_2$O DMSO, Tf$_2$O DMSO, (CH$_3$SO$_2$)$_2$O, HMPA (CH$_3$)$_2$Se, NCS	C$_6$H$_5$COCOC$_6$H$_5$ (95) " (77) " (97) " (99) " (93)	26 651 45 335 46
	DMSO, SO$_3$, Py	(79)	702
	DMSO, (COCl)$_2$	(91)	670

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, SO₃, Py	("exclusive")	181
	DMSO, CH₃COBr	(85)	298
4-C₂H₅O₂CC₆H₄N⟨⟩—OH	DMSO, DCC, Py, TFA	4-C₂H₅O₂CC₆H₄N⟨⟩=O (63)	—
	DMSO, DCC, CHCl₂CO₂H	(—)	315
C₆H₁₁CHOHCH₂SeC₆H₅	(CH₃)₂S, NCS	C₆H₁₁COCH₂SeC₆H₅ (74)	643
R¹=H, R²=CH₃; R¹=CH₃, R²=H	DMSO, TFAA	(75)	703, 704
	DMSO, (COCl)₂	(93)	705
	DMSO, TFAA	(80)	673
	DMSO, SO₃, Py	(92)	706, 707, 708
C₆H₅SeCH₂CHOHC₆H₁₃-n	DMSO, DCC, Py, TFA (CH₃)₂S, NCS	" (61) C₆H₅SeCH₂COC₆H₁₃-n (60)	707 449
	DMSO, (COCl)₂	(5) + ("major")	709
	DMSO, DCC, H₃PO₄	(76)	644
	DMSO, TFAA	(68)	710
separate epimers	DMSO, TFAA	(84–91)	122

TABLE III.   Oxidation of Secondary Alcohols (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)$_2$	(87)	711
	(CH$_3$)$_2$S, NCS	(>60)	712
	(CH$_3$)$_2$S, NCS	(74)	713
	DMSO, (COCl)$_2$	(95)	714
	DMSO, TFAA	(>65)	715
	DMSO, DCC, H$_3$PO$_4$	(67)	676
	DMSO, DCC, Py, TFA	(91)	716
(CH$_3$)$_2$C=C=C(C$_4$H$_9$-t)CHOHC$_4$H$_9$-t and t-C$_4$H$_9$C≡CC(CH$_3$)$_2$CHOHC$_4$H$_9$-t mixture	DMSO, (COCl)$_2$	(CH$_3$)$_2$C=C=C(C$_4$H$_9$-t)COC$_4$H$_9$-t (70) and t-C$_4$H$_9$C≡CC(CH$_3$)$_2$COC$_4$H$_9$-t	81
	DMSO, TFAA	*trans* (98) *cis* (100)	717
	DMSO, (COCl)$_2$	(88)	709
	DMSO, (COCl)$_2$	(—)	718
	DMSO, (COCl)$_2$	(~100)	719

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

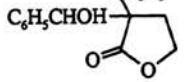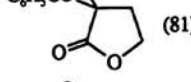| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	$C_6H_5SCH_3$, electrochemical	(82)	20
	DMSO, (COCl)$_2$	(—)	424
	DMSO, (COCl)$_2$	(61)	720
	DMSO, Py, SO$_3$	(86)	721
C$_{15}$ $C_6H_5CH=CHCHOHC_6H_5$	(CH$_3$)$_2$Se, NCS	$C_6H_5CH=CHCOC_6H_5$ (81)	46
	DMSO, DEC, Py, TFA	(20)	722
$C_6H_5CH(CH_3)CHOHC_6H_5$	DMSO, FDPT (2-fluoro-1,3-dimethylpyridinium tosylate)	$C_6H_5CH(CH_3)COC_6H_5$ (82)	216
	DMSO, Ac$_2$O	(46)	723
(ArOCH$_2$)$_2$CHOH	DMSO, DCC, Py, TFA	(ArOCH$_2$)$_2$CO	
Ar = C$_6$H$_5$		(42)	724
Ar = 2,4,5-Cl$_3$C$_6$H$_2$		(28)	724
Ar = 4-ClC$_6$H$_4$		(73)	724
Ar = 3-ClC$_6$H$_4$		(26)	724
Ar = 2-ClCl$_6$H$_4$		(25)	724
Ar = 4-FC$_6$H$_4$		(31)	724
Ar = 4-BrC$_6$H$_4$		(13)	724
Ar = 4-IC$_6$H$_4$		(75)	724
(ArSCH$_2$)$_2$CHOH	DMSO, DCC, Py, TFA	(ArSCH$_2$)$_2$CO	
Ar = C$_6$H$_5$		(14)	724
Ar = 4-ClC$_6$H$_4$		(19)	724
	DMSO, (COCl)$_2$	(87)	84
E,Z isomers	DMSO, (COCl)$_2$	E (90) Z (82)	84
	DMSO, DCC, Cl$_2$CHCO$_2$H	(83)	315
	DCMSO, Ac$_2$O	" (92)	725
	DMSO, SO$_3$, Py	(48) β: α at C$_2$, 2:1	726

458

459
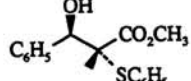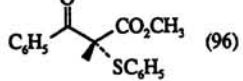
TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
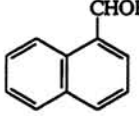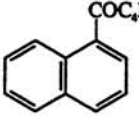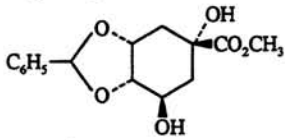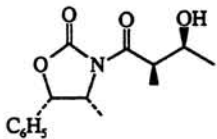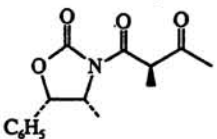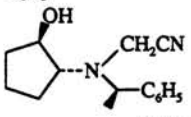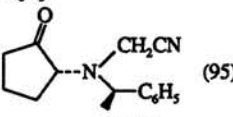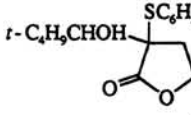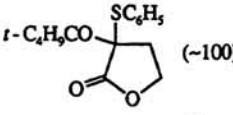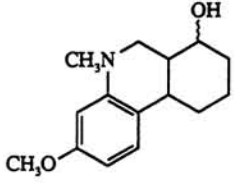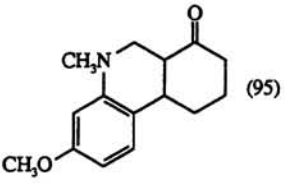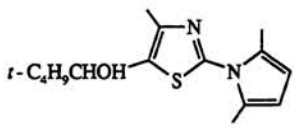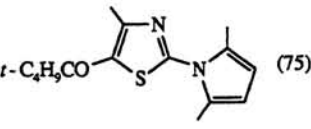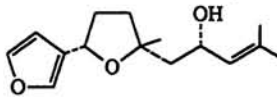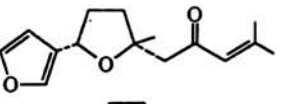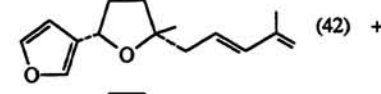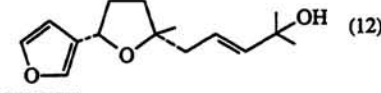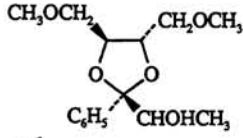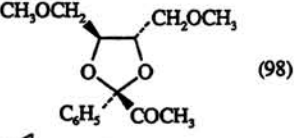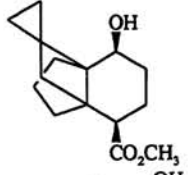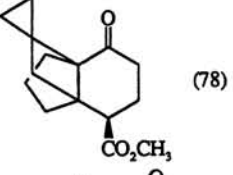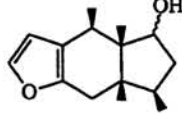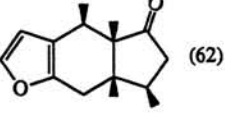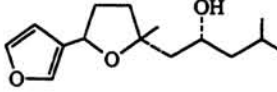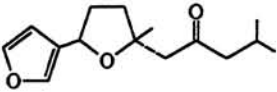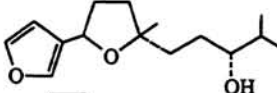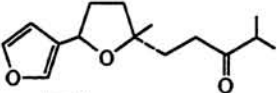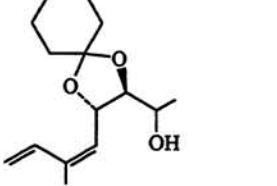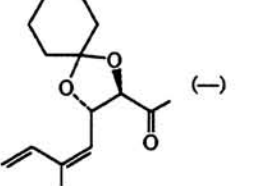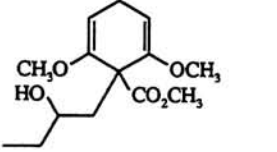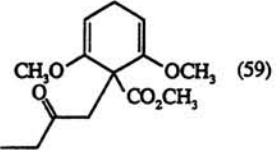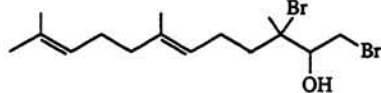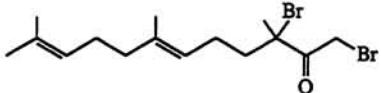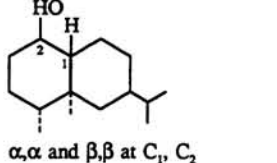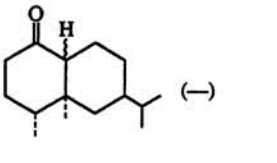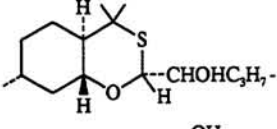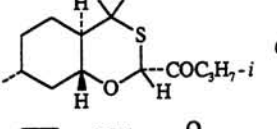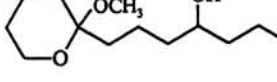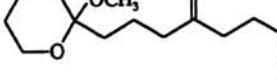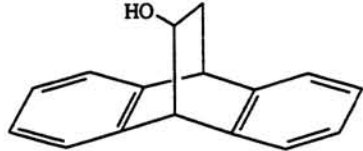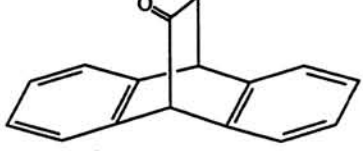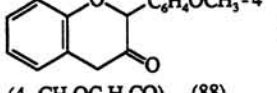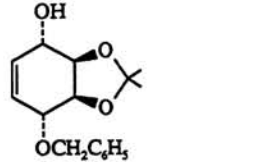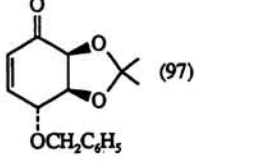
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac$_2$O	(—)	472
	DMSO, (COCl)$_2$	(45)	727
	DMSO, SO$_3$, Py	(~90)	674
	DMSO, (COCl)$_2$	(95)	728
	DMSO, (COCl)$_2$	(~100)	670
	DMSO, DCC, Py, TFA	(95)	729
	DMSO, Ac$_2$O	(75)	730
	DMSO, (COCl)$_2$	(23) + (42) + (12)	129
	DMSO, (COCl)$_2$	(98)	678
	DMSO, (COCl)$_2$	(78)	731
	DMSO, Ac$_2$O	(62)	732
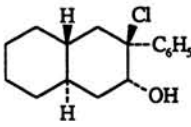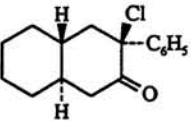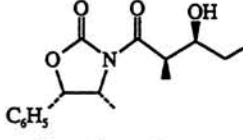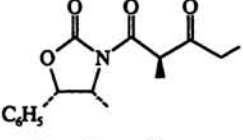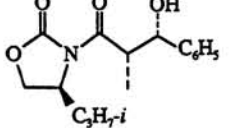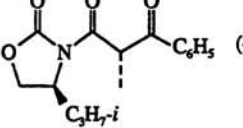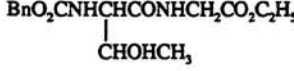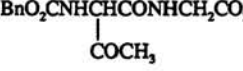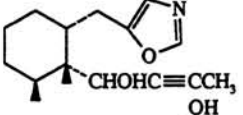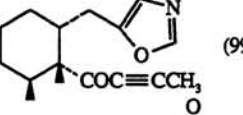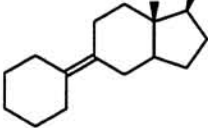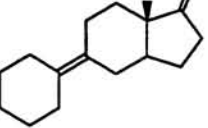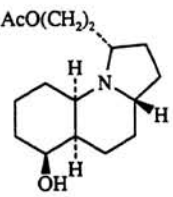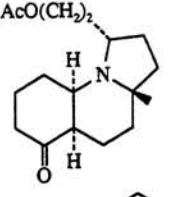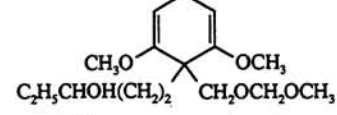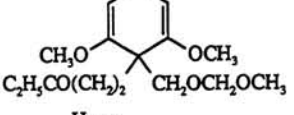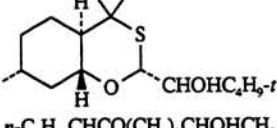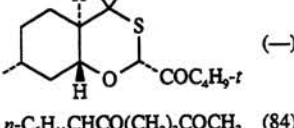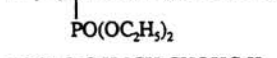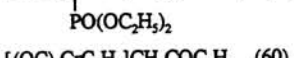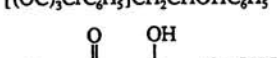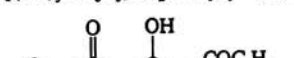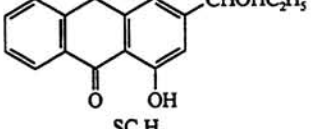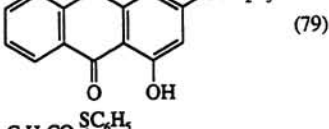
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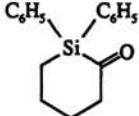
TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)$_2$	(70)	733
	DMSO, (COCl)$_2$	(23)	733
	DMSO, (COCl)$_2$	(—)	389
	DMSO, DCC, Py, TFA	(59)	734
	(CH$_3$)$_2$S, NCS	(90)	735
 α,α and β,β at C$_1$, C$_2$	DMSO, DCC	(—)	736
	DMSO, TFAA	(—)	737
	DMSO, TFAA	(72)	738
n-C$_5$H$_{11}$CHCO(CH$_2$)$_2$CHOHCH$_3$ $\quad$PO(OC$_2$H$_5$)$_2$	DMSO, (COCl)$_2$	n-C$_5$H$_{11}$CHCO(CH$_2$)$_2$COCH$_3$ (56) $\quad$PO(OC$_2$H$_5$)$_2$	62
n-C$_6$H$_{13}$CH(SeCH$_3$)CHOHC$_6$H$_{13}$-n	(CH$_3$)$_2$S, NCS	n-C$_6$H$_{13}$CH(SeCH$_3$)COC$_6$H$_{13}$-n (52)	449
C$_{16}$ (OC)$_3$CrC$_6$H$_5$CHOHC$_6$H$_5$	DMSO, Ac$_2$O	(OC)$_3$CrC$_6$H$_5$COC$_6$H$_5$ (65)	378
	DMSO, DCC, Py, TFA	(90)	739
	DMSO, DEC, Py, TFA	(21)	722
4-CH$_3$OC$_6$H$_4$COCHOHC$_6$H$_4$OCH$_3$-4	DMSO, Ac$_2$O DMSO, (COCl)$_2$	(4-CH$_3$OC$_6$H$_4$CO)$_2$ (88) " (90)	651 26
3-CH$_3$OC$_6$H$_4$COCHOHC$_6$H$_4$OCH$_3$-3	DMSO, P$_2$O$_5$ DMSO, Tf$_2$O	(3-CH$_3$OC$_6$H$_4$CO)$_2$ (71) " (51)	320 45
	DMSO, (COCl)$_2$	(97)	740

462

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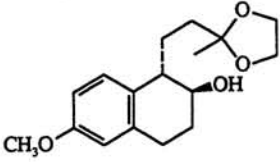TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

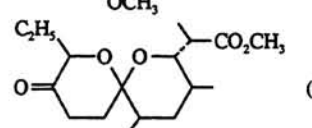| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac$_2$O	(—)	741
	DMSO, SO$_3$, Py	(~90)	674
	DMSO, SO$_3$, Py	(~90)	674
BnO$_2$CNHCHCONHCH$_2$CO$_2$C$_2$H$_5$ $\quad$ CHOHCH$_3$	DMSO, DCC, H$_3$PO$_4$	BnO$_2$CNHCHCONHCH$_2$CO$_2$C$_2$H$_5$ (70) $\quad$ COCH$_3$	87
CHOHC≡CCH$_3$	DMSO, (COCl)$_2$	COC≡CCH$_3$ (99)	84, 430
	DMSO, DCC, TFA, Py	(93)	742
AcO(CH$_2$)$_2$	DMSO, (COCl)$_2$	AcO(CH$_2$)$_2$ (89)	743
CH$_3$O $\quad$ OCH$_3$ C$_2$H$_5$CHOH(CH$_2$)$_2$ $\quad$ CH$_2$OCH$_2$OCH$_3$	DMSO, DCC	CH$_3$O $\quad$ OCH$_3$ (>59) C$_2$H$_5$CO(CH$_2$)$_2$ $\quad$ CH$_2$OCH$_2$OCH$_3$	744
CHOHC$_4$H$_9$-t	DMSO, TFAA	COC$_4$H$_9$-t (—)	737
n-C$_5$H$_{11}$CHCO(CH$_2$)$_3$CHOHCH$_3$ $\quad$ PO(OC$_2$H$_5$)$_2$	DMSO, (COCl)$_2$	n-C$_5$H$_{11}$CHCO(CH$_2$)$_3$COCH$_3$ (84) $\quad$ PO(OC$_2$H$_5$)$_2$	62
C$_{17}$ [(OC)$_3$CrC$_6$H$_5$]CH$_2$CHOHC$_6$H$_5$	DMSO, Ac$_2$O	[(OC)$_3$CrC$_6$H$_5$]CH$_2$COC$_6$H$_5$ (60)	378
CHOHCH$_2$H$_5$	DMSO, DCC, P$_2$O$_5$	COC$_2$H$_5$ (79)	745
SC$_6$H$_5$ C$_6$H$_5$CHOH	DMSO, (COCl)$_2$	C$_6$H$_5$CO $\quad$ SC$_6$H$_5$ (81)	670
OH C$_6$H$_5$ $\quad$ CO$_2$CH$_3$ $\quad$ SC$_6$H$_5$	DMSO, (COCl)$_2$	C$_6$H$_5$ $\quad$ CO$_2$CH$_3$ (96) $\quad$ SC$_6$H$_5$	670

TABLE III. Oxidation of Secondary Alcohols (*Continued*)
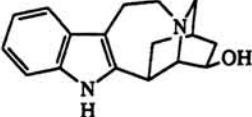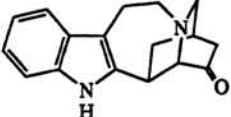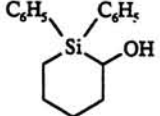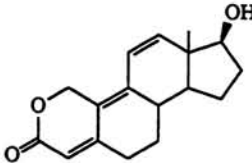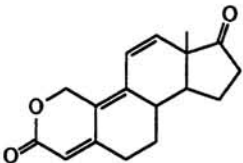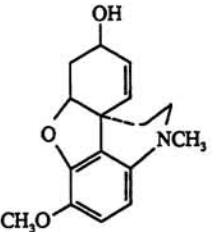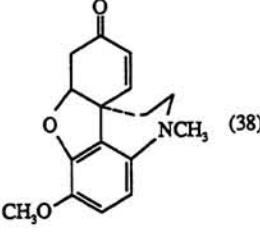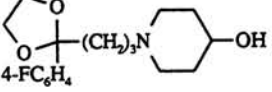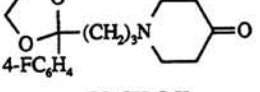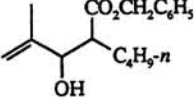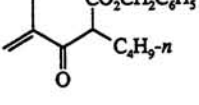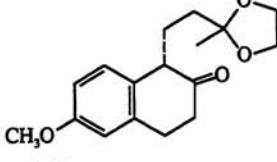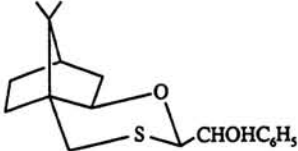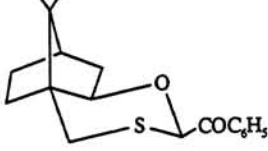
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
(ArOCH₂)₂CHOH	DMSO, DCC, Py, TFA	(ArOCH₂)₂CO	
Ar = 4-CH₃C₆H₄		(69)	724
Ar = 2-CH₃C₆H₄		(37)	724
Ar = 3-CH₃C₆H₄		(38)	724
Ar = 4-CH₃OC₆H₄		(66)	724
Ar = 2-CH₃OC₆H₄		(49)	724

$(ArOCH_2)_2CHOH$

$Ar = 4\text{-}CH_3C_6H_4$ (69) 724
$Ar = 2\text{-}CH_3C_6H_4$ (37) 724
$Ar = 3\text{-}CH_3C_6H_4$ (38) 724
$Ar = 4\text{-}CH_3OC_6H_4$ (66) 724
$Ar = 2\text{-}CH_3OC_6H_4$ (49) 724

DMSO, SO₃, Py — (88) — 746

C₁₇

DMSO, DCC, Py, TFA — (70) — 747

$C_6H_5CH_2OCH_2CHOHCH_2OCH_2C_6H_5$ — (CH₃)₂S, NCS — $C_6H_5CH_2OCH_2COCH_2OCH_2C_6H_5$ (83) — 748

DMSO, Ac₂O — (74) — 749

+ methylthiomethyl ether (12)

DMSO, Ac₂O — (38) — 11

(CH₃)₂S, NCS — (74) — 750

DMSO, (COCl)₂ — (—) — 718

DMSO, SO₃, Py — (85) — 751

DMSO, (COCl)₂ — (>65) — 752

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
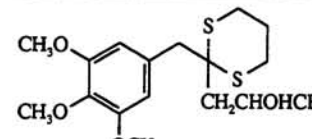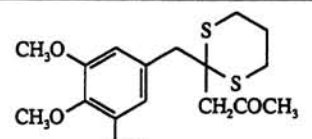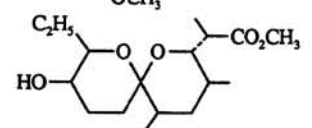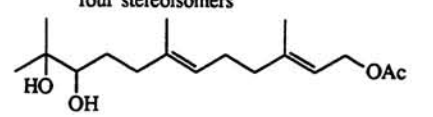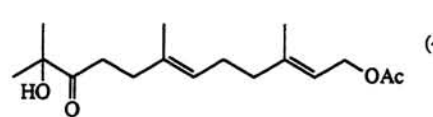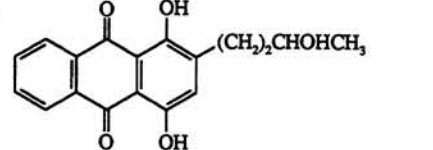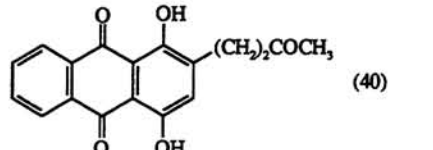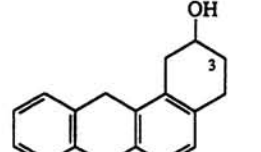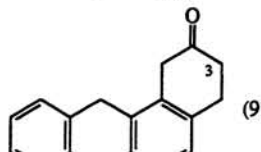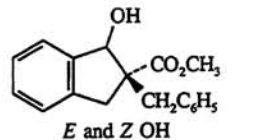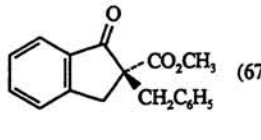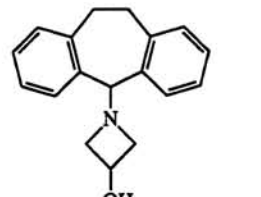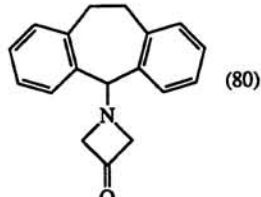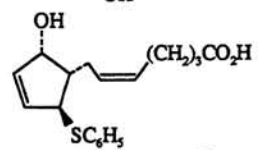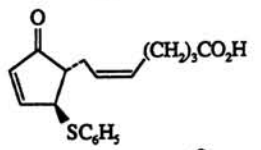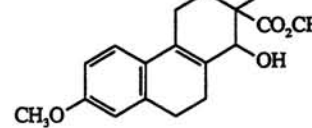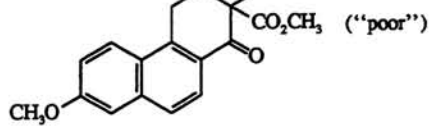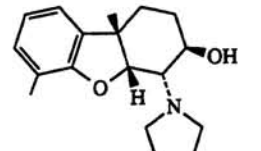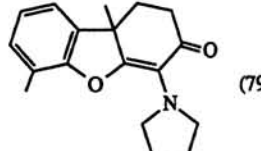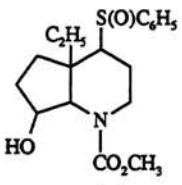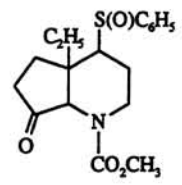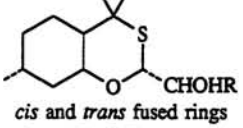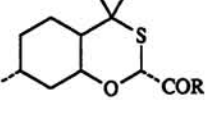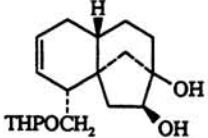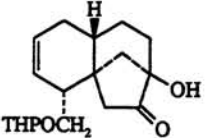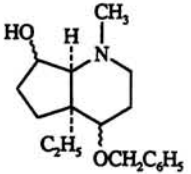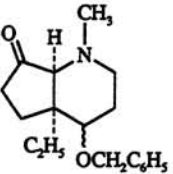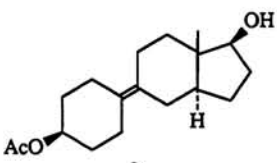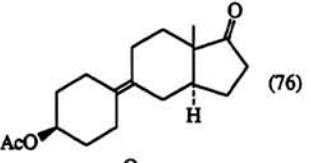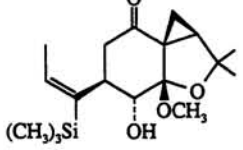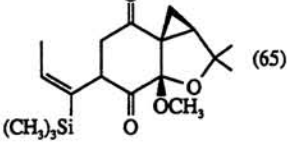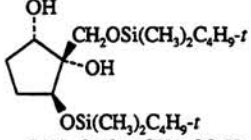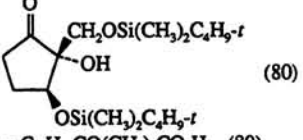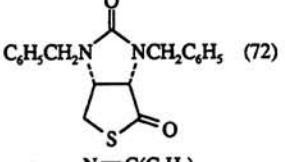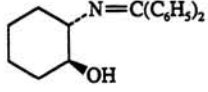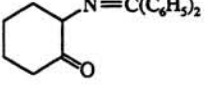
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, DCC, Py, TFA	(90)	753
four stereoisomers	DMSO, (COCl)$_2$	(93–97)	754
	(CH$_3$)$_2$S, NCS	(~100)	755
C$_{18}$	DMSO, Ac$_2$O	(40)	745
mixture with 3-OH isomer	DMSO, TFAA	+3-oxo isomer (91)	756
E and *Z* OH	DMSO, DCC, Py, TFA	(67–69)	757
	(CH$_3$)$_2$S, NCS	(80)	758
	DMSO, SO$_3$, Py	(68)	759
	DMSO, Ac$_2$O	("poor")	183
	DMSO, TFAA	(79)	180

TABLE III. Oxidation of Secondary Alcohols (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)₂	(>38)	760
cis and *trans* fused rings	DMSO, TFAA		
R = (E)-C₆H₅		(91)	717
R = (Z)-C₆H₅		(63)	717
R = n-C₆H₁₃		(90)	717
R = C₆H₁₁		(—)	717
	DMSO, (CCl₃CO)₂O	(80)	761
	DMSO, (COCl)₂	(>60)	762
	DMSO, DCC, TFA, Py	(76)	763
	DMSO, (COCl)₂	(65)	764
	DMSO, TFAA	(80)	720
n-C₁₄H₂₉CHOH(CH₂)₂CO₂H	DMSO, (COCl)₂, −10°	n-C₁₄H₂₉CO(CH₂)₂CO₂H (80)	22
n-C₆H₁₃CHOH(CH₂)₁₀CO₂H	DMSO, (COCl)₂, −10°	n-C₆H₁₃CO(CH₂)₁₀CO₂H (75)	22
C₁₉	DMSO, TFAA	(72)	765
	DMSO, (COCl)₂	(76)	766, 767

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
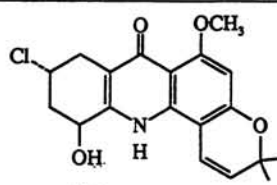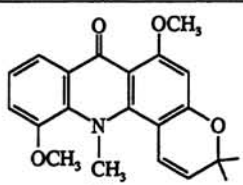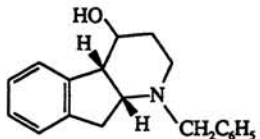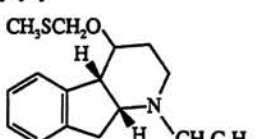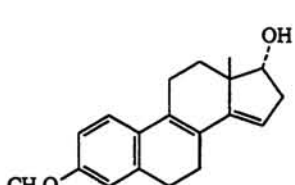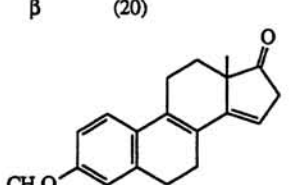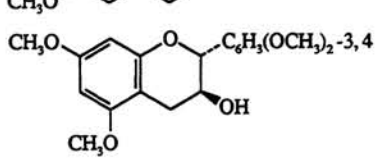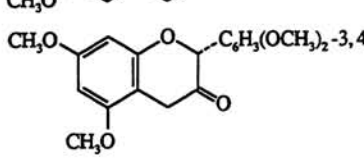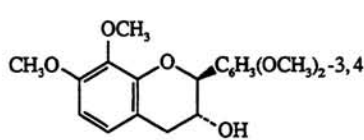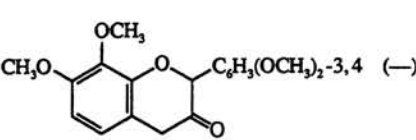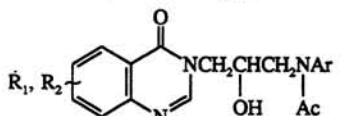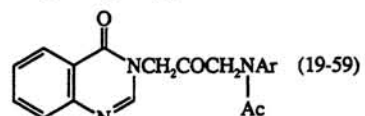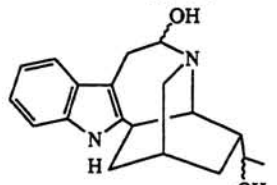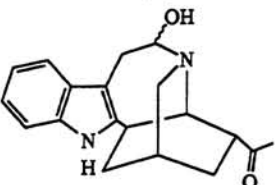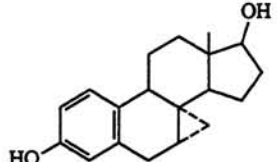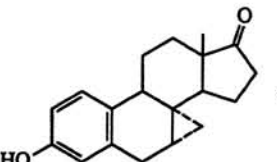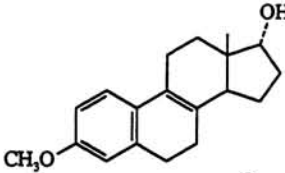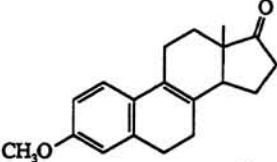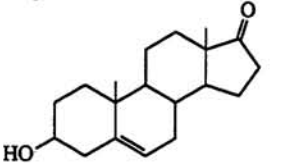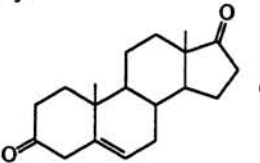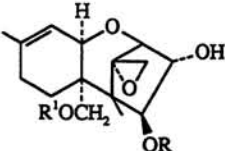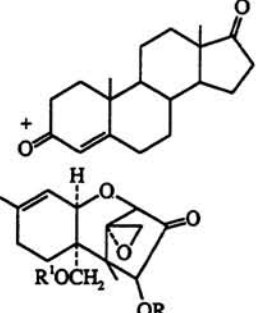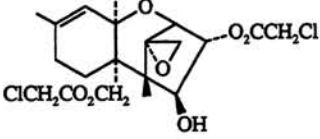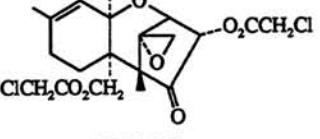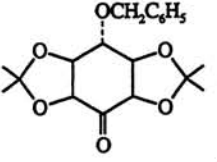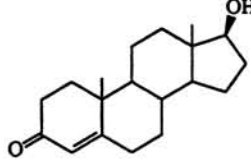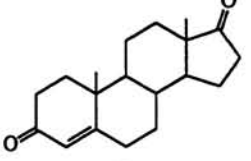
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	1. DMSO, DCC, Py, TFA 2. CH₃I	(15)	768
	DMSO, Ac₂O	+ α (15) (55) β (20) (48)	769 769
	DMSO, DCC, TFA, Py	(70)	125, 770
	DMSO, DCC, Py, TFA	(28)	771
	DMSO, DCC, Py, TFA	(—)	722
 R₁, R₂=H, H; H, Cl; Cl, Cl Ar=C₆H₅, 4-CH₃OC₆H₄, 4-CH₃C₆H₄, 4-ClC₆H₄	DMSO, Ac₂O	(19-59)	772

(ArOCH₂)₂CHOH   DMSO, DCC, Py, TFA   (ArOCH₂)₂CO

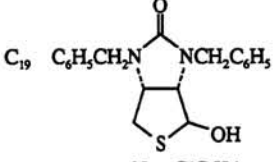| Ar			
4-C₂H₅C₆H₄		(60)	724
4-C₂H₅OC₆H₄		(63)	724
3,5-(CH₃)₂-4-ClC₆H₂		(27)	724
2-Cl-4,5-(CH₃)₂C₆H₂		(59)	724

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, DCC	(50)	773
	DMSO, SO₃, (C₂H₅)₃N	(52)	774
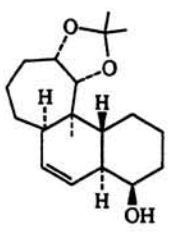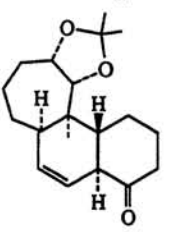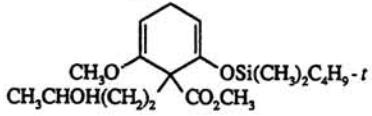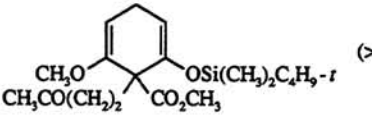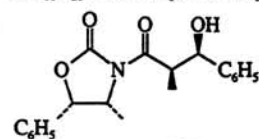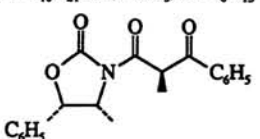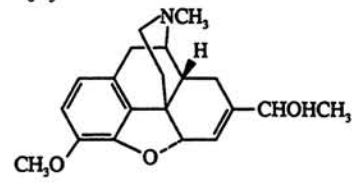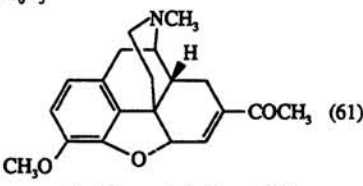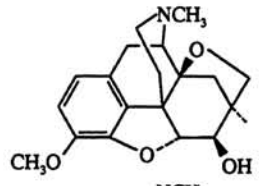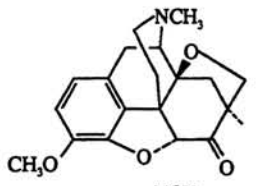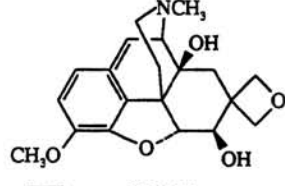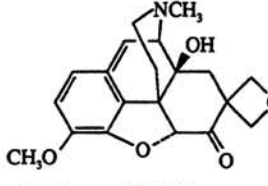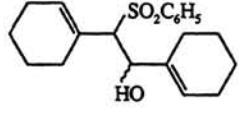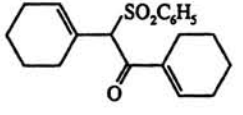
472

473

TABLE III. Oxidation of Secondary Alcohols (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, DCC, Py, TFA	(56)	775
	DMSO, DCC, Py, TFA	(90)	30, 776
	DMSO, RC≡CN(C₂H₅)₂ (R = CH₃, C₆H₅)	,, (60, 70)	54
	DMSO, DCC, H₃PO₄	,, (—)	30
	DMSO, TFAA		

R	R¹			
Ac	Ac		(98)	777
ClCH₂CO	ClCH₂CO		(93)	777
ClCH₂CO	Ac		(86)	777

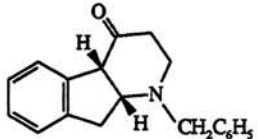| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, TFAA	(23)	777
	DMSO, Ac₂O	(22)	778
	DMSO, DCC, Py, TFA	(92)	30
	DMSO, DCC, H₃PO₄	,, (92)	30
	DMSO, Ms₂O, HMPA	,, (99)	335
	DMSO, MsCl	,, (—)	335
	DMSO, TsCl, HMPA	,, (77)	335
	DMSO, C₆H₅SO₂Cl	,, (85)	335
	DMSO, Ts₂O	,, (85)	335
	DMSO, C₆H₅COCl	,, (75)	335
	DMSO, cyanuric chloride	,, (99)	335
	DMSO, Ac₂O	,, (34)	11
(17β)	DMSO, Py, SO₃, 25°, <1 min	,, (~100)	13
(17α)	DMSO, Py, SO₃, 25°, 35 min	,, (~100)	13

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
(17β)	DMSO, (COCl)$_2$	" (99)	22
	DMSO, RC≡CN(C$_2$H$_5$)$_2$	" (60, 70)	54
	(R = CH$_3$, C$_6$H$_5$)	"	
	DMSO, (C$_6$H$_5$)$_2$C=C=NC$_6$H$_4$CH$_3$-4	" (82)	54

| | DMSO, (COCl)$_2$ | (97) | 123 |

| | DMSO, DCC | (>65) | 744 |

| (E)-n-C$_6$H$_{13}$CHOHCH$_2$CH=CH(CH$_2$)$_7$CO$_2$CH$_3$ | DMSO, (COCl)$_2$, −10° | (E)-n-C$_6$H$_{15}$COCH$_2$CH=CH(CH$_2$)$_7$CO$_2$CH$_3$ (79) | 22 |
| n-C$_{10}$H$_{21}$CH(SeCH$_3$)CHOHC$_6$H$_{13}$-n | (CH$_3$)$_2$S, NCS | n-C$_{10}$H$_{21}$CH(SeCH$_3$)COC$_6$H$_{13}$-n (78) | 449 |

C$_{20}$

| | DMSO, SO$_3$, Py | (~90) | 674 |

| | DMSO, Ac$_2$O | COCH$_3$ (61) | 779 |

+ methylthiomethyl ether (18)

| | DMSO, TFAA | (91) | 780 |

| | DMSO, TFAA | (90) | 780 |

| | DMSO, DCC, CHCl$_2$CO$_2$H | (85) | 781 |

| | DMSO, (COCl)$_2$ | (88) | 782 |

| | DMSO, TFAA | (~100) | 783 |

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
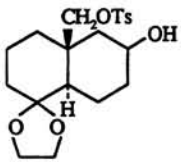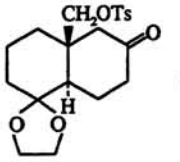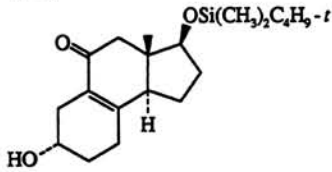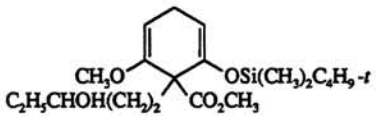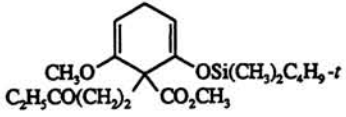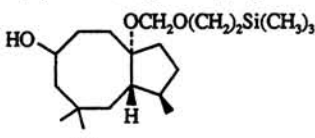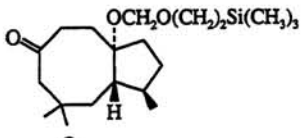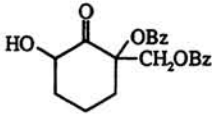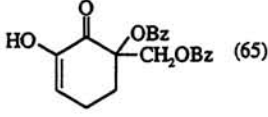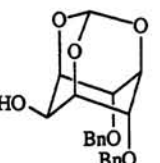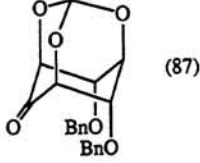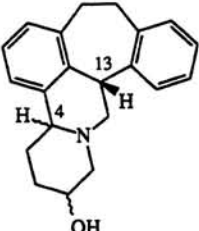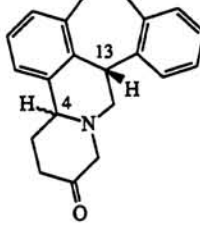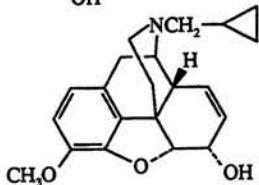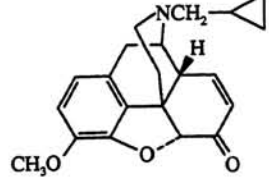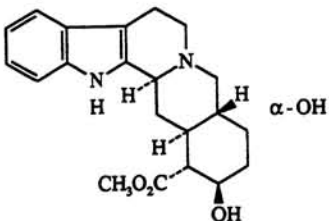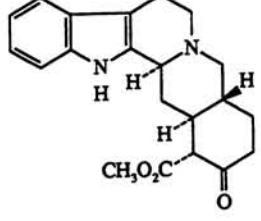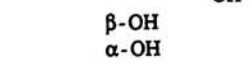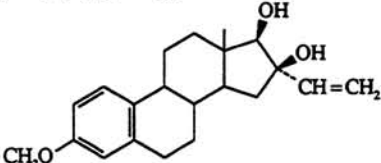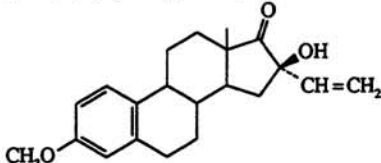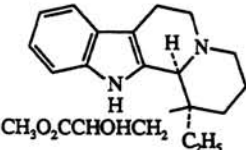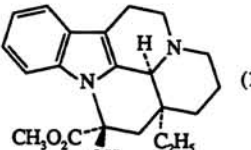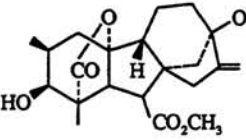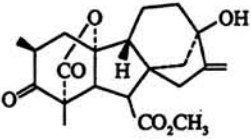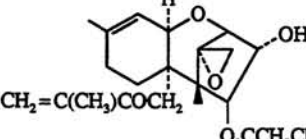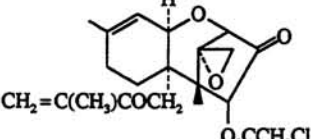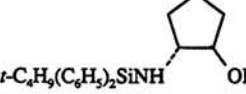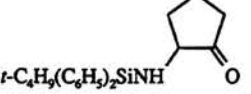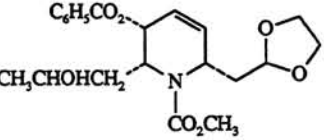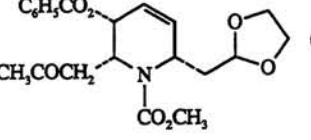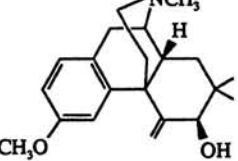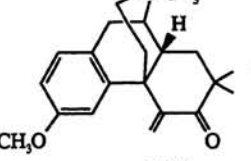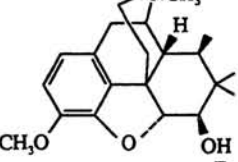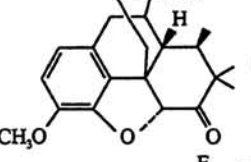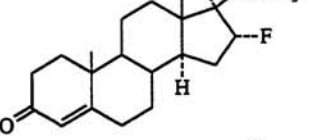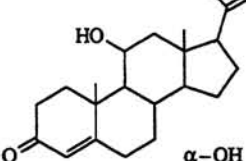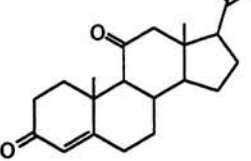
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, NCS	(84)	784
	DMSO, SO₃, Py	(79)	785
	DMSO, DCC, Py, TFA	(60)	734, 744
	DMSO, (COCl)₂	(>79)	73
C₂₁	DMSO, TFAA	(65)	317
	DMSO, (COCl)₂	(87)	198
	DMSO, SO₃, (C₂H₅)₃N	4, 13-Z (79) 4, 13-E (49)	786
	DMSO, TFAA	(99)	787
α-OH	DMSO, Ac₂O	(80)	11
β-OH	DMSO, Ac₂O	" (40)	11
α-OH	DMSO, Ms₂O	" (75)	335
	DMSO, cyanuric chloride	" (56)	335

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
$(n\text{-}C_3H_7C_6H_4OCH_2)_2CHOH$	DMSO, DCC, Py, TFA	$(n\text{-}C_3H_7C_6H_4OCH_2)_2CO$ (51)	724
	DMSO, SO₃, Py	(90)	788
	DMSO, SO₃, Py, H₂O (0.01%)	(10)	789
	DMSO, (COCl)₂	(60)	790
	DMSO, TFAA	(97)	777
	DMSO, (COCl)₂	(87)	791
	DMSO, TFAA	(80)	792
	DMSO, TFAA	(85)	793
	DMSO, TFAA	(67)	783
	DMSO, (COCl)₂	(83)	794
	DMSO, TFAA	(~100)	27

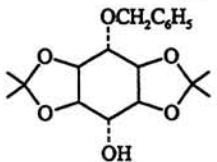TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
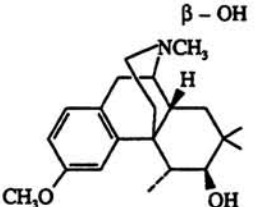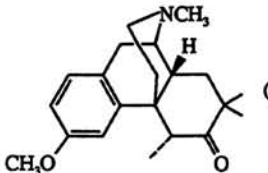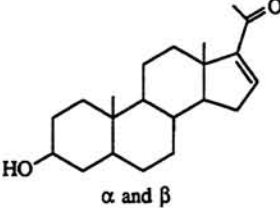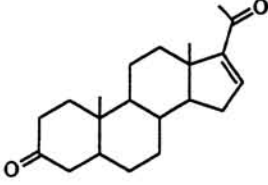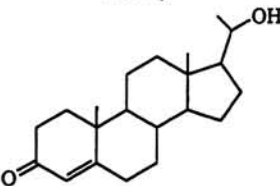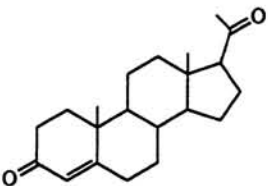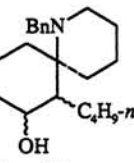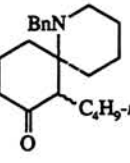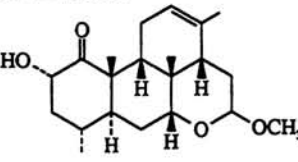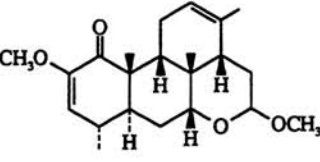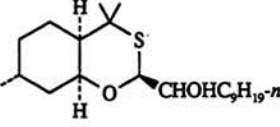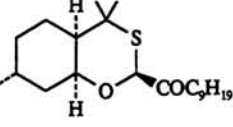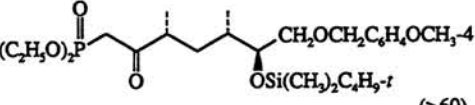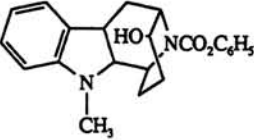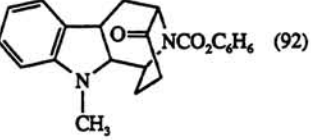
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac$_2$O	" (30)	11
	DMSO, (C$_6$H$_5$)$_2$C=C=NC$_6$H$_4$CH$_3$-4	" (62)	54
	1. COCl$_2$ 2. DMSO	" (24)	16
	DMSO, (COCl)$_2$, −10°	" (99)	22
	DMSO, RC≡CN(C$_2$H$_5$)$_2$ (R = CH$_3$, C$_6$H$_5$)	" (53−62)	54
	DMSO, DCC, Py, TFA	" (~100)	30
	DMSO, Py, SO$_3$	" (70)	13
	DMSO, Py, SO$_3$	" (~0)	13

β − OH

| | DMSO, TFAA | (82) | 793 |

α and β

| | DMSO, DCC | (—) | 30 |

| | DMSO, Py, SO$_3$ | (—) | 13 |

two *E* isomers

| | DMSO, (COCl)$_2$ | (44) | 795 |

| | 1. DMSO, NaOCH$_3$, 55°
 2. CH$_3$I | (93) | 71 |

trans ring-fused isomer
also oxidized

| | DMSO, TFAA | (58) | 796 |

| | DMSO, (COCl)$_2$ | (>60) | 456 |

| | DMSO, (COCl)$_2$ | (92) | 797 |

482

483

TABLE III. Oxidation of Secondary Alcohols (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, SO₃	(86)	706
C₂₂	DMSO, TFAA	(—)	317
both diastereomers	DMSO, TFAA	(—)	317
	DMSO, Py, SO₃	(20)	798
	DMSO, (COCl)₂	(55)	75
	DMSO, TFAA	(—)	783
	DMSO, (COCl)₂	(98)	799
	DMSO, Ac₂O, K₂CO₃	(50)	140
	DMSO, DCC, TFA, Py	(87)	742

TABLE III. Oxidation of Secondary Alcohols (*Continued*)
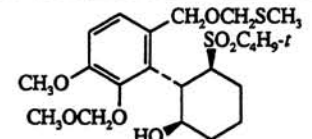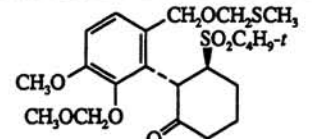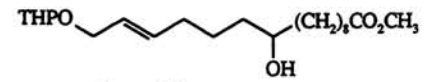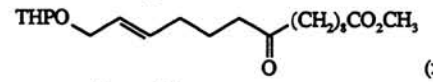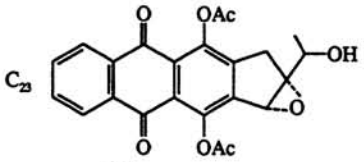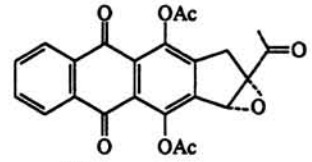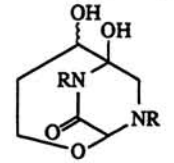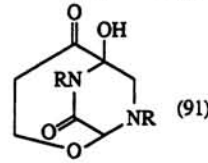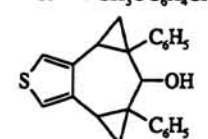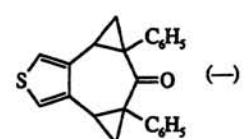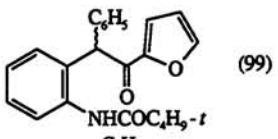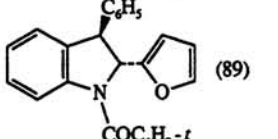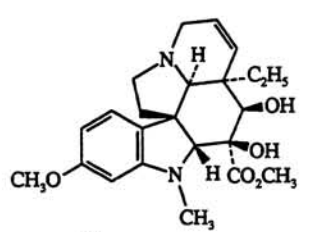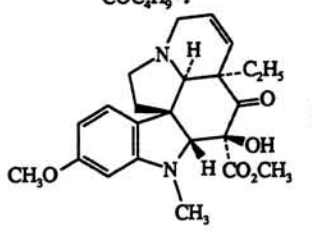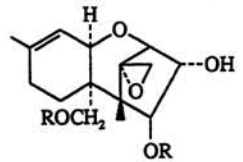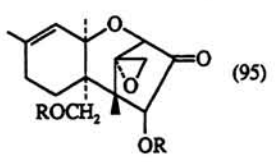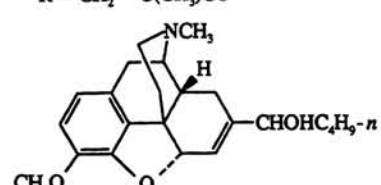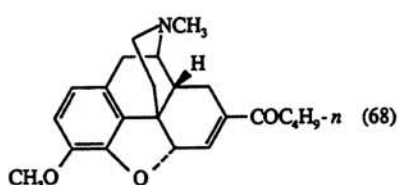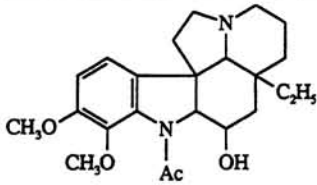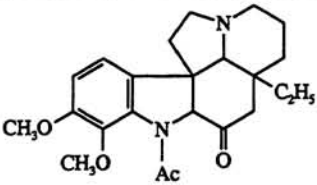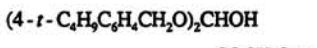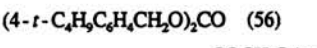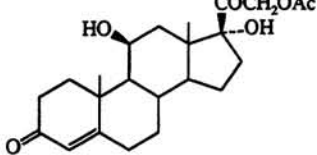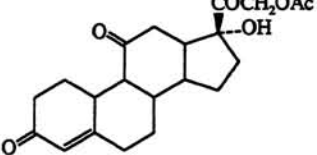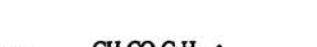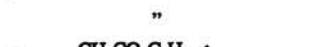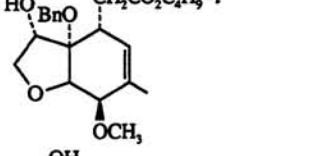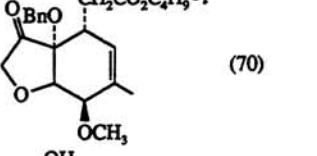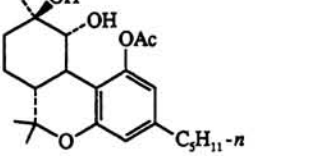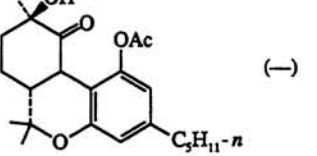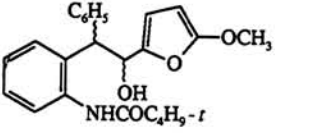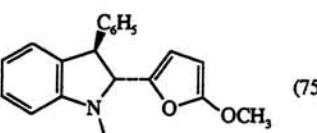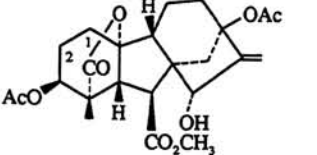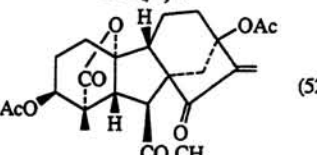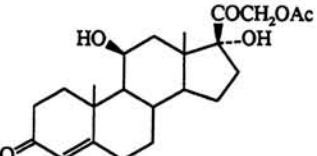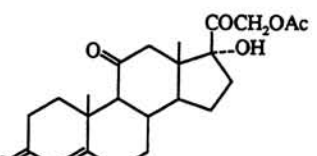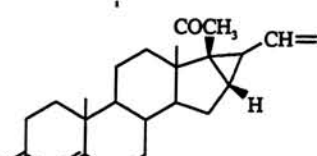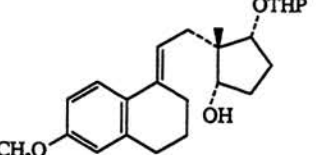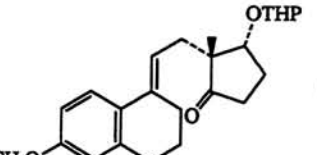
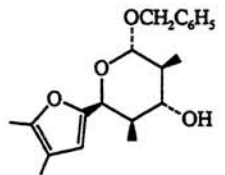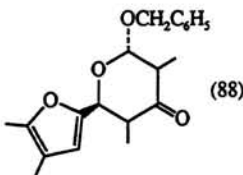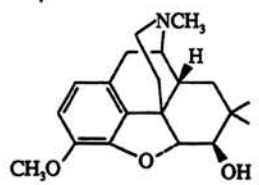| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, TFAA	(75)	800
	DMSO, (COCl)$_2$	(>75)	801
	DMSO, DCC, Py, TFA	(91)	802
R = 4-CH$_3$OC$_6$H$_4$CH$_2$	DMSO, (COCl)$_2$	(91)	803
	DMSO, Ac$_2$O	(—)	804
	1. DMSO, TFAA, −78° 2. TEA, −78°	(99)	160
	1. DMSO, TFAA, −78° 2. TEA, 0°	(89)	160
	DMSO, Py, SO$_3$	(73)	798
R = CH$_2$=C(CH$_3$)CO	DMSO, TFAA	(95)	777
	DMSO, Ac$_2$O	(68)	779

486

487

C$_{23}$

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

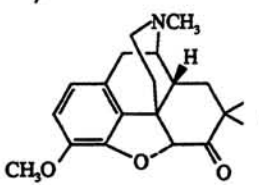| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, DCC, H₃PO₄	(83)	30
(4-*t*-C₄H₉C₆H₄CH₂O)₂CHOH	DMSO, DCC, Py, TFA	(4-*t*-C₄H₉C₆H₄CH₂O)₂CO (56)	724
	DMSO, TFAA	(~100)	27
	DMSO, Ac₂O, 92 h	„ (53)	11
	DMSO, (COCl)₂	(70)	611
	DMSO, Ac₂O	(—)	805
	DMSO, TFAA	(75)	160
also Δ-1, 2	1. DMSO, (COCl)₂ 2. DIPEA	(52)	75
	DMSO, (COCl)₂	(58)	38
	DMSO, DCC	(low)	806
	DMSO, DCC, TFA, Py	(100)	125, 770
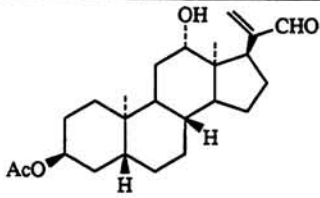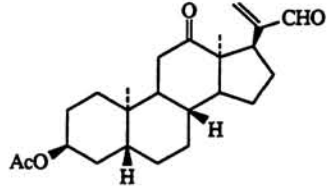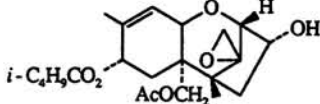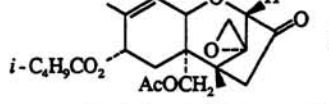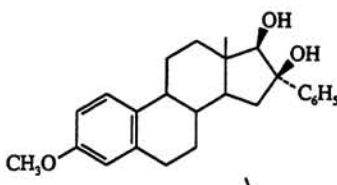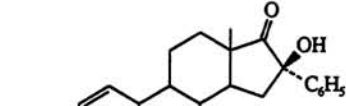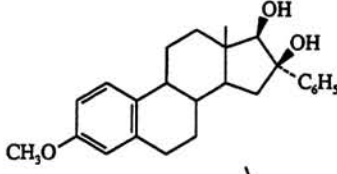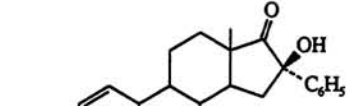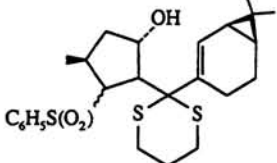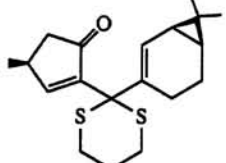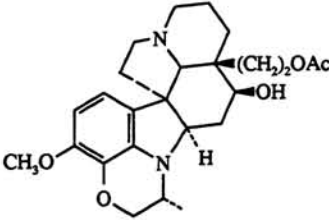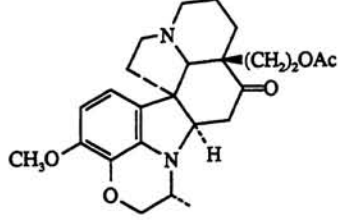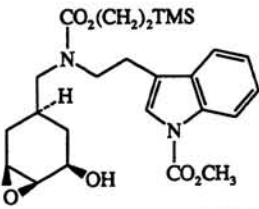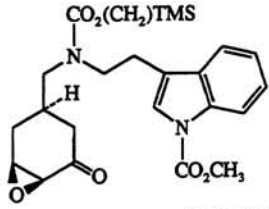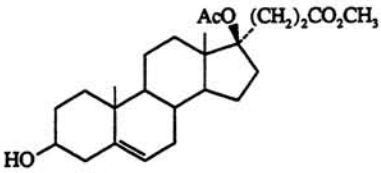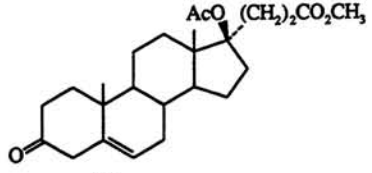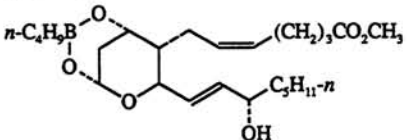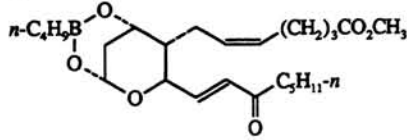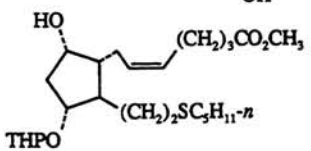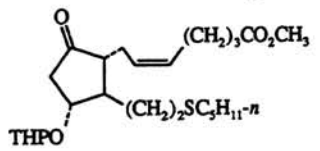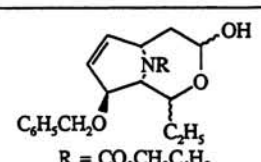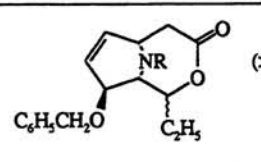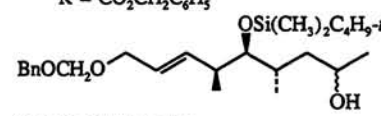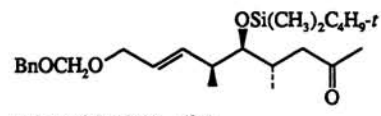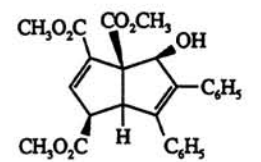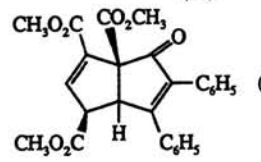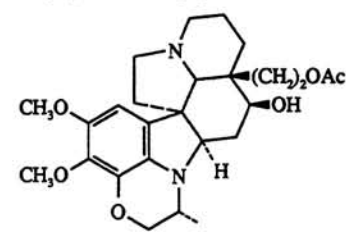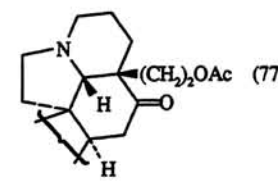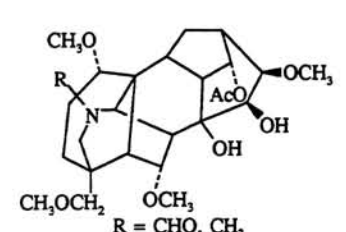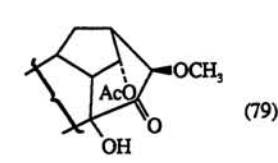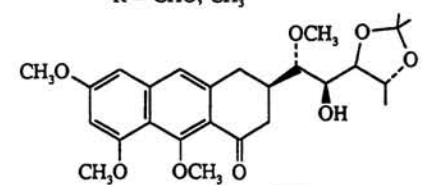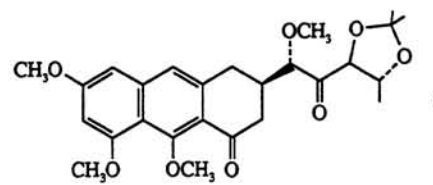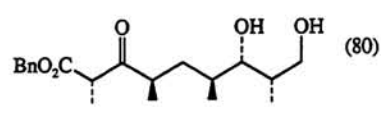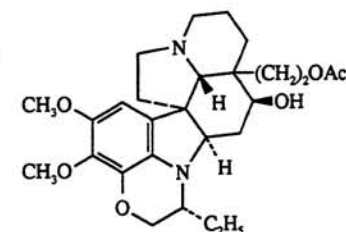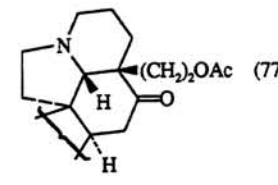
TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)$_2$	(90)	807
	(CH$_3$)$_2$S, NCS	(96)	219
n-C$_{10}$H$_{21}$CH(SeC$_6$H$_5$)CHOHC$_6$H$_{13}$-n	(CH$_3$)$_2$S, NCS	n-C$_{10}$H$_{21}$CH(SeC$_6$H$_5$)COC$_6$H$_{13}$-n (70)	449
	DMSO, SO$_3$, Py	(91)	756
	1. DMSO, TFAA 2. NaOH	(70)	808
	DMSO, DCC, H$_3$PO$_4$	(73)	809
	DMSO, (COCl)$_2$	(93)	810
	DMSO, SO$_3$, Py	(92)	811
	DMSO, DCC, CHCl$_2$CO$_2$H	(74)	812
	DMSO, DCC	(>74)	813

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

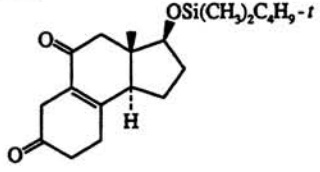| Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, TFAA	(>70)	814
	DMSO, (COCl)$_2$	(85)	111
C$_{26}$ (C$_6$H$_5$)$_3$CCHOHC$_6$H$_5$	DMSO, Ac$_2$O DMSO, O$_2$, reflux	(C$_6$H$_5$)$_3$CCOC$_6$H$_5$ (95) " (50)	634 634
	(CH$_3$)$_2$S, NCS	(—)	815
	DMSO, DCC, H$_3$PO$_4$	(CH$_2$)$_2$OAc (77)	809
R = CHO, CH$_3$	DMSO, TFAA	(79)	816, 817
	DMSO, TFAA	(85)	818
	1. DMSO, (COCl)$_2$, DIPEA 2. H$_2$O$_2$	(80)	72
C$_{27}$	DMSO, DCC, H$_3$PO$_4$	(CH$_2$)$_2$OAc (77)	809

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
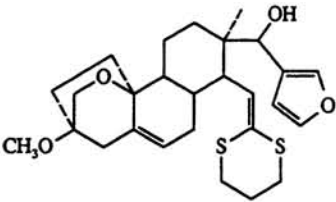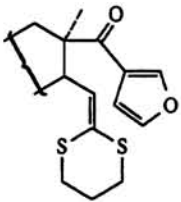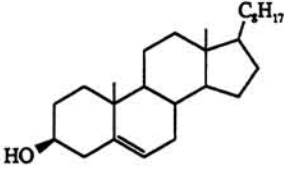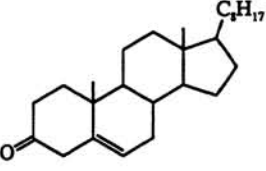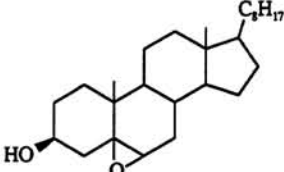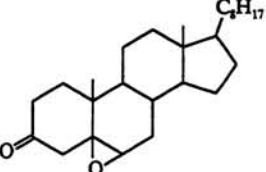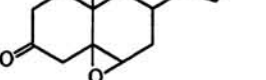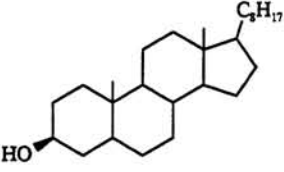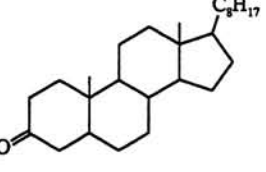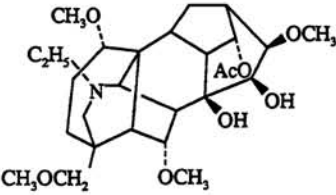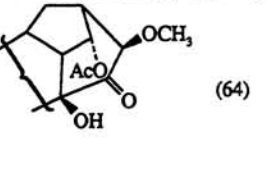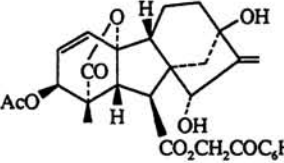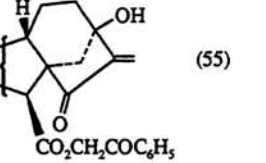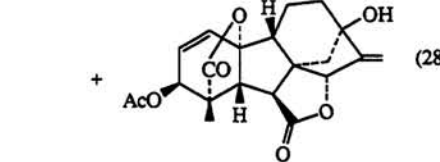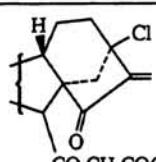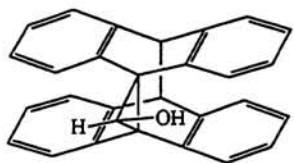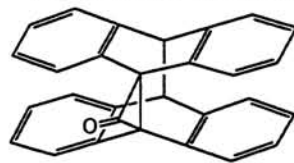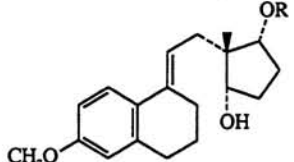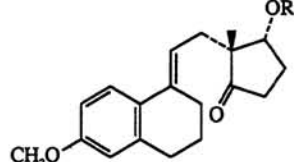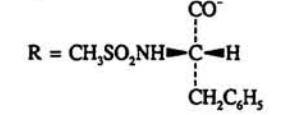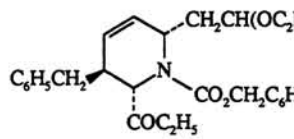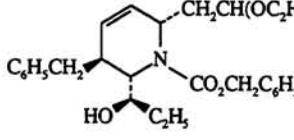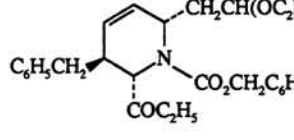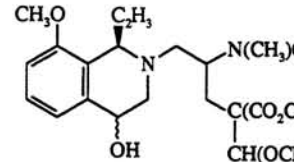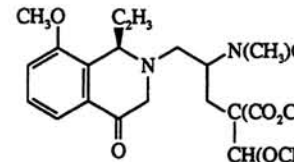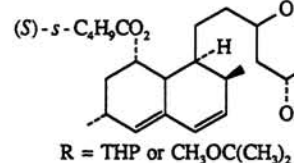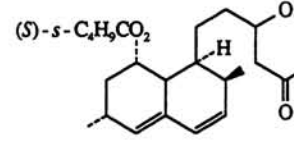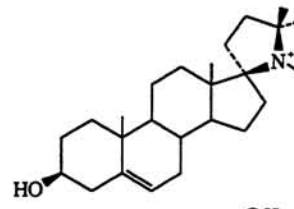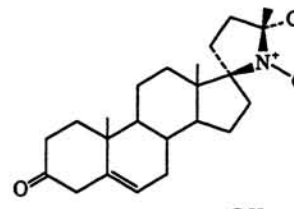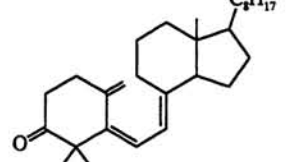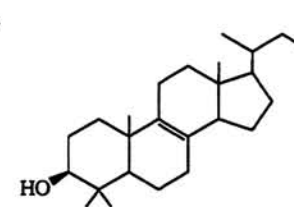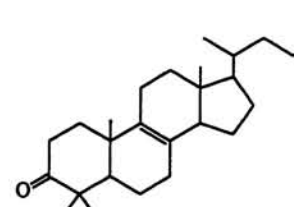
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, TFAA	(48)	819
	DMSO, DCC, Py, TFA	(66)	30, 776
	DMSO, (COCl)$_2$, −10°	(95)	22
	DMSO, TFAA	(~100)	27
		Δ5 : Δ4 = 2 : 1	
	DMSO, Tf$_2$O	(60)	45
	DMSO, CH$_3$C≡CN(C$_2$H$_5$)$_2$	(55)	54
	DMSO, DCC, Py, TFA	α - epoxide (52)	820
		β - epoxide (36)	820
	DMSO, (COCl)$_2$	(96)	22
	DMSO, Tf$_2$O	(73)	45
	DMSO, SO$_3$, Py	(83)	13
	1. COCl$_2$	(80)	14
	2. DMSO		
	DMSO, DCC, Py, TFA	(80)	30
	DMSO, DCC, Py, H$_3$PO$_4$	(67)	30
		+ methylthiomethyl ether (8)	
C$_{28}$	DMSO, TFAA	(64)	817
C$_{29}$	1. DMSO, (COCl)$_2$	(55)	75
	2. DIPEA		
		(28)	

494

495

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)
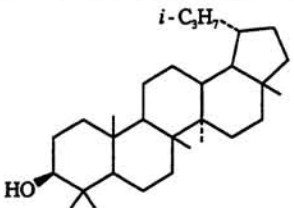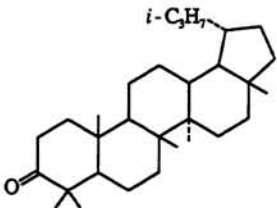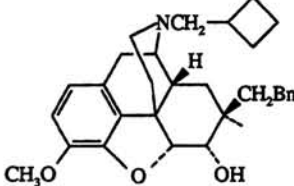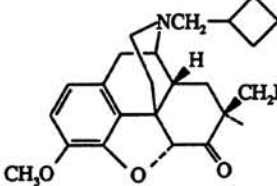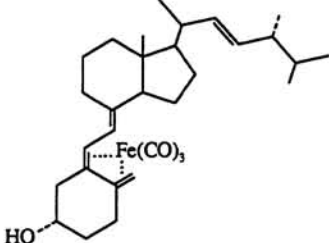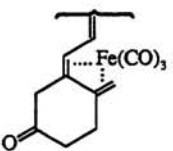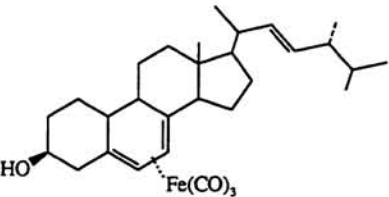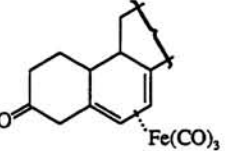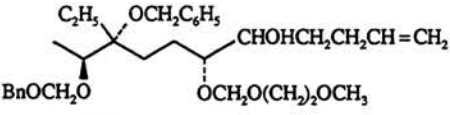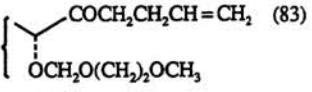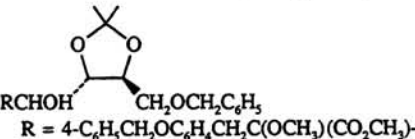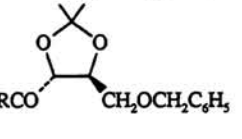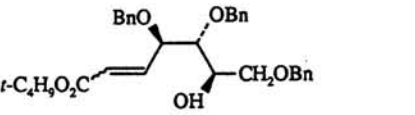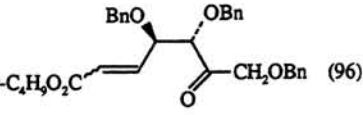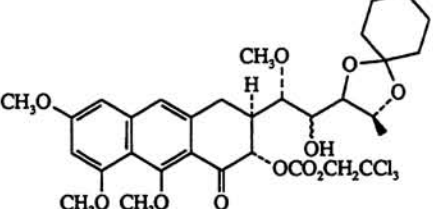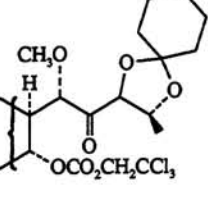
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	1. DMSO, (COCl)₂ 2. TEA	(58) + "small amounts" two products above	75
	DMSO, DIPC, Py, TFA	(—)	821
	DMSO, DCC, Py, TFA	(80)	125, 770
	DMSO, TFAA	(83)	814
	DMSO, (COCl)₂	(83)	822
	DMSO, TFAA	(87)	823
	(CH₃)₂S, NCS	(~100)	171
	DMSO, DEC, Py, TFA	(82)	200
	DMSO, DCC, Py, TFA	(94)	824

496

497

C₃₀

R = CH₃SO₂NH—C—H
CH₂C₆H₅
CO⁻

R = THP or CH₃OC(CH₃)₂

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)$_2$	(86)	825
	DMSO, TFAA	(77)	525
C$_{31}$	(CH$_3$)$_2$S, NCS	(90)	826
	(CH$_3$)$_2$S, NCS	(46)	826
	DMSO, (COCl)$_2$	(83)	559
C$_{32}$ RCHOH R = 4-C$_6$H$_5$CH$_2$OC$_6$H$_4$CH$_2$C(OCH$_3$)(CO$_2$CH$_3$)-	DMSO, (COCl)$_2$	(>62)	827
	DMSO, (COCl)$_2$	(96)	828
	DMSO, TFAA	(85)	829

TABLE III. OXIDATION OF SECONDARY ALCOHOLS (Continued)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, TFAA	(100)	525
	DMSO, SO₃, Py	(80)	830, 831
	DMSO, DCC, Cl₂CHCO₂H	(69)	832
C₃₃	DMSO, TFAA	(96)	525
C₃₄	DMSO, TFAA	(81)	524
22−R 22−S	(CH₃)₂, NCS	(80) (75)	833
C₃₆	(CH₃)₂S, NCS	(>90)[b]	18

500

501

[a] This product was formed by air oxidation.

[b] The product was isolated as the dinitrophenylhydrazone.

[c] The product was isolated as the i-C₃H₇(CH₃)₂Si ester.

TABLE IV. Oxidation of Secondary Carbohydrate Alcohols
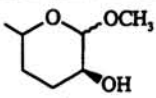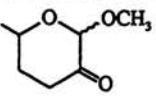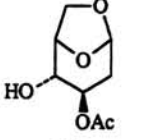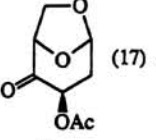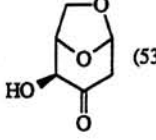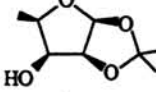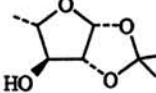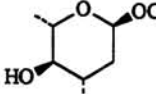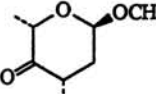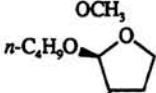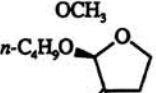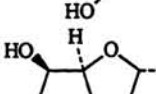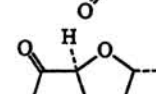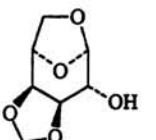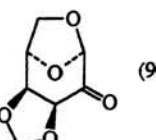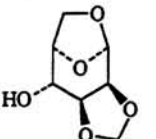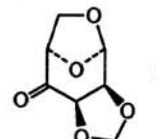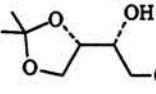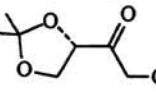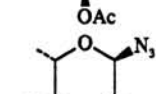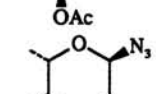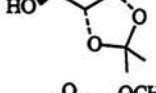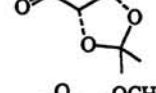
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C₇ mixture	DMSO, DCC, Py, TFA	(70)	834
C₈	DMSO, (COCl)₂	(17) + (53)	835
	DMSO, (COCl)₂	(—)	836
	DMSO, DCC, Py, H₃PO₄	(—)	837
	DMSO, DCC	(~50)	838
	DMSO, DCC, H₃PO₄	(—)	839
C₉	DMSO, P₂O₅	(40)	35, 320
	DMSO, Ac₂O	(90)	316, 840, 841
	DMSO, Ac₂O	(77)	842, 843
	DMSO, (COCl)₂	(85)	844
	DMSO, (COCl)₂	(96)	616
	DMSO, TFAA	(98)	845
	DMSO, Ac₂O	(18)	846

502

503

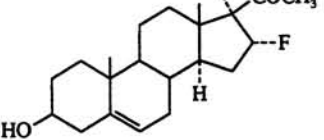TABLE IV.   OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)
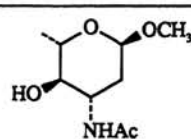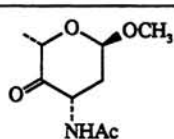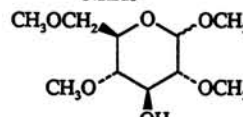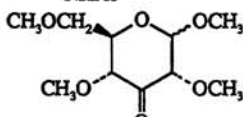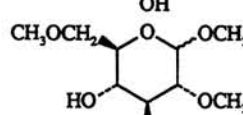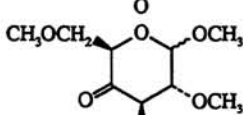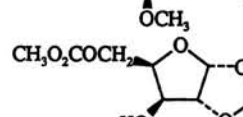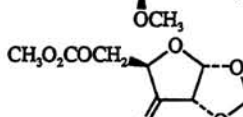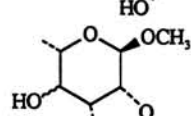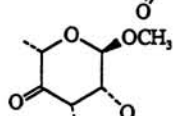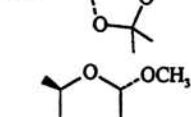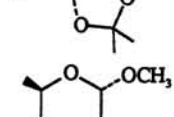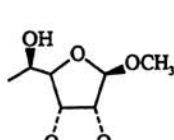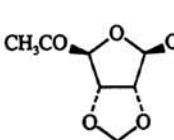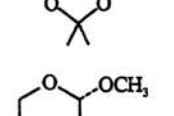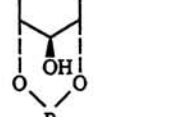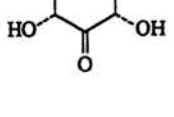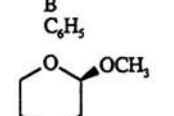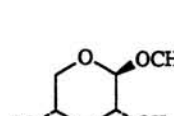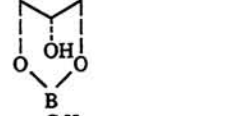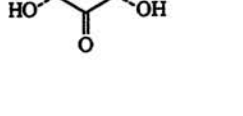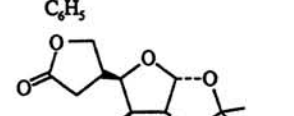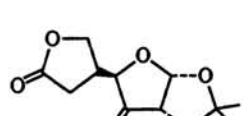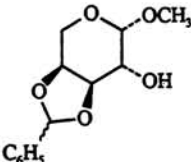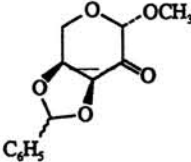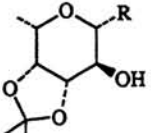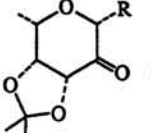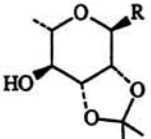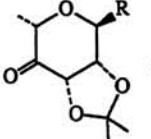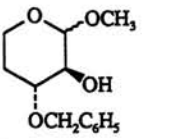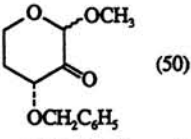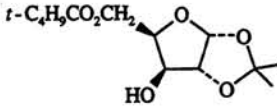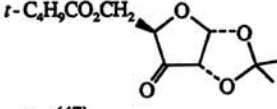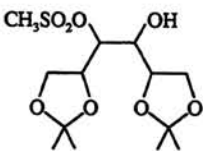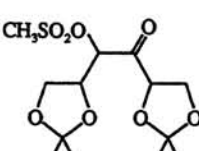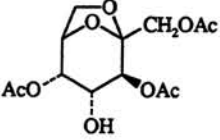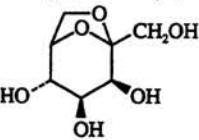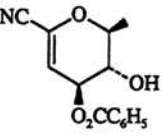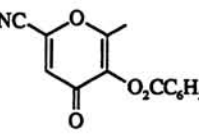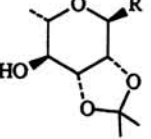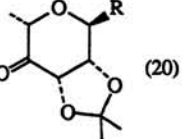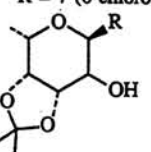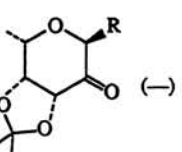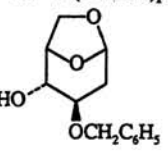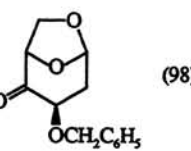
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, TFAA	(63)	847
C$_{10}$	DMSO, P$_2$O$_5$, DMF	(85)	207
	DMSO, P$_2$O$_5$, DMF	(80)	207
	DMSO, DCC, H$_3$PO$_4$, Py	(82)	848
	DMSO, TFAA	(87)	849
	DMSO, P$_2$O$_5$	(81)	850
	DMSO, DCC, Py, TFA	(71)	851
	DMSO, Ac$_2$O	" (81)	851
C$_{11}$	1. DMSO, Ac$_2$O, 40° 2. H$_2$O, 45°	(50)	843, 852
	"	(80)	852
	DMSO, P$_2$O$_5$, DMF	(83)	853
	DMSO, (COCl)$_2$	(85)	57, 311

504

505

TABLE IV. Oxidation of Secondary Carbohydrate Alcohols (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac₂O	(44)	854
	DMSO, P₂O₅	ʺ (63)	854
C₁₂	DMSO, SO₃, Py	(34)	855
	DMSO, DCC	(—)	147
	DMSO, Ac₂O	(70)	856, 857
	DMSO, AcCl	ʺ (76)	236
	DMSO, DCC, H₃PO₄, Py	ʺ (85)	858
	DMSO, P₂O₅	(65)	12
			316
	DMSO, DCC, H₃PO₄	ʺ (70)	26
	DMSO, (COCl)₂	ʺ (83)	849
	DMSO, TFAA	ʺ (85)	849, 859,
	DMSO, Ac₂O	ʺ (>88)	860
	DMSO, Ac₂O	(100)	842
	DMSO, DCC	ʺ (35)	842
	DMSO, DCC, H₃PO₄	(50)	851
	DMSO, P₂O₅	ʺ (34)	851
C₁₃	DMSO, DCC, Py, TFA	(—)	861
R = 7-theophyllinyl	DMSO, DCC	(—)	147

TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac$_2$O	β-C$_6$H$_5$ (45) α-C$_6$H$_5$ (60)	862
R = 1-(5-fluoro)uracylyl	DMSO, DCC	(—)	147
R = 1-(5-fluoro)uracylyl	DMSO, DCC	(—)	147
	DMSO, DCC, H$_3$PO$_4$	(50)	863
	DMSO, DCC, Py, TFA	(80)	152
	DMSO, Ac$_2$O	„ (47) + 3 - acetate (11)	152
	DMSO, DCC, H$_3$PO$_4$	(74)	864
	1. DMSO, Ac$_2$O 2. NaBH$_4$	(>33)	865
C$_{14}$	DMSO, (COCl)$_2$	(—)	185
R = 7-(6-chloro)purinyl	DMSO, DCC, Cl$_2$CHCO$_2$H	(20)	866
R = 7-(6-chloro)purinyl	DMSO, DCC, Py, TFA	(—)	867
	DMSO, (COCl)$_2$	(98)	614, 868

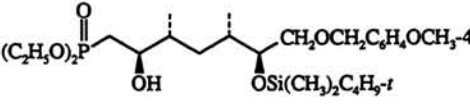TABLE IV.   OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac₂O	(65)	870
	DMSO, Ac₂O	" (—)	870
3-OH isomer	DMSO, Ac₂O	(80)	870, 871
	DMSO, Ac₂O	3-keto isomer (90)	872
	DMSO, TFAA	" (89)	849
	DMSO, (COCl)₂	(55)	844
	DMSO, DCC, Py, TFA	(60)	834
both epimers	DMSO, Ac₂O	(84)	144
	DMSO, SO₃, Py	(—)	873
	DMSO, DCC, CH₃PO₃H₂	(80)	874
	DMSO, (COCl)₂	(62)	875
	DMSO, DCC, Py, TFA	(62)	876
	DMSO, Ac₂O	" (31)	877
	DMSO, (COCl)₂	(98)	617

TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)
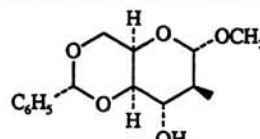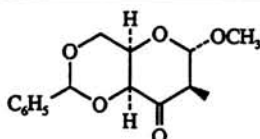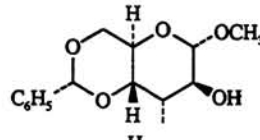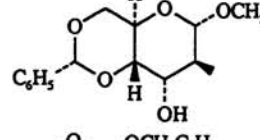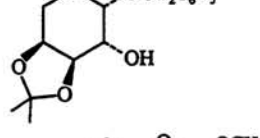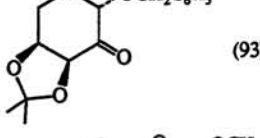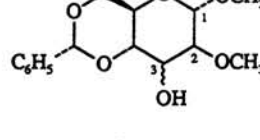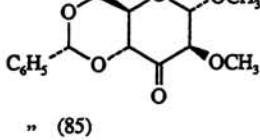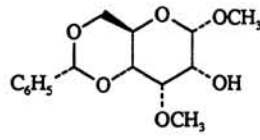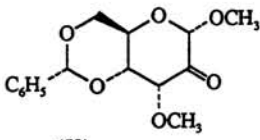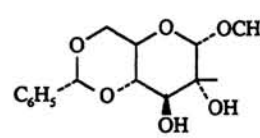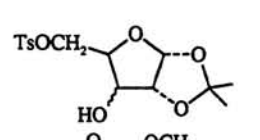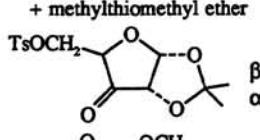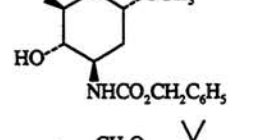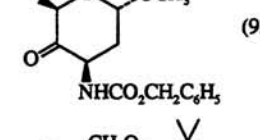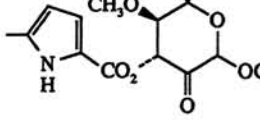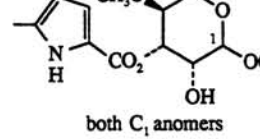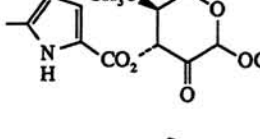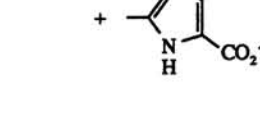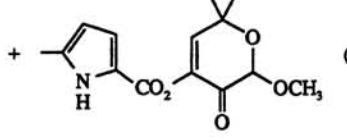
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac₂O, 4 h	(83)	43
	DMSO, Ac₂O, 4 h	(—)	43
	DMSO, Ac₂O, 4 h	(—)	43
	DMSO, (COCl)₂	(93)	495
1 - β, 2,3 - α	DMSO, TFAA	(98)	849
	DMSO, Ac₂O	„ (85)	849
	DMSO, TFAA	„ 1 - β, 2 - α (89)	878
	DMSO, TFAA	(93)	849
	DMSO, Ac₂O	„ (52)	849
	DMSO, TFAA	(48) + methylthiomethyl ether (36)	879
	DMSO, P₂O₅	β (35) α (31)	35
	DMSO, TFAA	(93)	880
both C₁ anomers	DMSO, DCC, H₃PO₄	(75) + (—)	881

512

513

TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)
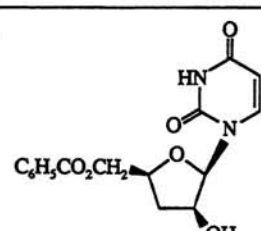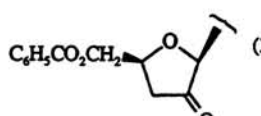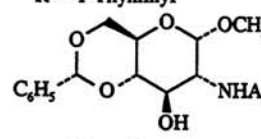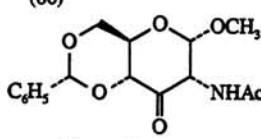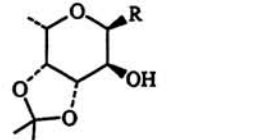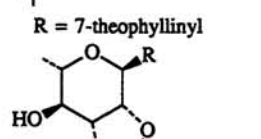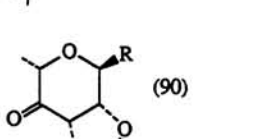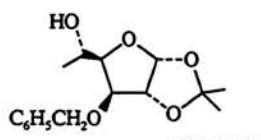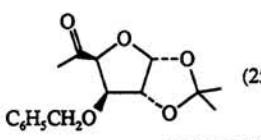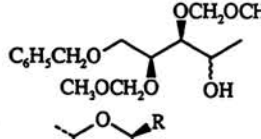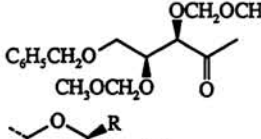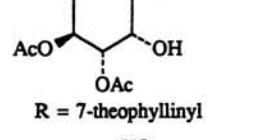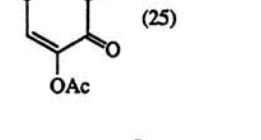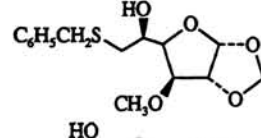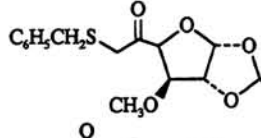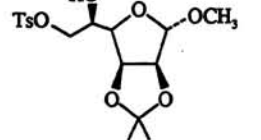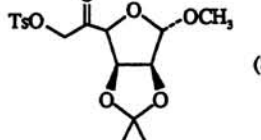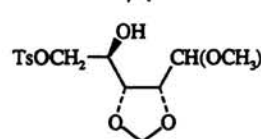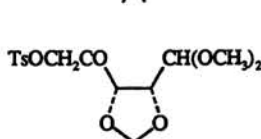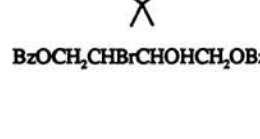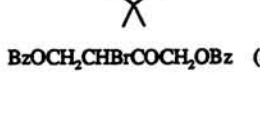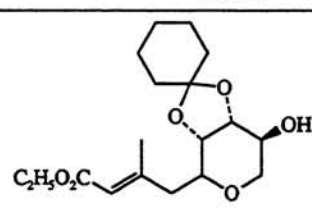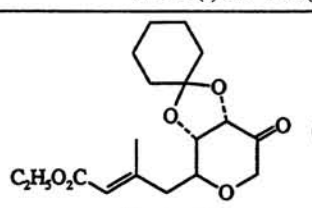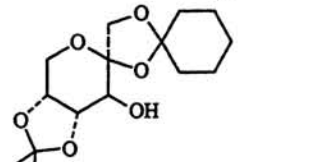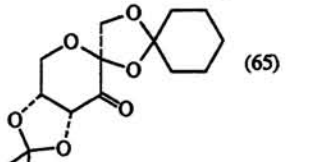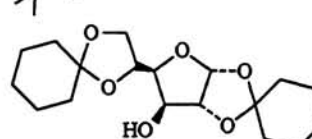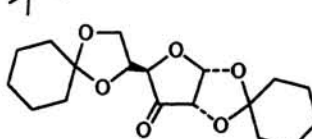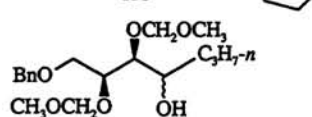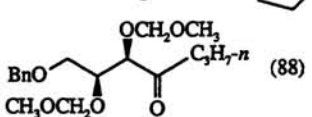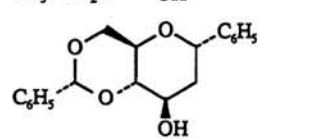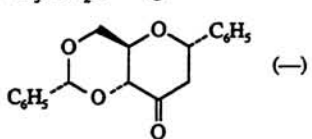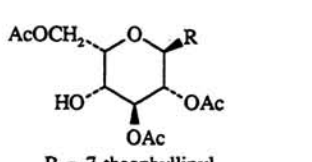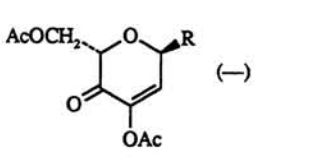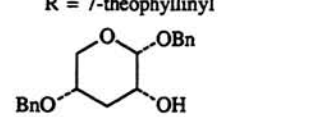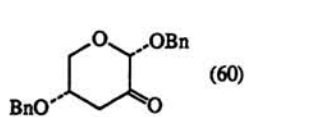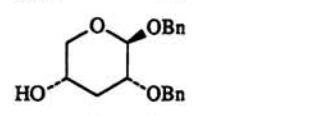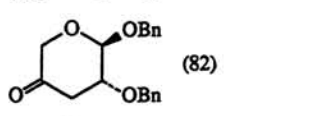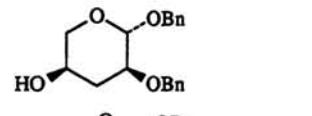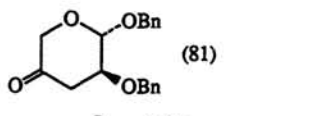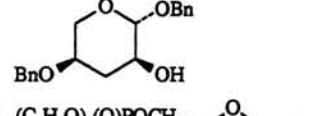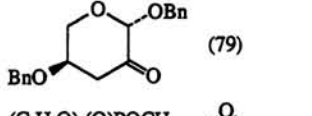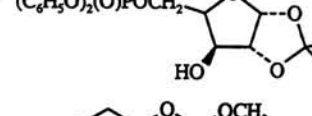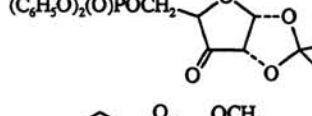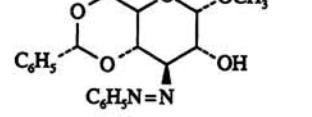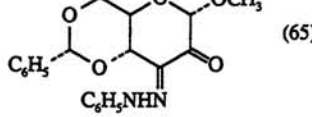
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{16}$			
(uracil nucleoside structure) C$_6$H$_5$CO$_2$CH$_2$ ... OH	DMSO, Ac$_2$O	C$_6$H$_5$CO$_2$CH$_2$ ... =O (38)	882
C$_6$H$_5$CH$_2$O(CH$_2$)$_2$CHOHCH$_2$R R = 9-Adeninyl R = 9-Guaninyl R = 1-Thyminyl	DMSO, DCC, CH$_3$PO$_3$H$_2$	C$_6$H$_5$CH$_2$O(CH$_2$)$_2$COCH$_2$R (18) (42) (80)	874 874 874
(pyranose structure) C$_6$H$_5$ ... OCH$_3$, NHAc, OH	DMSO, P$_2$O$_5$	C$_6$H$_5$ ... OCH$_3$, =O, NHAc (71)	35, 320
(pyranose structure) R, OH; R = 7-theophyllinyl	DMSO, DCC, Py, TFA	R, =O (—)	867
HO (pyranose structure) R; R = 7-theophyllinyl	DMSO, DCC, CHCl$_2$CO$_2$H	O= ... R (90)	866
HO (furanose structure) C$_6$H$_5$CH$_2$O	DMSO, Ac$_2$O	O= (furanose structure) C$_6$H$_5$CH$_2$O (25)	883
C$_6$H$_5$CH$_2$O ... OCH$_2$OCH$_3$, CH$_3$OCH$_2$O, OH	DMSO, (COCl)$_2$	C$_6$H$_5$CH$_2$O ... OCH$_2$OCH$_3$, CH$_3$OCH$_2$O, =O (99)	884
C$_{17}$			
(pyranose structure) R, AcO, OH, OAc; R = 7-theophyllinyl	DMSO, DCC, CHCl$_2$CO$_2$H	R, =O, OAc (25)	885
HO, C$_6$H$_5$CH$_2$S (furanose structure) CH$_3$O	DMSO, DCC, Py, H$_3$PO$_4$	O=, C$_6$H$_5$CH$_2$S (furanose structure) CH$_3$O (76)	886
HO, TsO (furanose structure) OCH$_3$	DMSO, Ac$_2$O	O=, TsO (furanose structure) OCH$_3$ (85)	887
TsOCH$_2$ ... OH, CH(OCH$_3$)$_2$	DMSO, (COCl)$_2$	TsOCH$_2$CO ... CH(OCH$_3$)$_2$ (90)	888
BzOCH$_2$CHBrCHOHCH$_2$OBz	DMSO, DCC, Py, TFA	BzOCH$_2$CHBrCOCH$_2$OBz (82)	889

TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, SO$_3$, Py	(—)	889
	DMSO, Ac$_2$O	(65)	856
C$_{18}$	DMSO, Ac$_2$O	(50)	856, 891 892
	DMSO, (COCl)$_2$	(88)	884
C$_{19}$	DMSO, Ac$_2$O	(—)	869
R = 7-theophyllinyl	DMSO, DCC	(—)	147
	DMSO, (COCl)$_2$	(60)	893
	DMSO, (COCl)$_2$	(82)	893
	DMSO, (COCl)$_2$	(81)	893
	DMSO, (COCl)$_2$	(79)	893
C$_{20}$	DMSO, P$_2$O$_5$	(35)	35
	DMSO, DCC, H$_3$PO$_4$	(65)	114

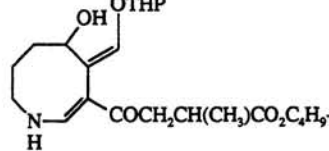TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)
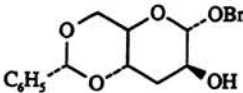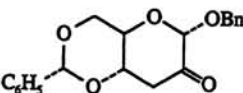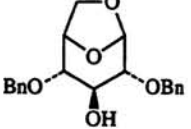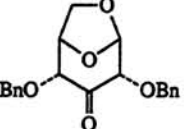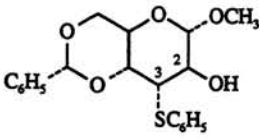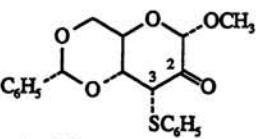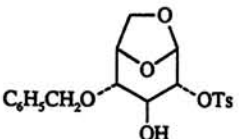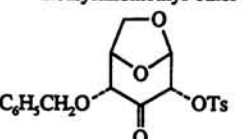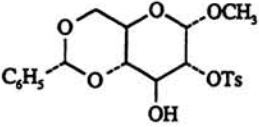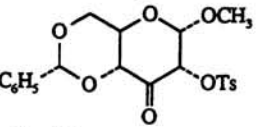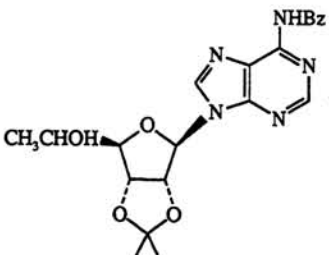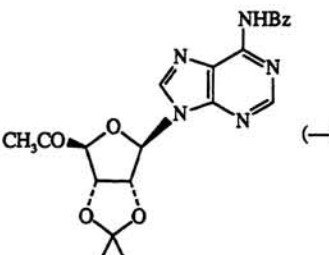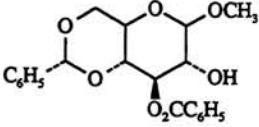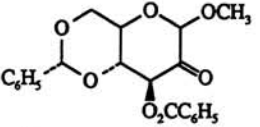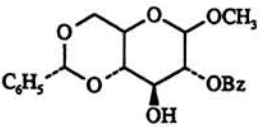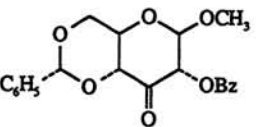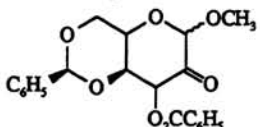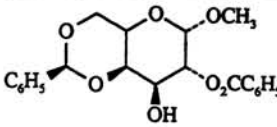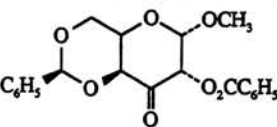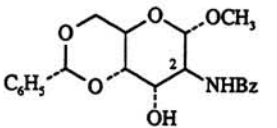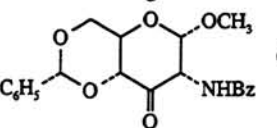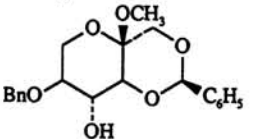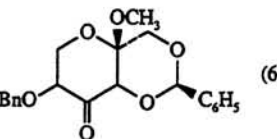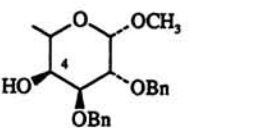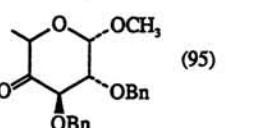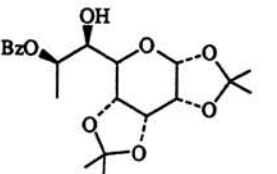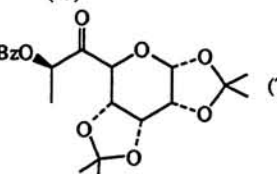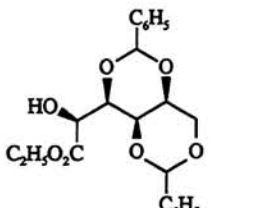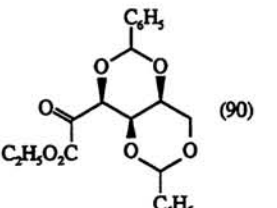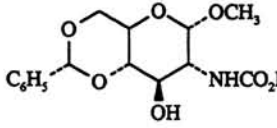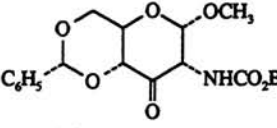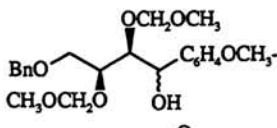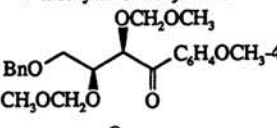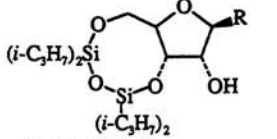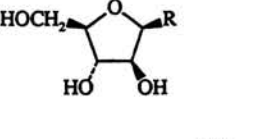
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac₂O	(76)	894
	DMSO, Ac₂O, 100°	(45)	895
	DMSO, DCC, Py, TFA	(—)	896
	DMSO, Ac₂O	" (40) + methylthiomethyl ether	896
	DMSO, Ac₂O, 100°	(30)	895
	DMSO, P₂O₅	(49)	851
	DMSO, Ac₂O DMSO, DCC, H₃PO₄	" (49) " (80)	851 864
	DMSO, DCC, Py, TFA	(—)	897
	DMSO, TFAA	α-OCH₃ (87)	849
	DMSO, Ac₂O DMSO, DCC, H₃PO₄ DMSO, DCC, H₃PO DMSO, P₂O₅	" (46) " β-OCH₃ (90) " α-OCH₃ (88) " (~80)	849 898 898 899
α-OCH₃ 	DMSO, TFAA	(98) (β-OCH₃)	849
	DMSO, TFAA DMSO, Ac₂O DMSO, Ac₂O DMSO, DCC, H₃PO₄ DMSO, DCC, H₃PO₄	" α-OCH₃ (97) " β-OCH₃ (48) " α-OCH₃ (52) " β-OCH₃ (90) " α-OCH₃ (88)	849 849 849, 900 898 898
	DMSO, DCC, H₃PO₄	α (84) β (56)	901

C₂₁

518

519

TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
(structure: benzylidene methyl glycoside with O₂CC₆H₅, OH)	DMSO, DCC, H₃PO₄	*(structure)* (75)	901
(structure: benzylidene methyl glycoside, NHBz, OH) β at C₂	DMSO, DCC	*(structure)* (95)	902
α at C₂	DMSO, DCC	" (83)	902
(structure: OCH₃, BnO, OH, C₆H₅)	DMSO, P₂O₅	*(structure)* (60)	903
(structure: HO, OCH₃, OBn, OBn) α-4-OH	DMSO, P₂O₅	*(structure)* (95)	904
	DMSO, P₂O₅	" " "very slow"	904
	(CH₃)₂S, Cl₂	" (93)	905
(structure: BzO, OH, isopropylidene acetonide)	DMSO, DCC, Py, HCl	*(structure)* (78)	906
C₂₂ *(structure: C₆H₅ benzylidene, HO, C₂H₅O₂C)*	DMSO, TFAA	*(structure)* (90)	63
(structure: benzylidene methyl glycoside, NHCO₂Bn, OH)	DMSO, DCC, H₃PO₄	*(structure)* (77)	907
	DMSO, Ac₂O	" (76) + methylthiomethyl ether	907
(structure: OCH₂OCH₃, BnO, C₆H₄OCH₃-4, CH₃OCH₂O, OH)		*(structure)* (83)	884
(structure: (i-C₃H₇)₂Si-O-Si(i-C₃H₇)₂ tethered furanose, R, OH) R = 1-adeninyl R = diaminopurinyl R = 1-guaninyl	1. DMSO, Ac₂O 2. NaBH₄ 3. (n-C₄H₉)₄NF	*(structure: HOCH₂, R, HO, OH)* (63) (48) (41)	908

TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)
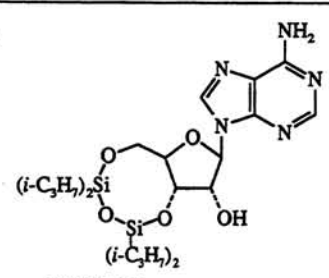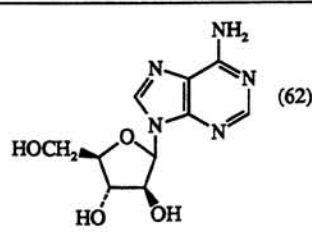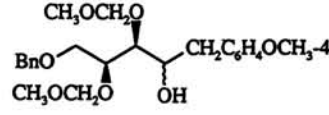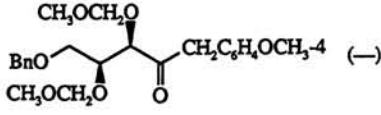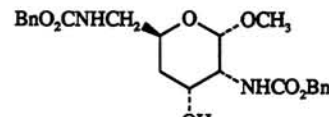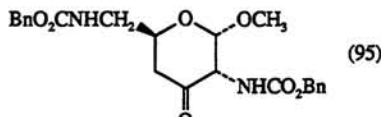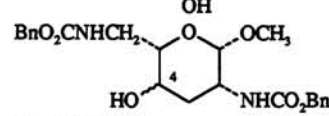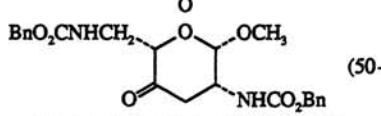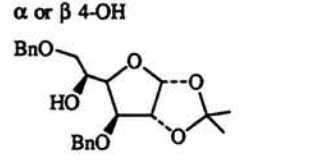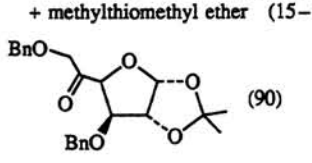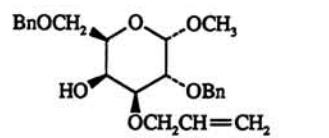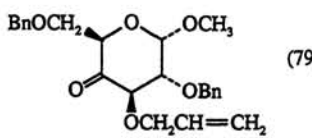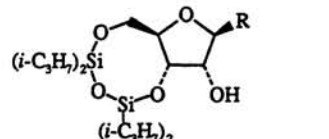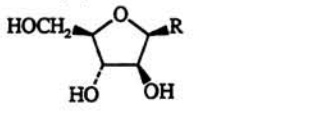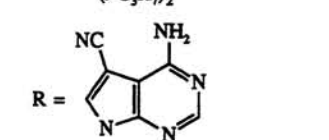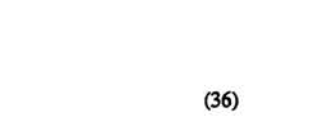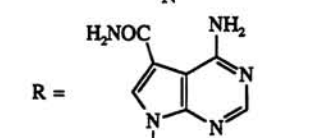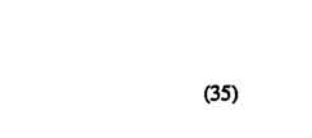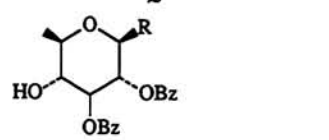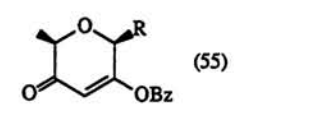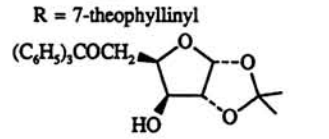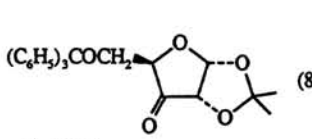
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C_{23}	1. DMSO, Ac_2O 2. $NaBH_4$ 3. $(n\text{-}C_4H_9)_4NF$	(62)	908
	DMSO, $(COCl)_2$	(—)	884
	DMSO, Ac_2O	(95)	909
α or β 4-OH	DMSO, Ac_2O	(50–52) + methylthiomethyl ether (15–18)	909
	DMSO, $(COCl)_2$	(90)	61
C_{24}	$(CH_3)_2S$, NCS	(79)	910
	DMSO, $(COCl)_2$	" (84)	910
	1. DMSO, Ac_2O 2. $NaBH_4$ 3. $(n\text{-}C_4H_9)_4NF$		
$R =$		(36)	908
$R =$		(35)	908
C_{27} R = 7-theophyllinyl	DMSO, DCC	(55)	147
	DMSO, DCC, Py, TFA	(80)	861, 911
	DMSO, Ac_2O	" (~30) + methylthiomethyl ether	861

TABLE IV. Oxidation of Secondary Carbohydrate Alcohols (*Continued*)
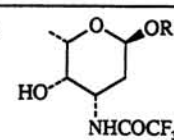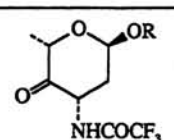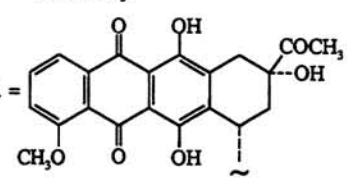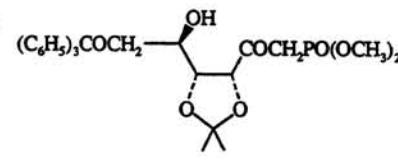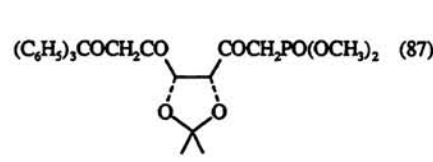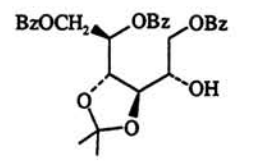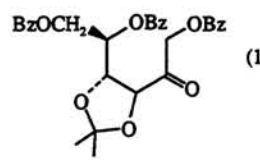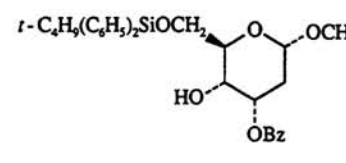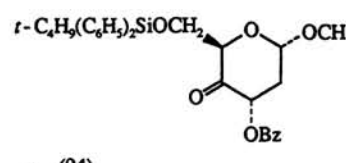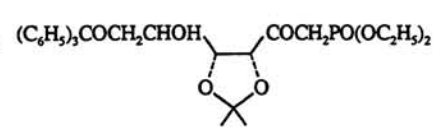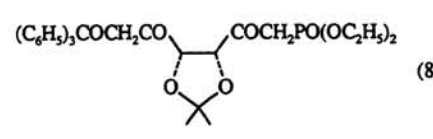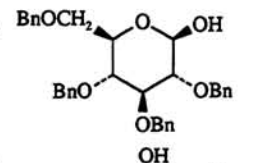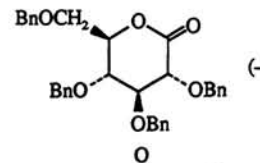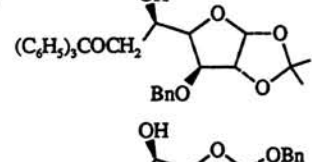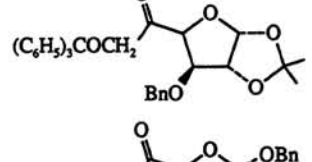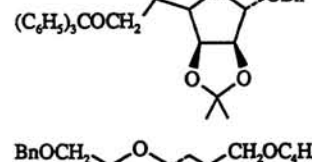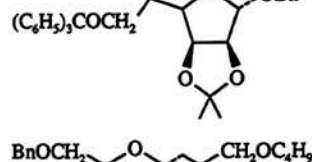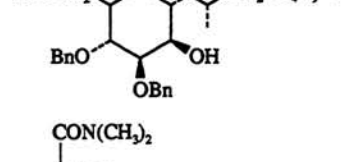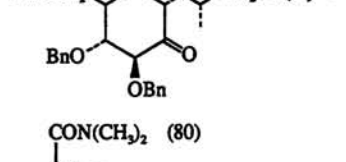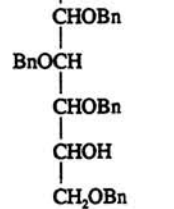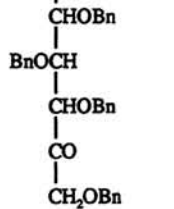
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.

C_{29} — DMSO, TFAA — (80) — 60

$R = $ [anthracycline structure with COCH₃, OH, CH₃O, OH substituents]

C_{30}

$(C_6H_5)_3COCH_2$ ... $COCH_2PO(OCH_3)_2$ — DMSO, TFAA — $(C_6H_5)_3COCH_2CO$ ... $COCH_2PO(OCH_3)_2$ (87) — 64

$BzOCH_2$, OBz, OBz — DMSO, Ac₂O — (100) — 293

$t\text{-}C_4H_9(C_6H_5)_2SiOCH_2$ ... OCH_3 — DMSO, Ac₂O — (80) — 53

DMSO, 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride, Py, TFA — ,, (94) — 53

C_{32} $(C_6H_5)_3COCH_2CHOH$ ... $COCH_2PO(OC_2H_5)_2$ — DMSO, TFAA — $(C_6H_5)_3COCH_2CO$ ... $COCH_2PO(OC_2H_5)_2$ (85) — 62

C_{34} $BnOCH_2$ ... OH, BnO, OBn, OBn — DMSO, (COCl)₂ — (—) — 58

C_{35} $(C_6H_5)_3COCH_2$ ... BnO — DMSO, Ac₂O — (91) — 912

$(C_6H_5)_3COCH_2$ ... OBn — DMSO, Ac₂O — (65) — 913

$BnOCH_2$ ... $CH_2OC_4H_9\text{-}t$, BnO, OH, OBn — DMSO, (COCl)₂ — (—) — 59

C_{36}

CON(CH₃)₂
|
CHOBn
|
BnOCH
|
CHOBn
|
CHOH
|
CH₂OBn

— DMSO, Ac₂O —

CON(CH₃)₂ (80)
|
CHOBn
|
BnOCH
|
CHOBn
|
CO
|
CH₂OBn

— 188

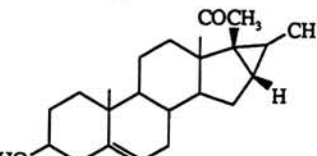TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)
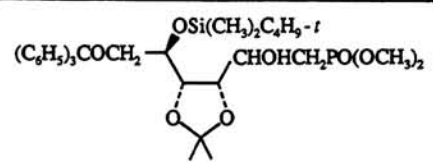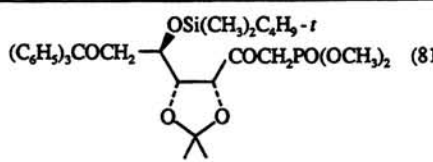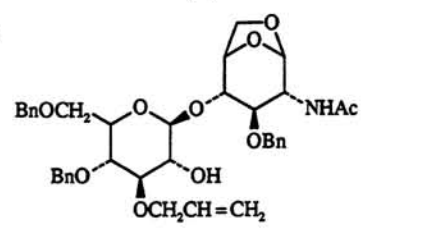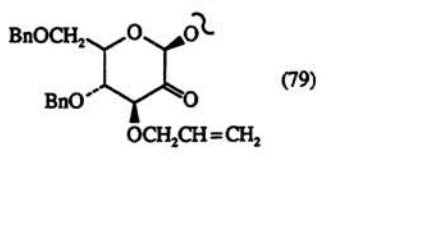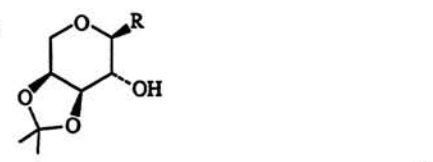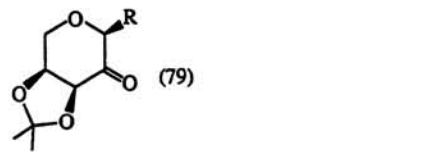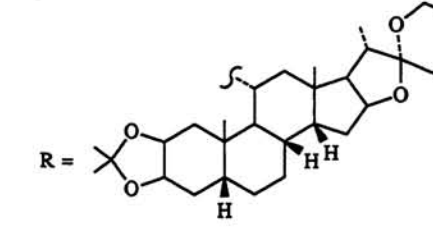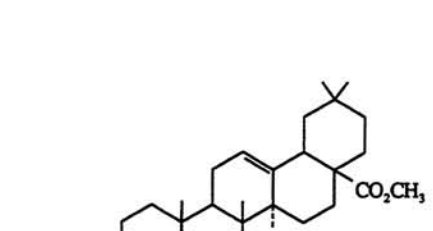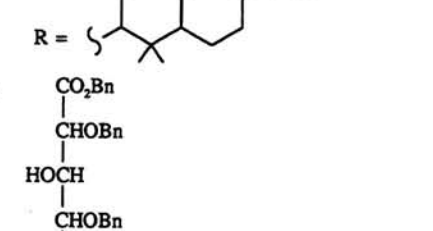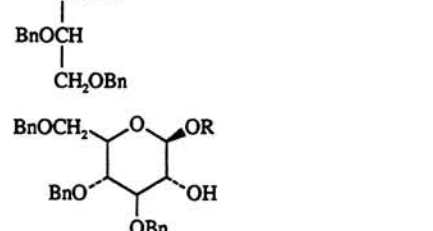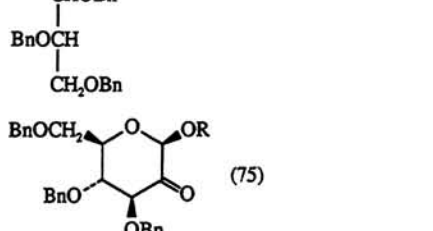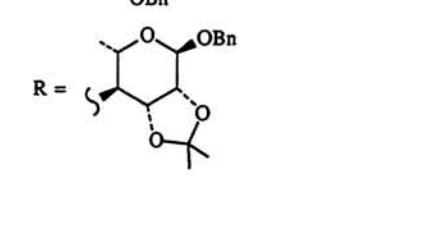
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, TFAA	(81)	64
C_{38}	DMSO, DCC, Py, TFA	(79)	914
C_{39}	DMSO, Ac$_2$O	(79)	915
	DMSO, Ac$_2$O	'' (82)	915
C_{41}	DMSO, DCC, Py, TFA	(45)	916
C_{43}	DMSO, Ac$_2$O	(75)	917

TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C₄₅	DMSO, Ac₂O	(86)	34, 319
C₄₆ R = 7-theophyllinyl	DMSO, DCC	(80)	147
C₄₇			

	R	R¹	R²				R	R¹	R²		
	H	(C₆H₅)₃C	1-cytosinyl	DMSO, DCC, CHCl₂CO₂H			=O	(C₆H₅)₃CO	1-cytosinyl	(70)	918
	H	(C₆H₅)₃C	1-uracylyl	DMSO, DCC, Py, TFA			=O	(C₆H₅)₃CO	1-uracylyl	(66)	919
				DMSO, P₂O₅			"	"	"	(57)	919
				DMSO, Ac₂O			"	"	"	(45)	919
	(C₆H₅)₃C	H	1-cytosinyl	1. DMSO, DCC, CHCl₂CO₂H 2. NH₄OH, CH₃OH			(C₆H₅)₃CO	=O	1-cytosinyl	(1)	918
	(C₆H₅)₃C	H	1-uracylyl	DMSO, DCC, Py, TFA			(C₆H₅)₃CO	=O	1-uracylyl	(63)	919
				DMSO, P₂O₅			"	"	"	(52)	919
				DMSO, Ac₂O			"	"	"	(56)	919

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
(C₆H₅)₃CO(CH₂)₂CHOHCH₂R	DMSO, DCC, CH₃PO₃H₂	C₆H₅)₃CO(CH₂)₂COCH₂R (86)	874
	DMSO, Ac₂O	(70)	143
	DMSO, Ac₂O	(64)	920
	DMSO, Ac₂O	(95)	921
C₄₉ R = 4-acetyl-1-cytosinyl	DMSO, AcO	(87)	918
	DMSO, DCC	" (86)	918
R = 4-acetyl-1-cytosinyl	DMSO, AcO	(81)	918

TABLE IV. OXIDATION OF SECONDARY CARBOHYDRATE ALCOHOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C_{51}	DMSO, Ac$_2$O	(56) + methylthiomethyl ether (16)	922
C_{53} CH$_2$OTr CHOBn BnOCH CHOBn CHOH CH$_2$OBn	DMSO, Ac$_2$O	CH$_2$OTr (79) CHOBn BnOCH CHOBn CO CH$_2$OBn	319
C_{68}	DMSO, Ac$_2$O	+ hydrate (—)	923

TABLE V. Oxidation of Diols and Polyols (*Continued*)
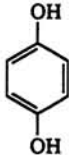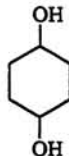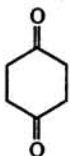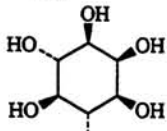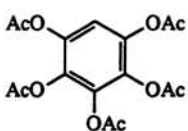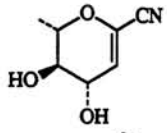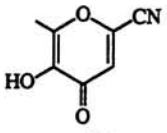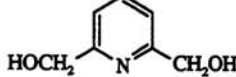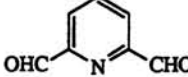
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C$_4$ HO(CH$_2$)$_4$OH	1. COCl$_2$ 2. DMSO	OHC(CH$_2$)$_2$CHO (80)	15
C$_6$	(CH$_3$)$_2$S, NCS	(~100)	193
	DMSO, DCC, H$_3$PO$_4$	" (—)	196
	DMSO, (COCl)$_2$	(95)	26
	DMSO, Ac$_2$O	(60)	924
C$_7$	DMSO, (COCl)$_2$	(—)	185
	(CH$_3$)$_2$SeO	(93)	47

TABLE V. Oxidation of Diols and Polyols
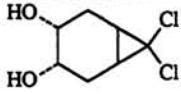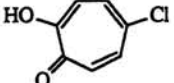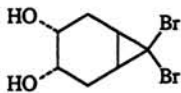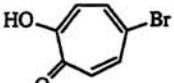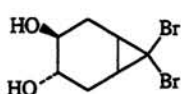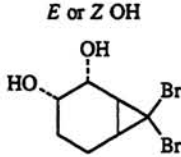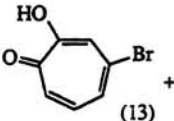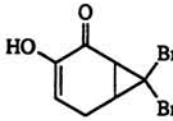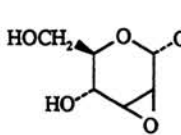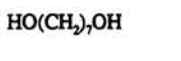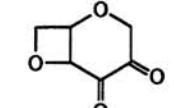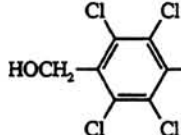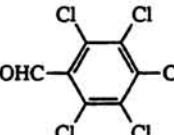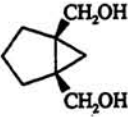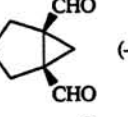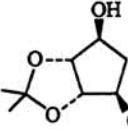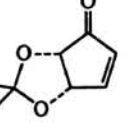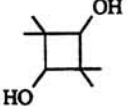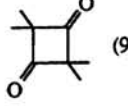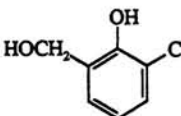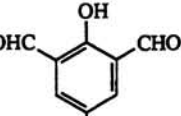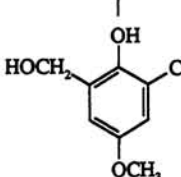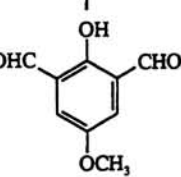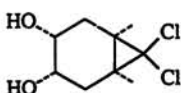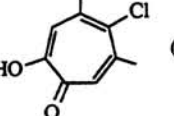
TABLE V. OXIDATION OF DIOLS AND POLYOLS

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
(dichlorobicyclic diol)	DMSO, TFAA	(hydroxy-chloro-tropone) (79)	925
(dibromobicyclic triol)	DMSO, TFAA	(hydroxy-bromo-tropone) (75)	925
(dibromobicyclic triol, E or Z OH)	DMSO, TFAA	" (73)	925
(bromo bicyclic diol)	DMSO, TFAA (2.1 eq)	(hydroxy-bromo-tropone) (13) + (bromo bicyclic ketone) (73)	925
	DMSO, TFAA (3.1 eq)	" (90)	925
HOCH$_2$...OCH$_3$ (epoxy sugar)	DMSO, BF$_3$	(bicyclic dione) (—)	167
HO(CH$_2$)$_7$OH	Polymeric sulfide, Cl$_2$, 4 h	HO(CH$_2$)$_6$CHO (44) + OHC(CH$_2$)$_5$CHO (40)	42
C$_8$ tetrachloro-bis(hydroxymethyl)benzene: HOCH$_2$...CH$_2$OH	DMSO, DCC, TFA, Py	OHC...CHO (40)	926
1,4-HOCH$_2$C$_6$H$_4$CH$_2$OH	DMSO, 2-fluoro-1-methylpyridinium tosylate	1,4-OHCC$_6$H$_4$CHO (71)	216
(spiro bis-CH$_2$OH)	DMSO, (COCl)$_2$	(spiro di-CHO) (—)	927
(acetonide cyclopentene diol)	DMSO, DCC, Py, TFA	(acetonide cyclopentenone) (—)	142
(dimethyl cyclobutane diol)	DMSO, (COCl)$_2$	(dimethyl cyclobutane dione) (90)	26
n-C$_6$H$_{13}$CHOHCH$_2$OH	DMSO, (COCl)$_2$	n-C$_6$H$_{13}$COCHO (>90)	311
C$_9$ HOCH$_2$...CH$_2$OH (phenol)	(CH$_3$)$_2$SeO	OHC...CHO (92)	47
HOCH$_2$...CH$_2$OH (OCH$_3$ phenol)	(CH$_3$)$_2$SeO	OHC...CHO (63)	47
(dichloro methyl bicyclic diol)	DMSO, TFAA	(chloro dimethyl tropone) (92)	925

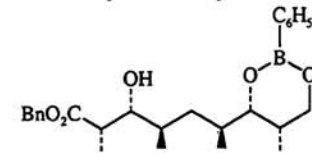TABLE V. OXIDATION OF DIOLS AND POLYOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, (COCl)$_2$	(—)	927
	DMSO, (COCl)$_2$	(—)	927
	DMSO, (COCl)$_2$	n-C$_4$H$_9$COCOSi(CH$_3$)$_3$ (41)	928
	DMSO, TFAA	(86)	925
	NCS, TEA	(100)	193
	(CH$_3$)$_2$SeO	(85)	47
	(CH$_3$)$_2$SeO	(94)	47
	DMSO, Ac$_2$O	(~100)	194
	DMSO, TFAA	(78)	925
	DMSO, (COCl)$_2$	(>54)	927
	DMSO, TFAA	(75)	925
	DMSO, (COCl)$_2$	n-C$_5$H$_{11}$COCO(CH$_3$)$_3$ (39)	928
	DMSO, DCC, H$_3$PO$_4$ 5 eq	carbonyl product	199, 929
	DMSO, (COCl)$_2$	C$_6$H$_5$COCOSi(CH$_3$)$_3$ (55)	928

C$_{10}$

C$_{11}$

TABLE V. OXIDATION OF DIOLS AND POLYOLS (*Continued*)
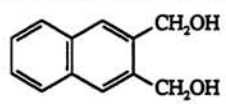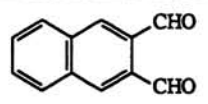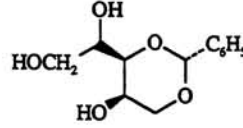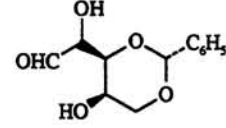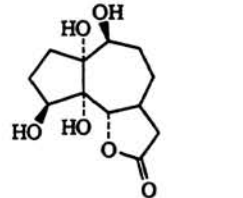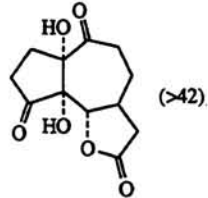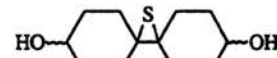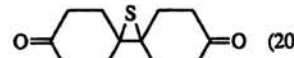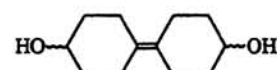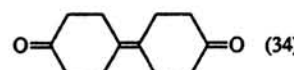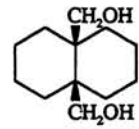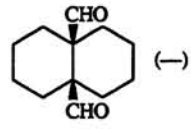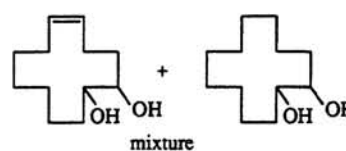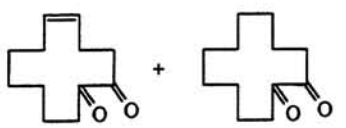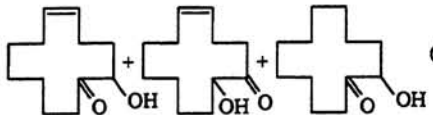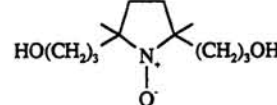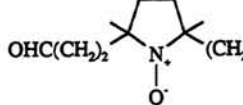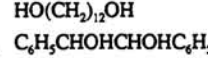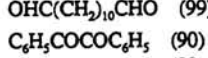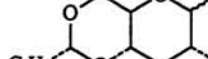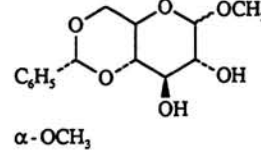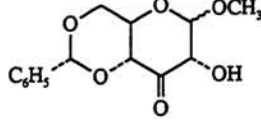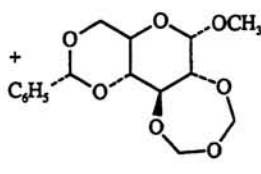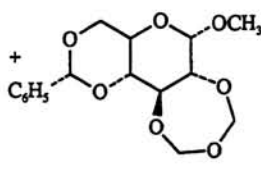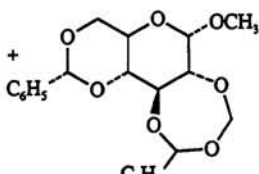
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}	$(CH_3)_2SeO$	(95)	47
	DMSO, DCC, Py, TFA, 25°	(85)	930
	DMSO, $(COCl)_2$	(>42)	931
	DMSO, DCC, TFA, Py	(20)	763
	DMSO, DCC, TFA, Py	(34)	763
	DMSO, $(COCl)_2$	(—)	927
mixture	DMSO, DCC, CCl_3CO_3H Py	(90)	932
	$(CH_3)_2S$, NCS	(90)	932
	DMSO, $(COCl)_2$	(69)	172
$HO(CH_2)_{12}OH$	DMSO, $(COCl)_2$	$OHC(CH_2)_{10}CHO$ (99)	23
C_{14} $C_6H_5CHOHCHOHC_6H_5$	DMSO, $(COCl)_2$	$C_6H_5COCOC_6H_5$ (90)	26
	$(CH_3)_2Se$, NCS	" (99)	46
	DMSO, Tf_2O	" (66)	45
	DMSO, TFAA	(15-20)	849
α-OCH_3	DMSO, P_2O_5	" α-OCH_3 (11)	933

536

537

TABLE V. OXIDATION OF DIOLS AND POLYOLS (*Continued*)
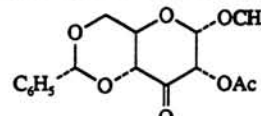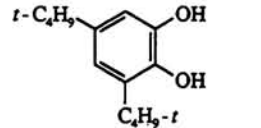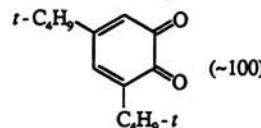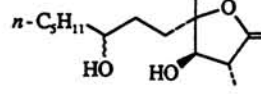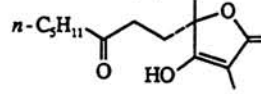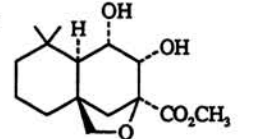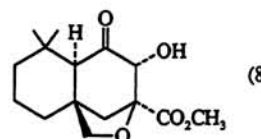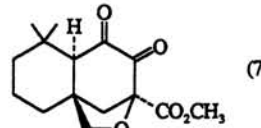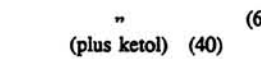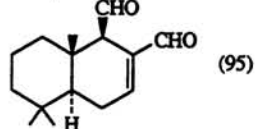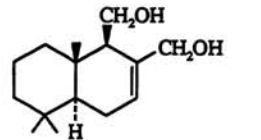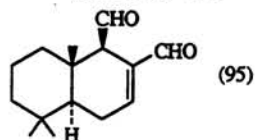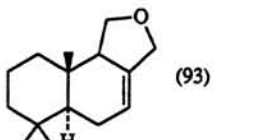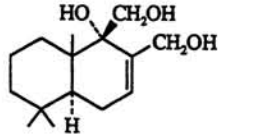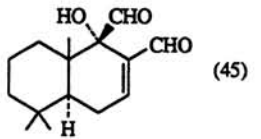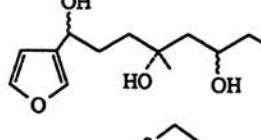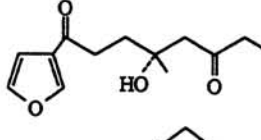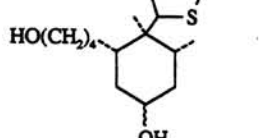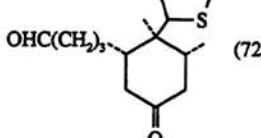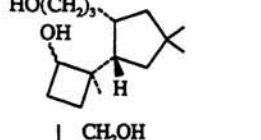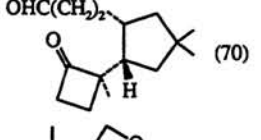
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Ac₂O	(24)	934
	(CH₃)₂S, NCS	(~100)	193
	DMSO, TFAA	(70)	673
C₁₅	1. DMSO, TFAA (1.67 eq) 2. HCl	(84)	201
	1. DMSO, TFAA 2. TEA	(78)	201
	1. DMSO, (COCl)₂ (1.4 eq) 2. TEA	" (60) (plus ketol) (40)	201
	1. DMSO, (COCl)₂ 2. TEA	(95)	158, 935, 936
	1. DMSO, (COCl)₂ 2. 25°	(93)	158
	DMSO, TFAA	(45)	158, 937
	DMSO, (COCl)₂	(17)	938
	DMSO, SO₃, Py	(72)	939
	DMSO, (COCl)₂	(70)	940
C₁₆	DMSO, DCC, Py, TFA	(—)	159

TABLE V. Oxidation of Diols and Polyols (*Continued*)
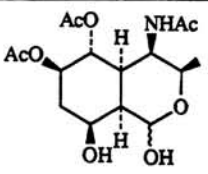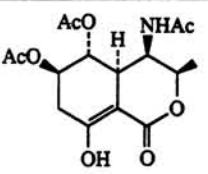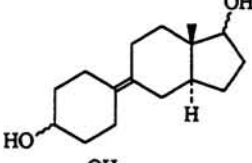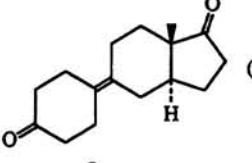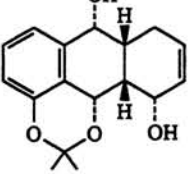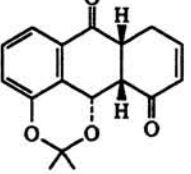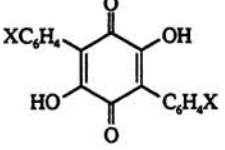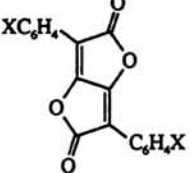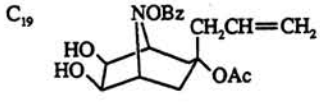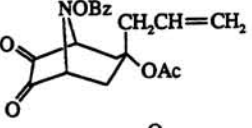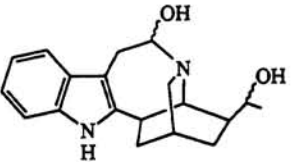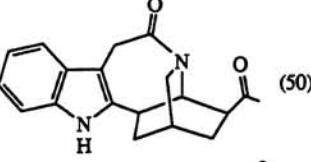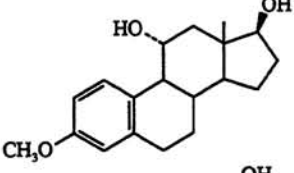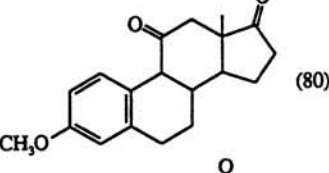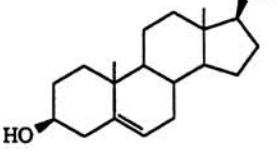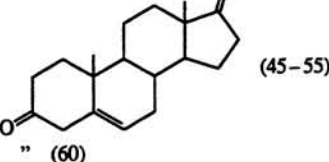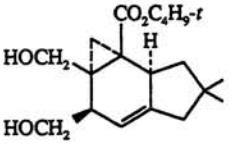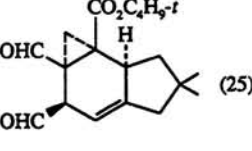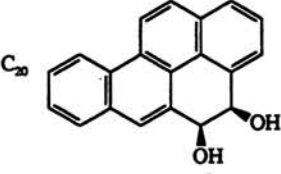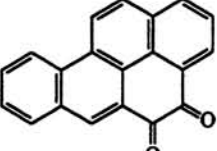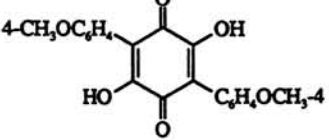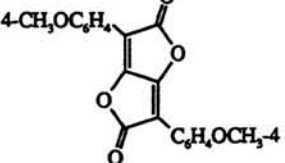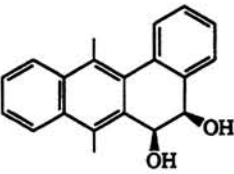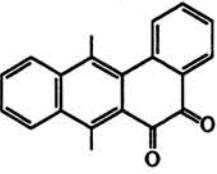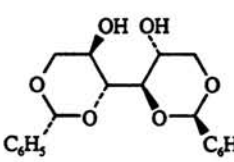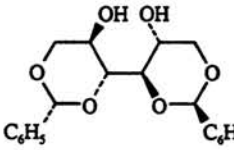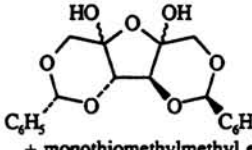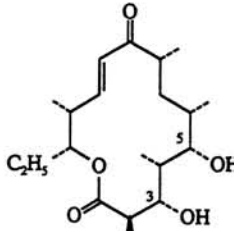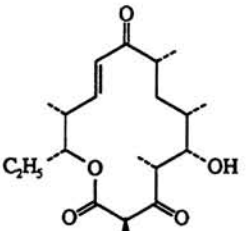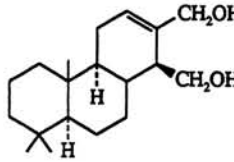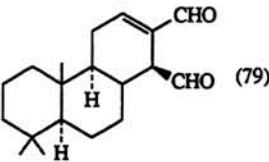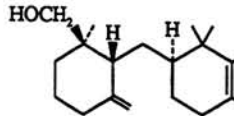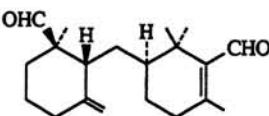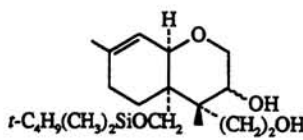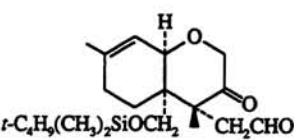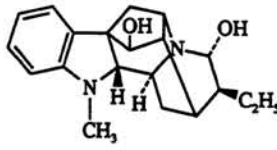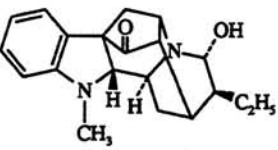
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, TFAA	(70)	99, 941
	DMSO, DCC, TFA, Py	(44)	763
	DMSO, (COCl)$_2$	(>60)	942
	DMSO, Ac$_2$O 60°, 15 min	(55)	197
X = 4-OH			
X = H	"	" (95)	197
C$_{19}$	(CH$_3$)$_2$S, NCS	(76)	943
	DMSO, DCC	(50)	773
	DMSO, DCC, CHCl$_2$CO$_2$H	(80)	944
	DMSO, RC≡CN(C$_2$H$_5$)$_2$ (R = CH$_3$, C$_6$H$_5$)	(45–55)	54
	DMSO, (C$_6$H$_5$)$_2$C=C=NC$_6$H$_4$CH$_3$-4	" (60)	54
	1. COCl$_2$, quinoline 2. DMSO 3. TEA	(25)	44

TABLE V. OXIDATION OF DIOLS AND POLYOLS

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, SO₃, Py	(85)	195
	DMSO, Ac₂O, 60°, 15 min	(90)	197
	DMSO, Ac₂O	(47)	194
	DMSO, Py, SO₃	" (98)	195
	DMSO, Ac₂O	(8) + monothiomethylmethyl ether (19)	945
	DMSO, DCC, H₃PO₄	+ 5-keto isomer (50) (40)	946
	DMSO, (COCl)₂	(79)	947, 948
	DMSO, (COCl)₂	(85)	156
	DMSO, (COCl)₂	(>63)	949
	1. DMSO, Ac₂O 2. NaOH, CH₃OH	(52) + methylthiomethyl ether (10)	11

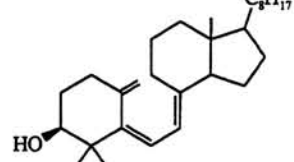TABLE V. OXIDATION OF DIOLS AND POLYOLS (*Continued*)
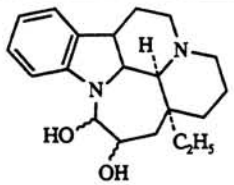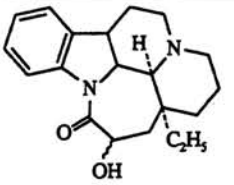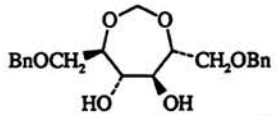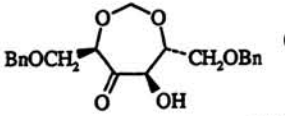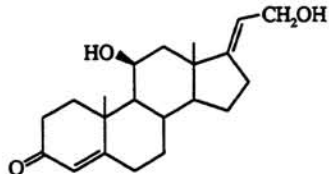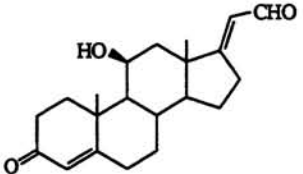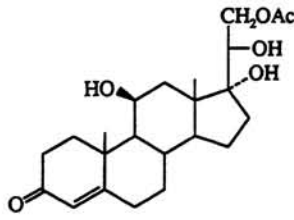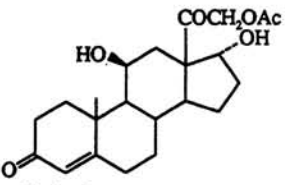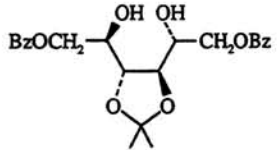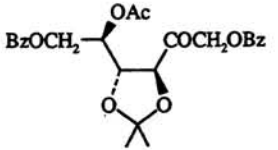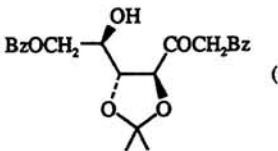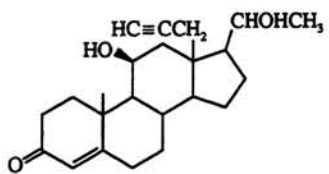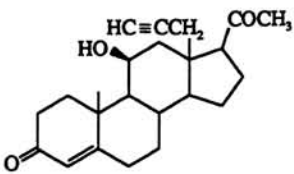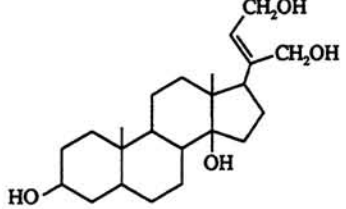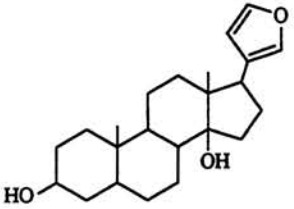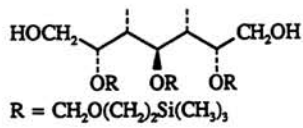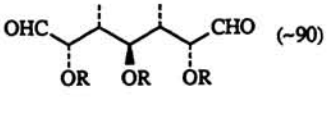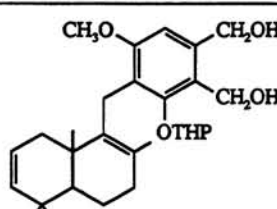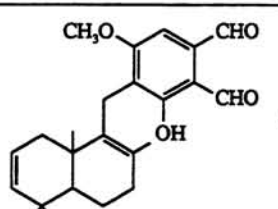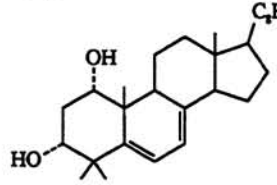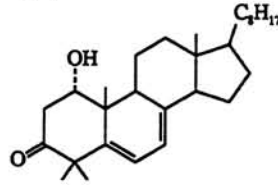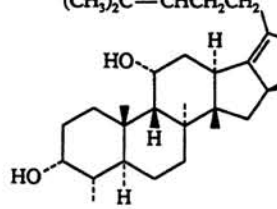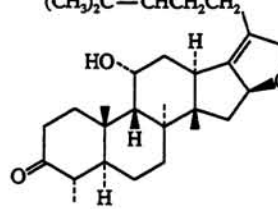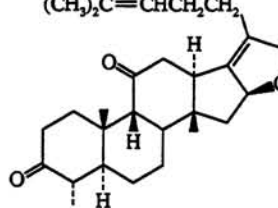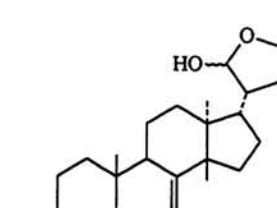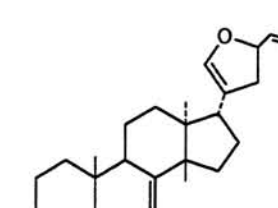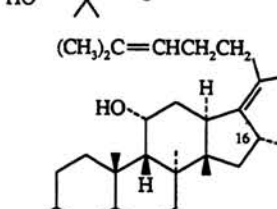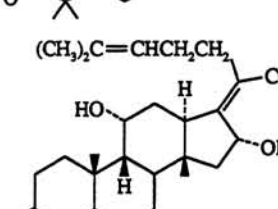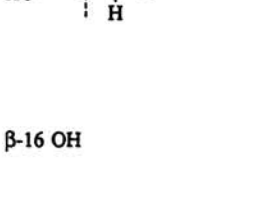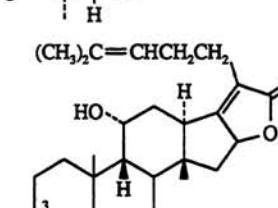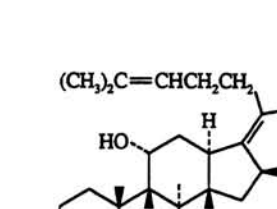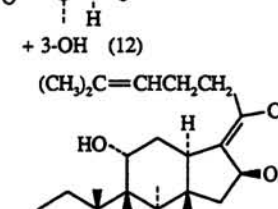
Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	DMSO, Py, SO₃, 1% H₂O	(85)	789
C₂₁	DMSO, Ac₂O	(68)	950
	DMSO, Py, SO₃	(70)	13
C₂₃	DMSO, SO₃, Py	(90)	13
	DMSO, DCC, Py, TFA, 16 h	" (—)	13
	DMSO, Ac₂O	(90)	293
	DMSO, P₂O₅	(19)	293
	DMSO, (COCl)₂	(62)	85
	DMSO, SO₃, TEA (1 eq)	(70)	162
C₂₇	DMSO, (COCl)₂	(~90)	951
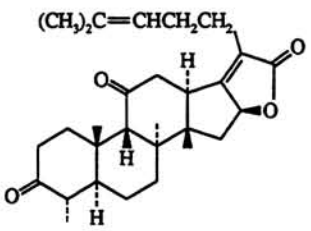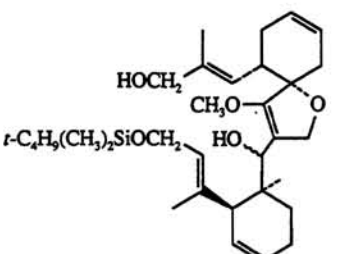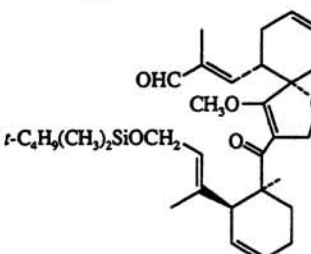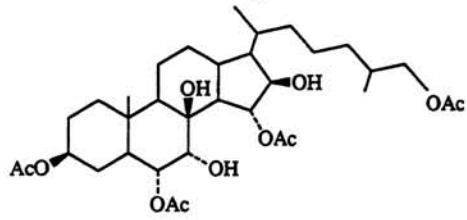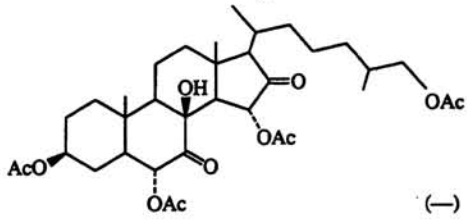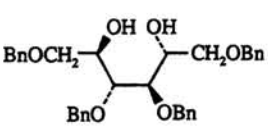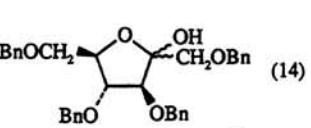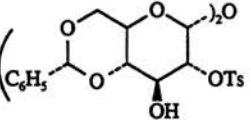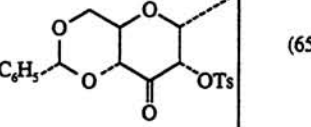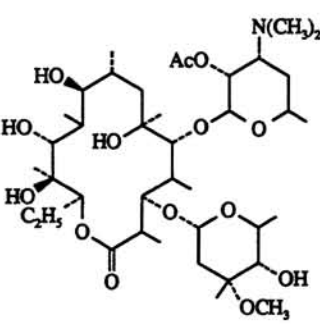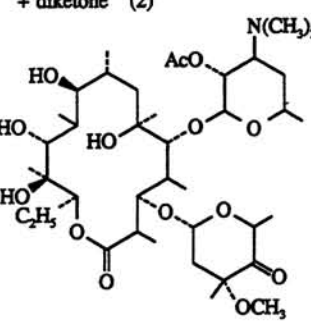
TABLE V. OXIDATION OF DIOLS AND POLYOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
	1. DMSO, (COCl)$_2$ 2. H$_3$O$^+$	(86)	952
	DMSO, DEC, Py, TFA	(52)	200
C$_{29}$ (CH$_3$)$_2$C=CHCH$_2$CH$_2$	(CH$_3$)$_2$S, NCS (1.2 eq)	(CH$_3$)$_2$C=CHCH$_2$CH$_2$ (63)	40
	(CH$_3$)$_2$S, NCS (4.0 eq)	(CH$_3$)$_2$C=CHCH$_2$CH$_2$ (78)	40
C$_{30}$	DMSO, DCC, Py, TFA	(47)	30
(CH$_3$)$_2$C=CHCH$_2$CH$_2$ CO$_2$CH$_3$	(CH$_3$)$_2$S, NCS (excess)	(CH$_3$)$_2$C=CHCH$_2$CH$_2$ CO$_2$CH$_3$ (85)	40
β-16 OH	(CH$_3$)$_2$S, NCS (excess)	(CH$_3$)$_2$C=CHCH$_2$CH$_2$ (65) + 3-OH (12)	40
C$_{32}$ (CH$_3$)$_2$C=CHCH$_2$CH$_2$ CO$_2$CH$_3$ OAc	(CH$_3$)$_2$S, NCS (1 eq)	(CH$_3$)$_2$C=CHCH$_2$CH$_2$ CO$_2$CH$_3$ OAc (85)	40

546

547

TABLE V.   OXIDATION OF DIOLS AND POLYOLS (*Continued*)

Alcohol	Oxidant and Conditions	Product(s) and Yield(s) (%)	Refs.
"	$(CH_3)_2S$, NCS (excess)	(80)	40
	DMSO, $(COCl)_2$	(>43)	113
C$_{33}$	DMSO, TFAA	(—)	953
C$_{34}$	DMSO, Ac$_2$O	(14)	954
C$_{40}$	DMSO, Ac$_2$O	(65) + bis(methylthiomethyl) ether (2) + diacetate (3) + diketone (2)	955
C$_{41}$	DMSO, TFAA	(~100)	956

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The Polonovski Reaction

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1. Introduction

In connection with their interest in the isolation and medicinal properties of the "gen alkaloids" (*N*-oxides), Max and Michel Polonovski reported in 1927 their discovery that the treatment of a tertiary amine *N*-oxide with acetic anhydride or acetyl chloride results in a rearrangement in which one of the alkyl groups attached to nitrogen is cleaved, and the *N*-acetyl derivative of the corresponding secondary amine and aldehyde are obtained (Eq. 1). (1-3)

$$RR'NCH_2R'' \xrightarrow[\text{or } CH_3COCl]{(CH_3CO)_2O} RR'NCOCH_3 \quad + \quad R''CHO \tag{1}$$
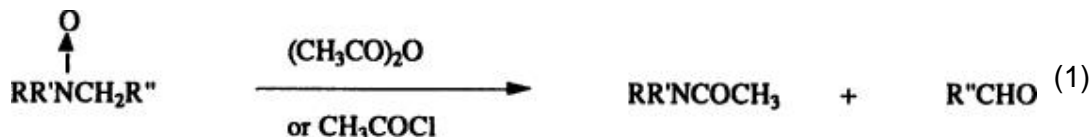
As the original work by the Polonovskis was mainly carried out on bicyclic tropane *N*-oxide derivatives, the products of the reaction were the demethylated amides and formaldehyde. The reaction was thus looked upon as a means of effecting *N*-demethylation of tertiary amines. As such it was, and still remains, a viable alternative to the use of cyanogen bromide (Von Braun), (4, 5) alkyl chloroformates, (6-8) azocarboxylic esters, (9, 10) or nitrous acid (10) for this purpose. These methods often require more drastic conditions and/or promote unwanted side reactions.

It is quite remarkable therefore that in spite of the considerable potential of the Polonovski reaction, nearly 30 years passed after its discovery before the scientific community began to study it seriously. Today, nearly 200 applications of this reaction have appeared in the literature, and it is now clear that its scope goes well beyond a simple means of effecting *N*-demethylation.

The central feature of the Polonovski reaction is the transformation of an *N*-oxide to an iminium ion intermediate. Depending on the structure of the substrate and the acid anhydride or other activating reagent employed, iminium ion formation can occur through loss of an α hydrogen, or through fragmentation of a C α $-$ carbon bond (Eqs. 2 and 3). Again, depending on conditions, the reaction will either stop at this stage and iminium ions become the Polonovski products, or proceed to give enamines or tertiary amides and/or secondary amines and aldehydes (Eqs. 4–6). The often close relationship

between structure and reaction conditions, which determine both product types and reaction regiochemistry, is discussed in the following sections.

$$R(CH_2)_3\overset{O\uparrow}{N}(CH_3)_2 \xrightarrow{(R'CO)_2O} R(CH_2)_2CH\overset{+}{=}N(CH_3)_2 \quad \text{and/or} \quad R(CH_2)_3(CH_3)\overset{+}{N}=CH_2 \quad (2)$$

$$\mathbf{1} \qquad\qquad\qquad\qquad\qquad \mathbf{2} \qquad\qquad\qquad\qquad \mathbf{3}$$

$$\mathbf{1} \quad\longrightarrow\quad RCH=CH_2 \quad + \quad CH_2\overset{+}{=}N(CH_3)_2 \qquad (3)$$

$$\qquad\qquad\qquad\qquad\quad \mathbf{4} \qquad\qquad\qquad \mathbf{5}$$

$$\mathbf{2} \quad\longrightarrow\quad R'CON(CH_3)_2 \quad \text{or} \quad HN(CH_3)_2 \quad + \quad R(CH_2)_2CHO \qquad (4)$$

$$\qquad\qquad\qquad\qquad\quad \mathbf{6} \qquad\qquad\qquad \mathbf{7}$$

$$\mathbf{3} \quad\longrightarrow\quad R(CH_2)_3(CH_3)NCOR' \quad \text{or} \quad R(CH_2)_3NHCH_3 \quad + \quad H_2CO \qquad (5)$$

$$\qquad\qquad\qquad\qquad\quad \mathbf{8} \qquad\qquad\qquad\qquad \mathbf{9}$$

$$\mathbf{2} \quad\longrightarrow\quad RCH_2CH=CHN(CH_3)_2 \qquad (6)$$

$$\qquad\qquad\qquad\qquad\quad \mathbf{10}$$
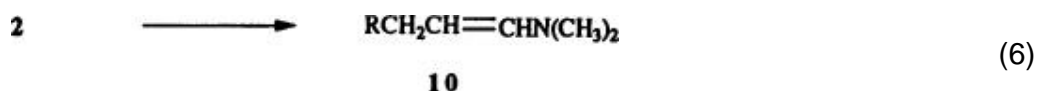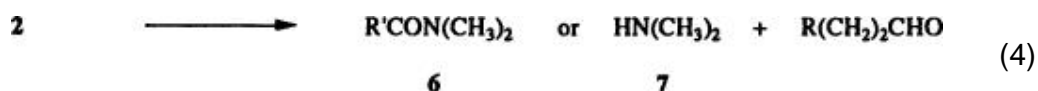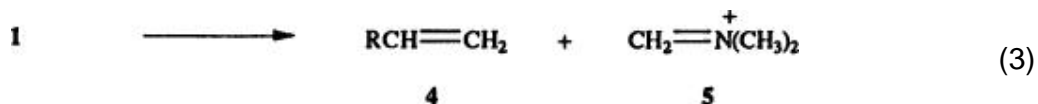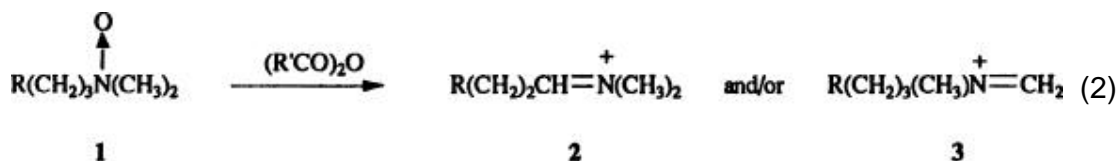
In its initial stages the Polonovski reaction resembles other reactions in which a tertiary amine is oxidized through interaction of the pair of electrons on nitrogen with an agent X followed by elimination of the elements of HX. Reagents like lead tetraacetate, N-bromosuccinimide, and in particular mercuric acetate have been employed for this purpose. (11) However, the Polonovski reaction can offer certain advantages in selectivity and experimental ease.

In principle, any reagent capable of activating the N-oxide oxygen could promote the Polonovski reaction. However, three major types of activating agents, acid anhydrides and chlorides (including chloroformate esters), iron salts and complexes, and sulfur dioxide, are usually employed.

Perhaps the most important contribution to the use of the Polonovski reaction in modern organic synthesis was the discovery in the 1960s that on replacing

acetic anhydride by trifluoroacetic anhydride the reaction could be stopped at the iminium ion stage. (12-15) Considering the rich chemistry of iminium ions, (16-19) many applications of this modified, or Polonovski–Potier, reaction have appeared in the literature, the most spectacular of which was the first successful approach to the synthesis of the indole antitumor agents of the vinblastine group (see page 133).

In this chapter the discussion is limited to examples of the Polonovski reaction in which the abovementioned activating reagents are employed. The coverage is restricted to tertiary amine oxides in which at least one of the substituents on nitrogen is an alkyl group. Both acyclic and cyclic amine oxides such as piperidine *N*-oxide fall into this category, whereas heteroaromatic *N*-oxides do not. With the exception of one special case, nitrones are also omitted from the discussion.

A number of early reviews on tertiary amine *N*-oxides discuss the Polonovski reaction, and several recent reviews provide illustrations of modern applications of the reaction. (20-26) The present literature coverage includes articles appearing before the end of August 1988.

2. Mechanism

The mechanism of the Polonovski reaction can essentially be divided into three stages:

1. Reaction (or complexation) of the *N*-oxide oxygen with an activating agent to produce the positively charged intermediate $R_3N^+ - OR'$.

2. Elimination of the elements of HOR′ from this highly labile species or fragmentation of a C α $-$ carbon bond to give an iminium ion intermediate which, depending upon the nucleophilicity of the counterion OR¢, may exist in equilibrium with its addition product, a carbinolamine derivative.

3. Elaboration of the iminium and/or carbinolamine intermediates to the amide (amine) plus aldehyde or enamine products.

These features are common to the reaction of amine oxides with acylating reagents, iron salts, and sulfur dioxide. However, among these three types of activating agents, fundamental differences exist in the precise mechanism for the crucial step wherein $R_3N^+ - OR'$ is converted into an iminium ion.

2.1. Acylating Reagents

The first step in the Polonovski reaction of an amine *N*-oxide **11** with an acid anhydride, acid chloride, or chloroformate ester is the formation of the *O*-acylimonium salt **12** (Scheme 1). Such species are highly unstable. However, if powerful acylating agents such as acetyl perchlorate, acetyl tetrafluoroborate, or acetyl hexafluoroantimonate are employed, the sensitive intermediate **12** $(R = CH_3, \quad X = ClO_4^-, \quad BF_4^-, \quad SbF_6^-)$ can be detected in situ (^{1}H NMR) or in certain cases actually isolated. (26-31) On subsequent treatment of these *O*-acylimonium salts with acetic anhydride, sodium acetate, or tetramethylammonium acetate, the expected tertiary amides and aldehydes are produced.

Scheme 1.

RCH₂N(CH₃)R' represented as:

$$\text{RCH}_2\text{N(CH}_3\text{)R'} \quad \mathbf{11} \xrightarrow{\text{(R''CO)}_2\text{O}} \quad \mathbf{12}$$

$-\text{R''CO}_2\text{H}$

$-\text{R''CO}_2\text{H}$

$$\text{RCH}=\overset{+}{\text{N}}(\text{CH}_3)\text{R'} \qquad \mathbf{13'}$$

$$\text{RCH}_2\overset{+}{\text{N}}\text{R'} \qquad \mathbf{13''}$$

$^-\text{OCOR''}$

$^-\text{OCOR''}$

$$\underset{\text{OCOR''}}{\text{RCHN(CH}_3\text{)R''}} \qquad \mathbf{14'}$$

$$\text{RCH}_2\text{N(R')CH}_2\text{OCOR''} \qquad \mathbf{14''}$$

$\text{(R''CO)}_2\text{O}$

$\text{(R''CO)}_2\text{O}$

$\mathbf{15'}$

$\mathbf{15''}$

$$\text{R''CON(CH}_3\text{)R'} \ + \ \text{RCHO}$$
$$\mathbf{16'} \qquad\qquad \mathbf{17'}$$

$$\text{RCH}_2\text{N(R')COR''} \ + \ \text{H}_2\text{CO}$$
$$\mathbf{16''} \qquad\qquad \mathbf{17''}$$
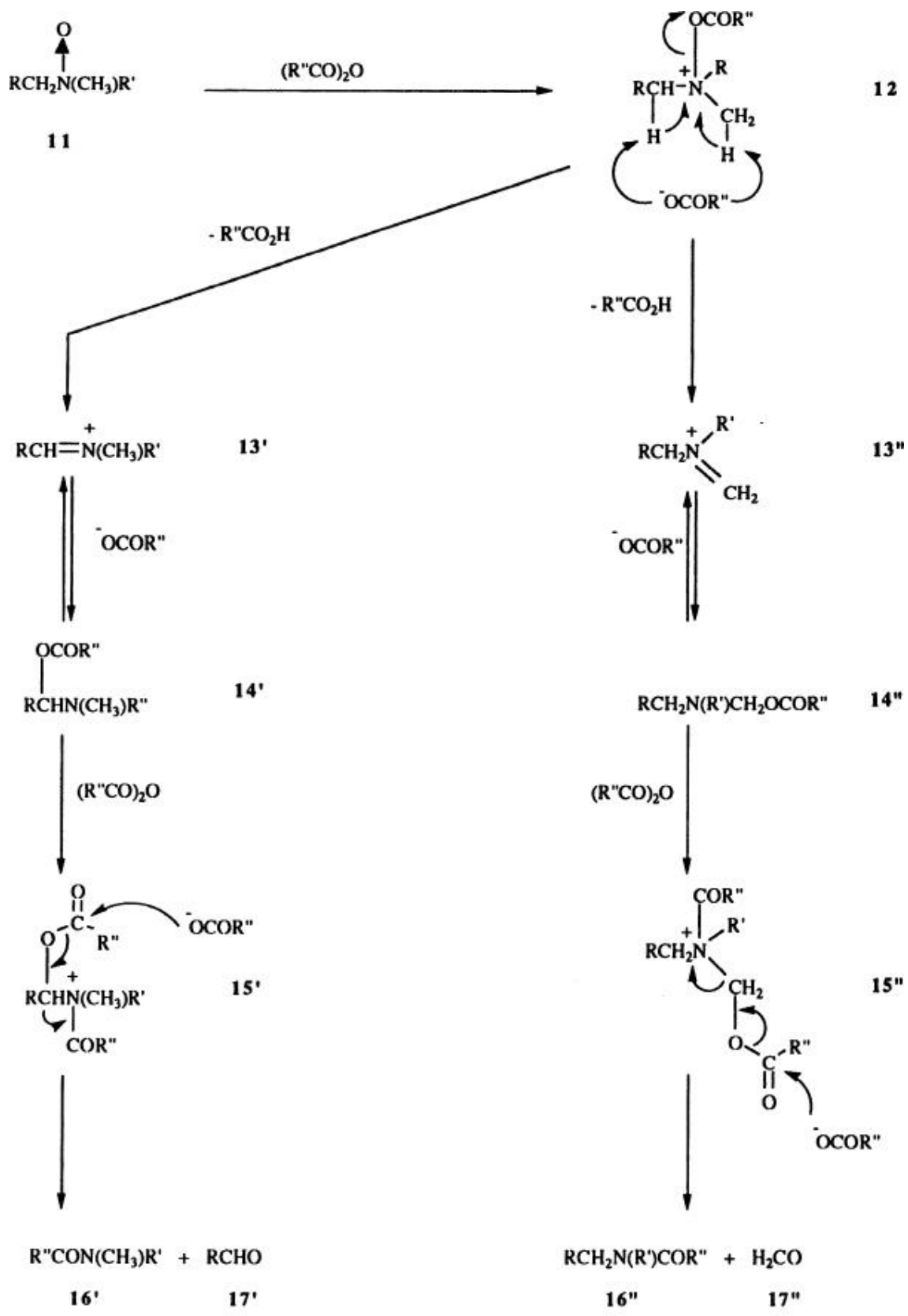
The conversion of **12** into one or both of the iminium ions **13′** and **13²** can also be followed by ^{1}H NMR, (30-32) and for this step three different mechanisms, ionic, radical, and ylide, have been considered. The evidence, however, favors an ionic E_2-type elimination mechanism. In support of this mechanism the Polonovski reaction is accelerated by the addition of acetate ion or amine bases (33) and markedly decelerated when carried out in acidic media. (31-34) These observations point to the involvement of the counterion $R''CO_2^-$ in the removal of the proton from the α-carbon atom. That such weak bases as trifluoroacetate ion or chloride ion are capable of promoting this elimination reaction is probably due in large part to the fact that the $C - H$ bond in question is adjacent to a positively charged nitrogen, which considerably increases its acidity. Perhaps the strongest support for the E_2 mechanism comes from studies which demonstrate that there is a pronounced preference in nonbiased systems for loss of the hydrogen that is *trans*-antiperiplanar to the $N - O$ bond. (35-37) These findings are in complete agreement with the established mechanism for E_2 eliminations. (38)

Although the regiochemistry of the elimination reaction leading to isomeric iminium ions such as **13¢** and **13²** is governed to a considerable extent by steric hindrance and conformational effects (see next section), electronic effects that alter the kinetic acidities of the α hydrogens, and differences in the leaving group $R''CO_2^-$ with variations in R², also influence the product distributions. Depending on the particular combination of these factors, the transition state for the elimination step may thus change from being strictly E_2-like to one possessing more or less E_1 or E_{1cb} character. (30, 39)

The subsequent position of the equilibrium reaction between the iminium ions **13** and their addition products **14** is a function of both the nucleophilicity of the counterion $R''CO_2^-$ and the acidity of the reaction medium. When $R''CO_2^-$ is acetate anion this equilibrium is displaced entirely toward intermediates **14**. Such α-acetoxymethylamines are very labile entities and were for a long time only presumed to be intermediates in the Polonovski reaction. However, by reacting trimethylamine *N*-oxide with an equimolar amount of acetic anhydride below 15° it was found that the α-acetoxymethylamine **14** (R = H, R¢ = R² = CH$_3$) can be isolated in 50% yield after careful workup. (40, 41) Similarly, compound **19** can be prepared by reaction of the *N*-mesityl-*N*-methyliminium ion **18** with tetramethylammonium acetate in chloroform/methylene chloride solutions. (42) Upon treatment of these products with acetic anhydride, the corresponding tertiary amides are obtained in high yield (>85%).

18   19 (50%)
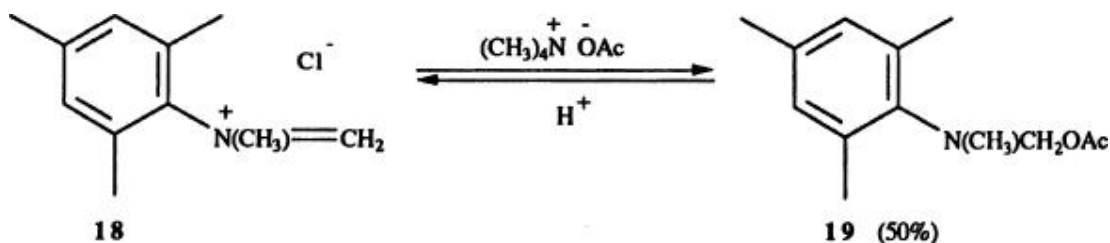
The latter study also showed that the iminium ion **18** could be regenerated from **19** by addition of strong acids such as hydrochloric or trifluoroacetic acid (see also refs. 31, 43, and 44). This reversibility and the low nucleophilicity of the trifluoroacetate anion explain why the modified Polonovski reaction using trifluoroacetic anhydride does not proceed beyond the iminium ion stage. This characteristic of the modified Polonovski reaction has considerable synthetic potential, as is discussed later.

The elaboration of the acetoxymethylamines **14** to the corresponding tertiary amides **16** can occur in situ under nonhydrolytic conditions by reaction with a further molecule of acetic anhydride followed by acetate ion promoted fragmentation of intermediates **15**. (33) However, if the reaction is stopped before this process is complete, it is still possible that any residual acetoxymethylamine would be hydrolyzed and the liberated secondary amine converted rapidly to the amide by the excess anhydride.

There is, however, one exception to the general mechanism outlined in Scheme 1. When formic–acetic anhydride is employed as the acylating agent, simple reduction of the *N*-oxide results (Eq. 7). (45) In this instance there is selective formation of the *O*-formyliminonium salt **12'** (R = H) which loses carbon dioxide to give the parent tertiary amine before elimination to the iminium ions **13** can occur.

$$11 \longrightarrow \underset{\textbf{12'}}{RCH_2N(CH_3)R'} \longrightarrow RCH_2N(CH_3)R' + CO_2 \qquad (7)$$
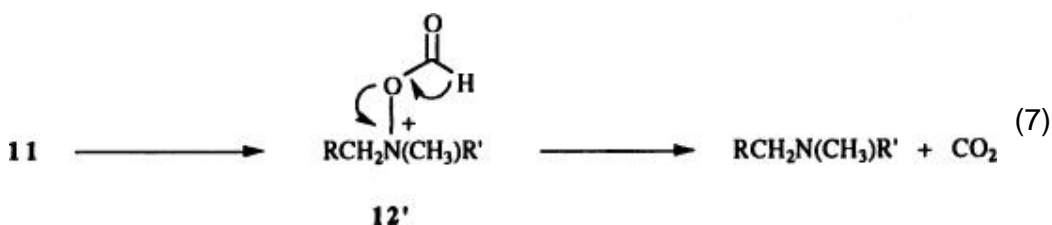
The alternative Polonovski reaction mode in which $C\alpha - C$ bond cleavage is observed can occur if two conditions are met (Eq. 8):

1. The C α — C bond to be broken is activated toward cleavage by an adjacent electron-donating center (double bond, aromatic ring, or heteroatom).
2. The C α — C and N — O bonds are antiperiplanar.

The fragmentation reaction by which amine **20** is transformed to **21** and iminium ion **22** is in fact a manifestation of the Grob reaction, (46) and is of considerable interest because extensive modification of the tertiary amine structure is achieved in a single operation.

$$RCH_2—CH_2 \quad CH_2—N(CH_3)R' \longrightarrow RCH=CH_2 + CH_2=\overset{+}{N}(CH_3)R' \quad (8)$$

20   **21**   **22**

A free-radical mechanism invoking homolysis of the N — O bond of **12** was proposed for the Polonovski reaction by analogy with the reaction of tertiary amines with peroxides, (47) and from the observation that the reaction of dimethylaniline *N*-oxide with acetic anhydride is effective in promoting the polymerization of styrene, methyl methacrylate, and acrylonitrile. (27, 28, 48-56) Radical species have in fact been detected by both ESR (55) and CIDNP techniques. (30, 57) However, it was not determined whether these radicals are intermediates leading to the parent tertiary amine or to the Polonovski products. In any event it is important to note that the former reactions were run at >60°. At lower temperatures (0–20°) polymerization does not occur to any measurable extent during the reaction of trimethylamine *N*-oxide with acetic anhydride in acrylonitrile, which produces dimethylacetamide in >80% yield. (33) It is likely that free-radical pathways represent only a minor component in the Polonovski reaction at room temperature.

The ylide mechanism was originally forwarded to deal with the Polonovski reaction of bridgehead *N*-oxides. (58) This mechanism has been rejected, however, since the reaction of quinuclidine *N*-oxide (**23**) with benzoyl chloride stops at formation of the remarkably stable *N*-benzoyloxyimonium salt **24**. (29) Furthermore, it has been shown that the formation of secondary products when styrene is an additive (59) does not require the involvement of ylide intermediates. (60)

23 → **24** (89-91%)

C₆H₅COCl
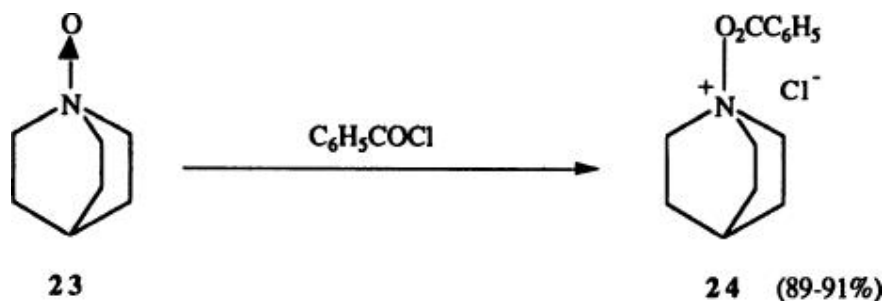
2.2. Iron-Based Reagents

In contrast to the ionic mechanism for the classical Polonovski reaction with acid anhydrides, the iron-catalyzed transformation of amine oxides to secondary amines occurs by two successive one-electron transfer steps involving Fe^{+2}/Fe^{+3} redox reactions of iron. The current mechanism for the iron-based reaction is illustrated in Eqs. 9–14. (61-63) In the first step coordination of the protonated amine oxide **25** to iron(II) is considered to take place with formation of a complex (depicted as **26**) which undergoes a one-electron reduction. As a consequence of this single electron transfer, the N — O bond is cleaved and the aminium radical cation **27** is generated. This energetic aminium radical then reacts in either of two ways: (1) it dissociates from the oxidized iron complex and undergoes further reduction by reaction with a second iron(II) ion to give the parent tertiary amine **28** (the principal side product in these reactions), or (2) it loses an a proton and undergoes electron reorganization while still bound to iron to give the more stable carbon-centered radical **29**. Oxidation of this intermediate by iron(III) then produces the iminium ion **30**, which under the aqueous acid conditions of the reaction is hydrolyzed to the secondary amine and aldehyde products.

$$\overset{OH}{\underset{25}{\overset{|+}{RR'NCH_2R''}}} \;+\; Fe(II) \;\longrightarrow\; \underset{26}{\left[\overset{OH}{\overset{|+}{(RR'NCH_2R''):Fe(II)}}\right]} \tag{9}$$

$$\underset{26}{26} \;\xrightarrow{\;H^+\;}\; \underset{27}{\overset{+\cdot}{RR'NCH_2R''}} \;+\; H_2O \;+\; Fe(III) \tag{10}$$

$$\textbf{27} \quad + \quad \text{Fe(II)} \quad \longrightarrow \quad \text{RR'NCH}_2\text{R''} \quad + \quad \text{Fe(III)} \tag{11}$$

$$\textbf{28}$$

$$\textbf{27} \quad \longrightarrow \quad \text{RR'NCHR''} \quad + \quad \text{H}^+ \tag{12}$$

$$\textbf{29}$$

$$\textbf{29} \quad + \quad \text{Fe(III)} \quad \longrightarrow \quad \text{RR'}\overset{+}{\text{N}}\!\!=\!\!\text{CHR} \quad + \quad \text{Fe(II)} \tag{13}$$

$$\textbf{30}$$

$$\textbf{30} \quad + \quad \text{H}_2\text{O} \quad \longrightarrow \quad \text{RR'}\overset{+}{\text{N}}\text{H}_2 \quad + \quad \text{R''CHO} \tag{14}$$
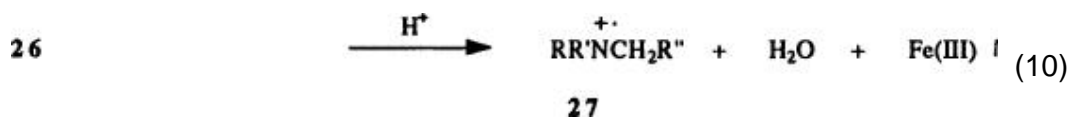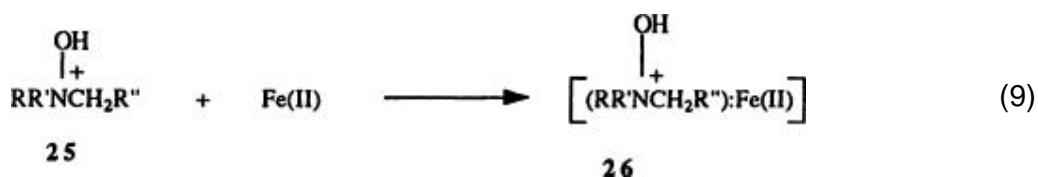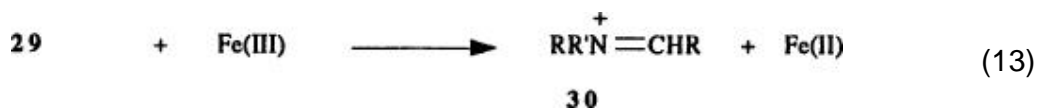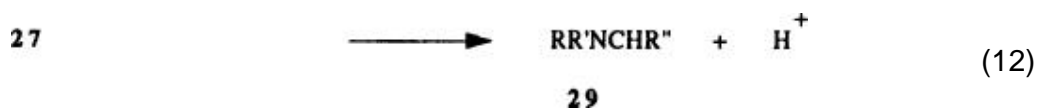
Various observations, including the polymerization of added styrene and methyl methacrylate, the stoichiometric oxidation of added alcohols to the corresponding carbonyl compounds, the intra- and intermolecular hydroxylation of compounds bearing nonactivated methylene groups, and the formation of bisbenzyl derivatives when phenethylamine *N*-oxides are reacted with iron(II) salts, lend support to this free radical mechanism. (62, 64-66)

That ferrous ion and not ferric ion (67-72) is the initiator of the reaction is demonstrated by experiments with iron(III) salts coordinated to nonreducing acids (sulfuric, succinic). Under these conditions the Polonovski transformation is not observed. However, when as little as 3% iron(II) sulfate is added to the medium, secondary amine production begins. (62)

Concerning the separate stages of the reaction, the observation that reaction rate and yield of aldehyde product depend upon the nature of the iron(II) counterion is taken as evidence that formation of the aminium radical cation **27** is rate determining. (62) In contrast, product selectivity (reaction regiochemistry) is determined by which of the α hydrogens is lost from **27** in the subsequent step. As is found for the reaction of aminium radical cations generated by other means, the hydrogen lost depends upon a number of factors, including the kinetic acidity of the α hydrogens, their statistical distribution, and the pH of the reaction medium, as well as steric and stereo-electronic effects. (63, 73-77)

It should be noted that in the light of recent findings concerning the acidity of aminium radical cations an alternative mechanism is proposed (78) wherein iminium salts are formed directly from aminium radical cations through abstraction of an α -hydrogen atom. In the context of the Polonovski reaction this would involve transfer of a hydrogen atom to iron followed by its reduction to the Fe^{+2} state and liberation of a proton, i.e. the sum of Eqs. 12 and 13.

A similar ambiguity exists as to the precise mechanism for the conversion of aminium radical cations derived from N-oxides or tertiary amines into iminium salts (carbinolamines) by iron porphyrins. (79-86) This interesting reaction, which occurs through redox reactions of higher oxidation states of iron, is a biomimetic version (87-90) of the Polonovski reaction, whose potential in synthesis is only beginning to be explored. (79, 84, 91-93)

2.3. Sulfur Dioxide

In the reaction of amine oxides with aqueous solutions of sulfur dioxide, mixtures of secondary and tertiary amines are generally obtained in proportions which depend upon substrate structure and in particular on reaction temperature. At elevated temperatures (60–100°), N-oxides are reduced to the parent tertiary amines in high yields, whereas at room temperature or below there is predominant and in some cases exclusive formation of the secondary amine (Polonovski) product.

Unlike the iron-catalyzed Polonovski reaction wherein a common aminium radical cation intermediate evolves toward the reduced and dealkylated amine products, in the reaction with sulfur dioxide these products are produced by separate radical and ionic pathways (pathways a and b, Scheme 2).

Scheme 2.
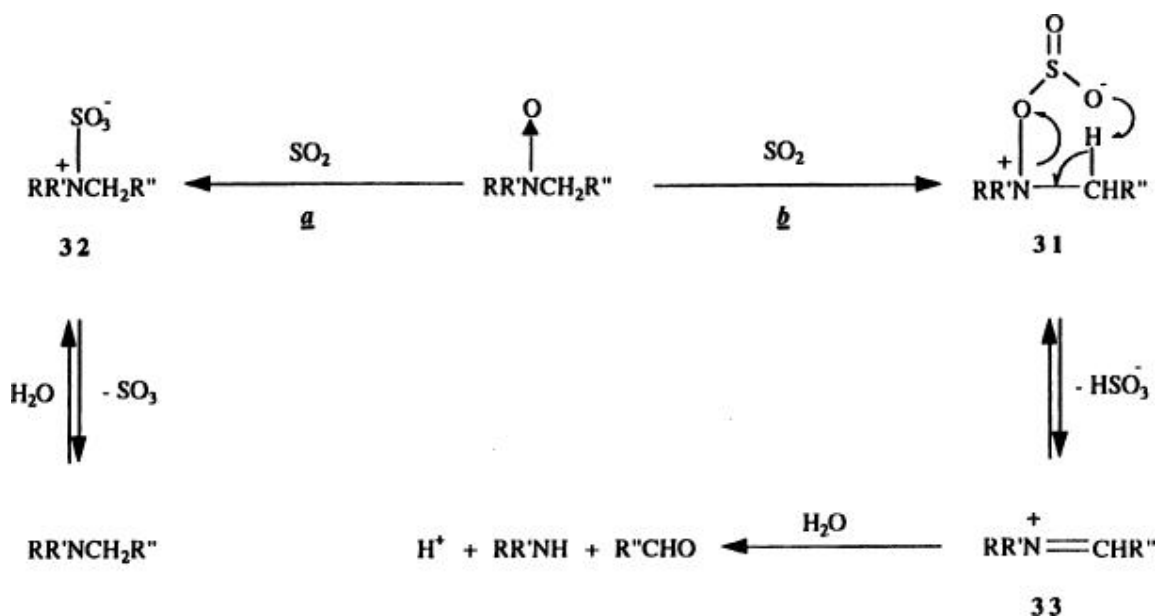
Fortunately, the initially formed sulfitoamine **31** and aminesulfamate **32** intermediates are sufficiently stable to permit isolation and characterization when the reaction is conducted under nonaqueous conditions, (94-96) or when bridgehead amine oxides such as strychnine *N*-oxide (96) and quinuclidine *N*-oxide (97) are employed as substrates.

Thus when trimethylamine *N*-oxide is reacted with sulfur dioxide in anhydrous benzene, the sulfitoamine **31** (R = R¢ = CH, R² = H) is obtained in 90% yield. (95) In one study, however, this same reaction was found to evolve beyond the formation of **31** to give $(CH_3)_2NCH_2OSO_2H$. (98) Although compound **31** is quite stable in hot ethanol, when dissolved in cold aqueous acid or base it reacts rapidly to produce dimethylamine, formaldehyde, and sulfur dioxide in almost quantitative yield. This reaction is presently viewed as involving an intramolecular elimination of bisulfite ion from **31** and hydrolysis of the resultant iminium ion **33**. Similarly, the sulfitoamine **35** is obtained by reacting strychnine *N*-oxide (**34**) with sulfur dioxide in anhydrous benzene. (96) Although this intermediate is transformed to the sulfamic acid derivative **36** in hot water, this does not represent a major pathway since compound **36** is obtained directly by reacting strychnine *N*-oxide with cold aqueous sulfur dioxide.
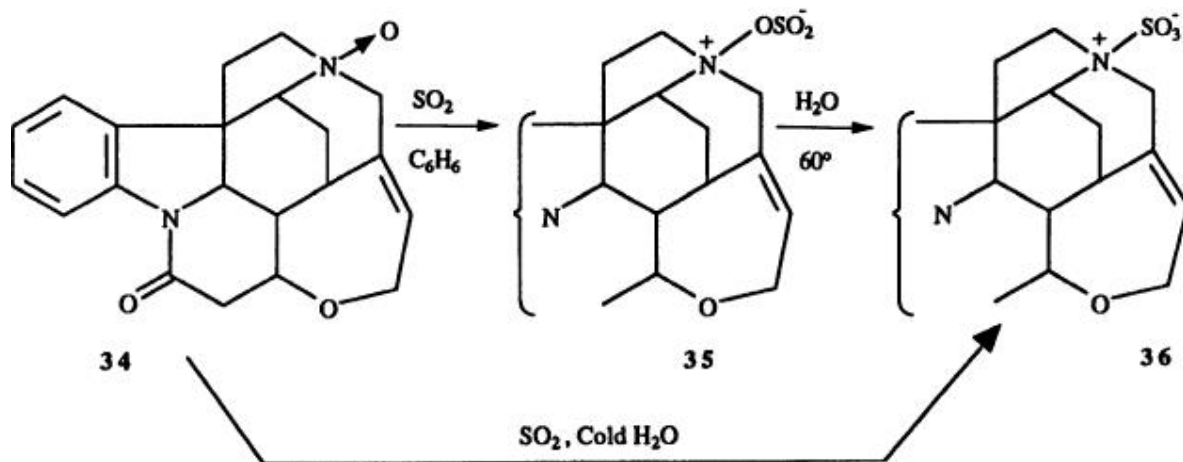
The observation that the yields of compound **36** are markedly diminished when these latter two reactions are carried out in the presence of hydroquinone in aqueous media strongly indicates a radical mechanism. The minor pathway represented by Eq. 15 is believed to involve decomposition of the sulfitoamine **35** to an aminium radical cation and sulfite radical anion followed by recombination of the two radical components to give the sulfamate. The principal pathway (Eq. 16) involves a similar process initiated by transfer of an electron from the protonated form of the amine oxide to sulfite ion followed by

combination of the two radical species. Sulfite ion is present in the reaction medium as a result of dissociation of sulfurous acid produced by bubbling sulfur dioxide into water.

$$R_3\overset{+}{N}\text{-O}\overset{-}{S}O_2 \longrightarrow R_3\overset{+}{N}{}^{\cdot} + \overset{\cdot\cdot}{S}\overset{-}{O}_3 \longrightarrow R_3\overset{+}{N}\!\!-\!\!\overset{-}{S}O_3 \quad (15)$$

$$R_3\overset{+}{N}\text{-OH} + \overset{-}{S}O_3 \longrightarrow R_3\overset{+}{N}{}^{\cdot} + \overset{\cdot\cdot}{S}\overset{-}{O}_3 + OH^{-} \longrightarrow R_3\overset{+}{N}\!\!-\!\!\overset{-}{S}O_3 \quad (16)$$
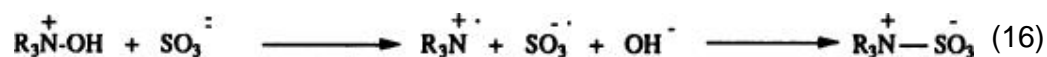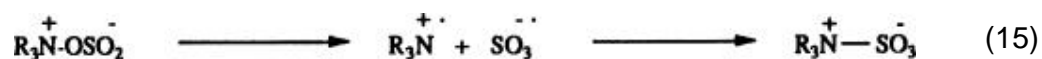
A completely different product **37** is isolated from the reaction of triethylamine *N*-oxide with sulfur dioxide in benzene (Eq. 17). (94) Formation of this sulfatoamine arises from reaction of excess amine oxide with the sulfitoamine **38** initially formed in the reaction (Eq. 18). This implies that the *N*-oxide, which is a very weak base in water, is able to take SO_3 from the stronger base triethylamine. As expected, compound **37** reacts with water in an identical manner to sulfitoamines, liberating diethylamine.

$$(C_2H_5)_3\overset{O}{\underset{\uparrow}{N}} \xrightarrow[\text{C}_6\text{H}_6]{\text{SO}_2} (C_2H_5)_3\overset{+}{N}\!\!-\!\!O\overset{-}{S}O_3 \xrightarrow{\text{H}_2\text{O}} (C_2H_5)_2NH + CH_3CHO \quad (17)$$

$$\qquad\qquad\qquad\qquad\qquad\mathbf{37}$$

$$(C_2H_5)_3\overset{+}{N}\!-\!O\overset{-}{S}O_2 + (C_2H_5)_3\overset{O}{\underset{\uparrow}{N}} \longrightarrow (C_2H_5)_3\overset{+}{N}\!-\!O\overset{-}{S}O_3 + (C_2H_5)_3N \quad (18)$$

$$\quad\mathbf{38}\qquad\qquad\qquad\qquad\qquad\qquad\qquad\mathbf{37}$$
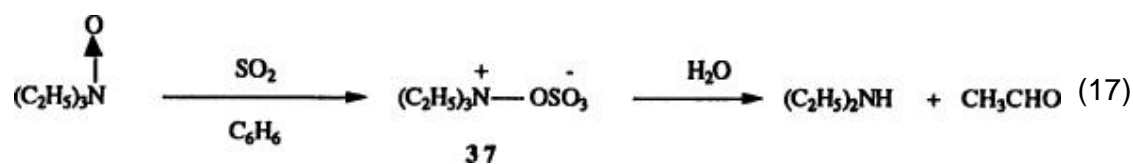
3. Scope and Limitations

3.1. Acylating Agents

As illustrated in Eqs. 2–6, reaction of a tertiary amine *N*-oxide with an acylating agent can produce a variety of products, including tertiary amides and/or secondary amines, aldehydes, iminium salts, and enamines or products derived therefrom. For the synthetic chemist it is thus of prime importance when applying the Polonovski reaction to a particular chemical problem to be able to direct the reaction toward the production of the desired product, and with unsymmetrical *N*-oxides, to the desired regioisomer.

In the search for optimum conditions the most important parameter to be considered is the choice of acylating agent. Up to the present almost exclusive use has been made of only two reagents, acetic and trifluoroacetic anhydrides, although in a small number of examples acetyl chloride and chloroformate esters have also been used. Despite this narrow range of investigation, however, marked alterations in product type and reaction regiochemistry are obtained by changing from one anhydride to the other.

3.2. Carbon–Hydrogen Elimination Reactions

Scheme 1 shows that formation of a particular product depends primarily upon the capacity of the intermediate iminium ions **13** to condense with their counterions. Thus in the reaction of trimethylamine *N*-oxide with acetic anhydride the *N*-demethylated product dimethylacetamide is formed in high yield, (33) whereas with trifluoroacetic anhydride under similar conditions the iminium ion **39**, a synthetically useful Mannich reagent, is generated in nearly quantitative yield. (99, 100) Further examples involving the reaction of more complicated *N*-oxides with these two reagents are presented in the section on Synthetic Applications.
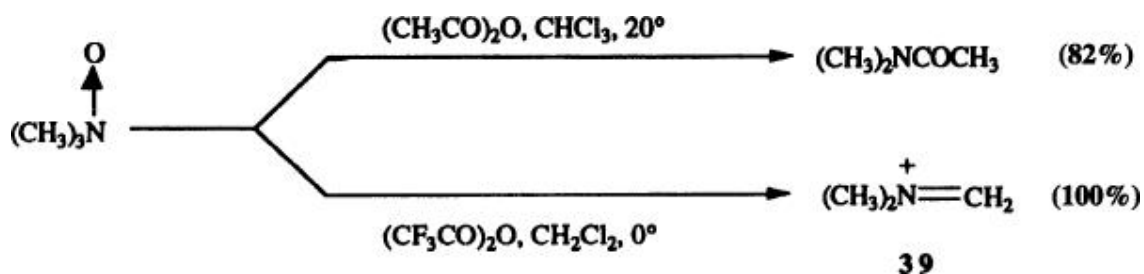
3.2.1. Regio- and Stereochemistry

3.2.1.1.1. Acyclic and Six-Membered Ring Systems

Scheme 1 also shows that the regiochemistry of the Polonovski reaction is determined by a preference for loss of a proton from one or the other of the

carbon centers α to nitrogen in the iminium ion-forming step **12** **13**. The anhydride plays a fundamental role in the orientation of this E_2 elimination reaction, since both the leaving group on nitrogen and the base are derived from it. As a rule it is found that the thermodynamically more stable iminium ion is produced when trifluoroacetic anhydride is employed, and with acetic anhydride the product obtained generally depends upon the kinetic acidity of the α hydrogens. These results reflect the fact that on reaction of an *N*-oxide such as **11** with trifluoroacetic anhydride, an excellent leaving group is generated along with a weak base, whereas with acetic anhydride a comparatively poorer leaving group and a much stronger base are produced. The elimination step is best considered in terms of Variable E_2-Transition State theory. (101-103) According to this picture, in the transition state for the reaction of an *N*-oxide with trifluoroacetic anhydride, departure of the leaving group on nitrogen will be advanced with respect to cleavage of the C α -H bond [E_1-like], and the stability of the product iminium ion is the controlling factor. Conversely, in the transition state for the reaction with acetic anhydride, a highly developed bond may form between the proton being abstracted and the base [E_{1cb}-like]. In this transition state model the kinetic acidity of the α protons is the regiochemical determining factor.

$$RR'NCH_2R'' \longrightarrow \underset{\overset{|}{\underset{B^-}{\nwarrow}}\,\overset{\displaystyle H}{|}}{\underset{RR'N-CHR''}{\overset{+}{\underset{|}{OR'''}}}}$$

OR''' : $(\bar{O}COCF_3 > \bar{O}COCH_3)$

B⁻ : $(\bar{O}COCH_3 > \bar{O}COCF_3)$
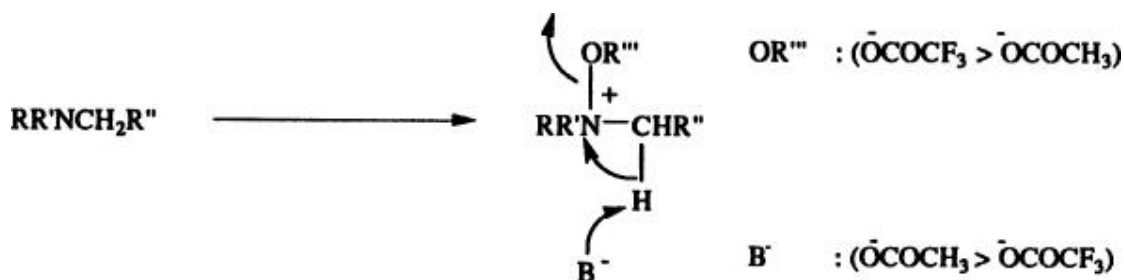
The results of several studies of the Polonovski reaction lend support to this analysis and illustrate the influence of structural parameters on the products obtained. For instance, in the Polonovski reaction of the simple unsymmetrical *N*-oxides **40–43** there is a greater preference for elimination to produce the more highly substituted iminium ion when trifluoroacetic anhydride is employed as the activating agent. (31) In the more complex steroidal *N*-oxide **44** a similar shift in product distribution is observed on changing from acetic to trifluoroacetic anhydride. (12) It is also interesting to note that the selectivity for reaction at the methine center of *N*-oxide **42** is even higher

$CH_3(CH_2)_3N(CH_3)_2 \rightarrow O$ **40**

$(CH_3)_2CHN(CH_3)_2 \rightarrow O$ **41**

$(CH_3CO)_2O$	(13%)	(87%)
$(CF_3CO)_2O$	(37%)	(63%)

	(50%)	(50%)
	(80%)	(20%)

cyclohexyl–$N(CH_3)_2 \rightarrow O$ **42**

cyclopentyl–$N(CH_3)_2 \rightarrow O$ **43**

$(CH_3CO)_2O$	(0%)	(100%)
$(CF_3CO)_2O$	(39%)	(61%)
CH_3COCl	(95%)	(5%)

	(68%)	(32%)
	(99%)	(1%)

44

$(CH_3CO)_2O$	(R= COCH₃)	(70%)	(20%)
$(CF_3CO)_2O$	(R= H)	(40%)	(55-60%)
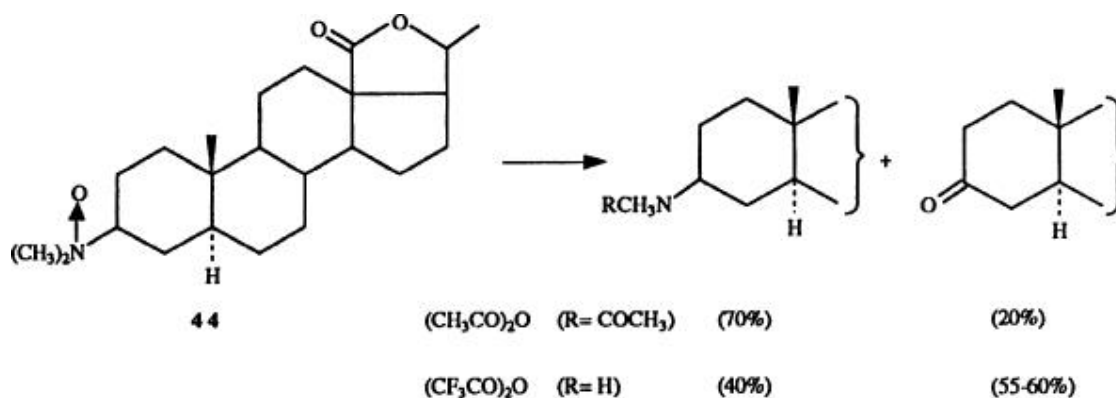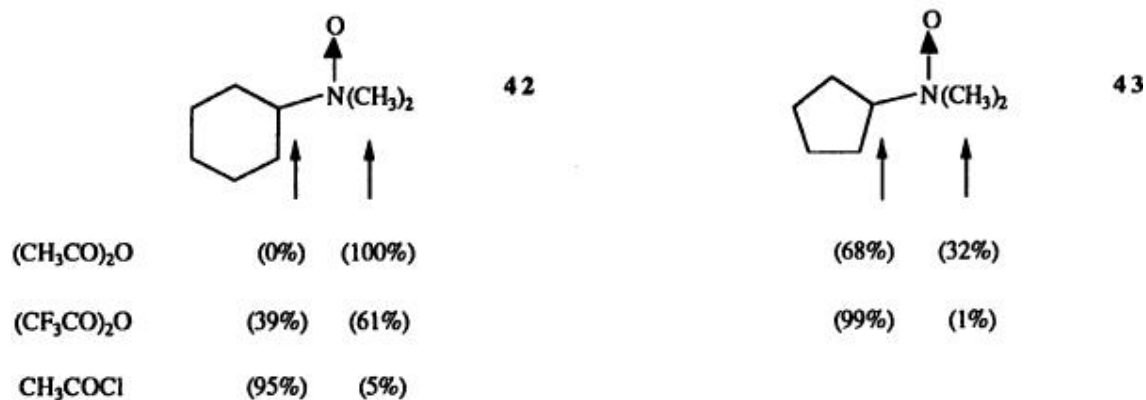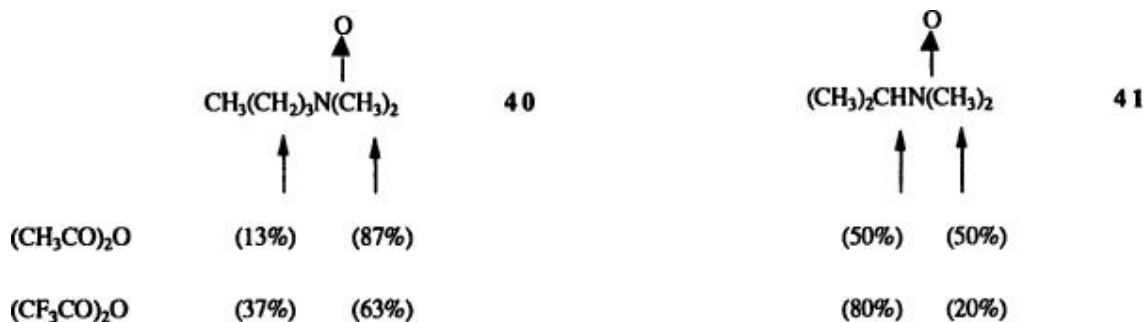
with acetyl chloride. (104) This result is interpreted as being due to the lower basicity of chloride ion relative to trifluoroacetate anion. That reaction at the more highly substituted carbon of N-oxide **43** predominates even under acetic anhydride conditions reflects the greater stability of an exocyclic double bond in a five-membered ring.

Identical arguments are evoked to explain the results obtained in the reaction of N-oxide **45** with different acid anhydrides. (105, 106) Thus with stronger bases $[(C_2H_5)_3N > CH_3CO_2^- > Cl^-]$ the E_{1cb} character of the transition state is considered to be enhanced, favoring the formation of **47** via the less stable iminium ion intermediate **46**. Opposed to this is the trend with better leaving groups $(CF_3SO_3^- > CF_3CO_2^- > CH_3CO_2^-)$ toward formation of compound **49** via

the more stable iminium ion **48**.

As might be expected, when the acidity of an α hydrogen is increased by the presence of an adjacent electron-withdrawing group, double bond, or aromatic ring, as in the *N*-benzyldimethylamine *N*-oxides **50a–e**, the Polonovski reaction occurs predominantly, if not exclusively, in the direction of the activated center. (38) In this case both *para* electron-donating and electron-withdrawing substituents on the aromatic ring of **50** augment the preference for debenzylation over demethylation. (30)

The influence of a phenyl or other electron-attracting functional group on the orientation of the Polonovski reaction can be overcome if the *N*-oxide nitrogen is incorporated into a piperidine ring. For example, reaction of the *N*-oxides **51** and **53** with trifluoroacetic anhydride (methylene chloride, 0°) followed by treatment with potassium cyanide leads to regioselective formation of the α -aminonitrile products **52** and **54** (43–55% yields). (107) Here the enhanced acidity of the exocyclic α hydrogens is outweighed by the greater stability of the intermediate endocyclic iminium ions.

Unfortunately, in 3-substituted piperidine *N*-oxides such as **55** there is generally little discrimination between the ring carbon centers α to nitrogen, and mixtures of regioisomeric products **56** and **57** are obtained. If, however, a $\triangle^{3,4}$ double bond is present in the starting *N*-oxide this functionality will direct the Polonovski reaction toward elimination of one of the allylic hydrogens. Two factors are responsible for this effect. First, the allylic protons are kinetically more acidic, and second, the resulting conjugated iminium ion
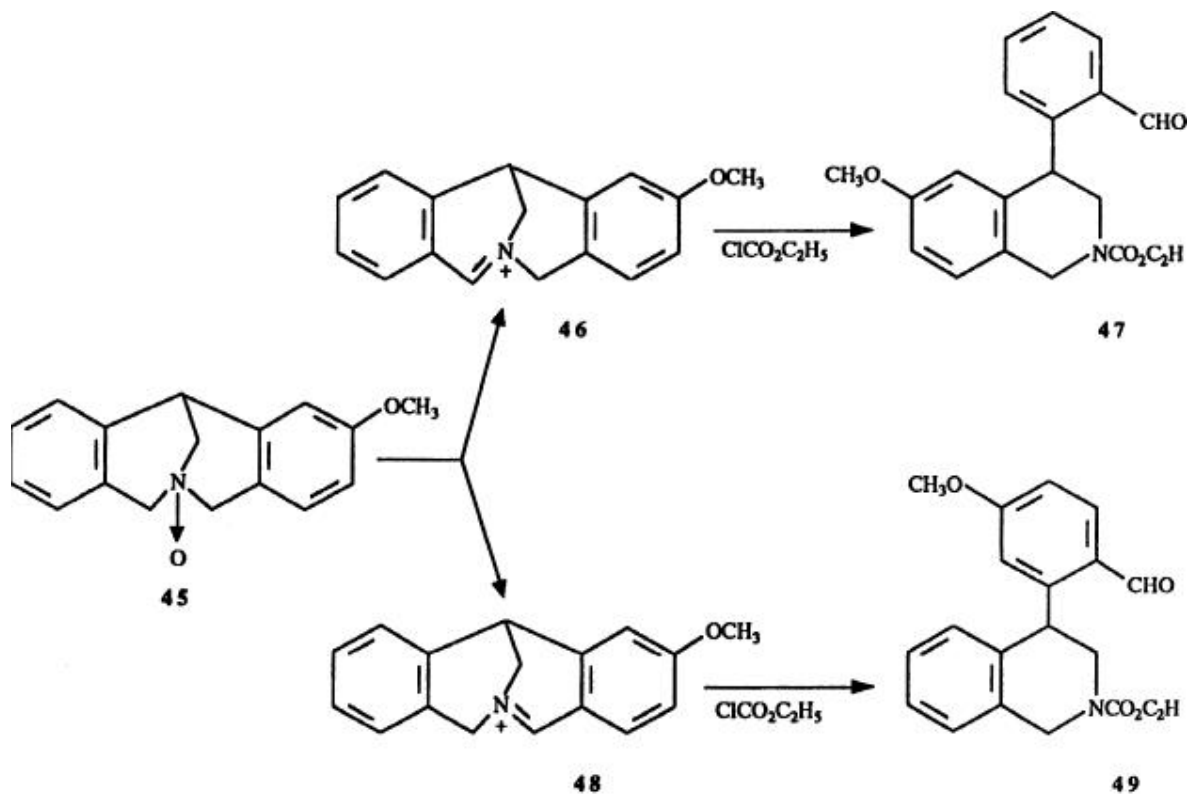
	47 : 49
(CH$_3$CO)$_2$O, 12h	2 : 1 (75)
(CH$_3$CO)$_2$O, (C$_2$H$_5$)$_3$N, 30 min	3 : 1 (71)
CH$_3$COCl	1 : 1 (92)
(CF$_3$CO)$_2$O	1 : 1 (95)
(CF$_3$SO$_2$)$_2$O	1 : 5 (89)
CF$_3$SO$_2$Cl	1 : 2 (25)
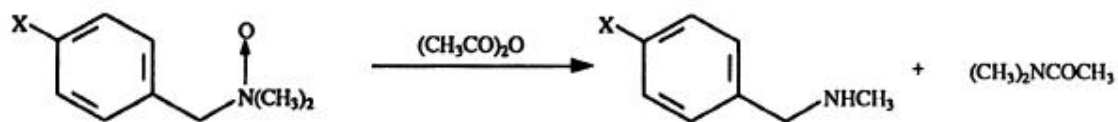
50a X= OCH$_3$	1 :	4.1
b X= CH$_3$	1 :	5.2
c X= H	1 :	2.9
d X= Cl	1 :	6.5
e X= NO$_2$	1 :	6.4

is thermodynamically more stable. Selective formation of the conjugated iminium ion **59** is thus observed on reaction of *N*-oxide **58** with trifluoroacetic anhydride. Treatment of this intermediate with sodium borohydride gives the (*Z*)-ethylidene product **60**. (108)
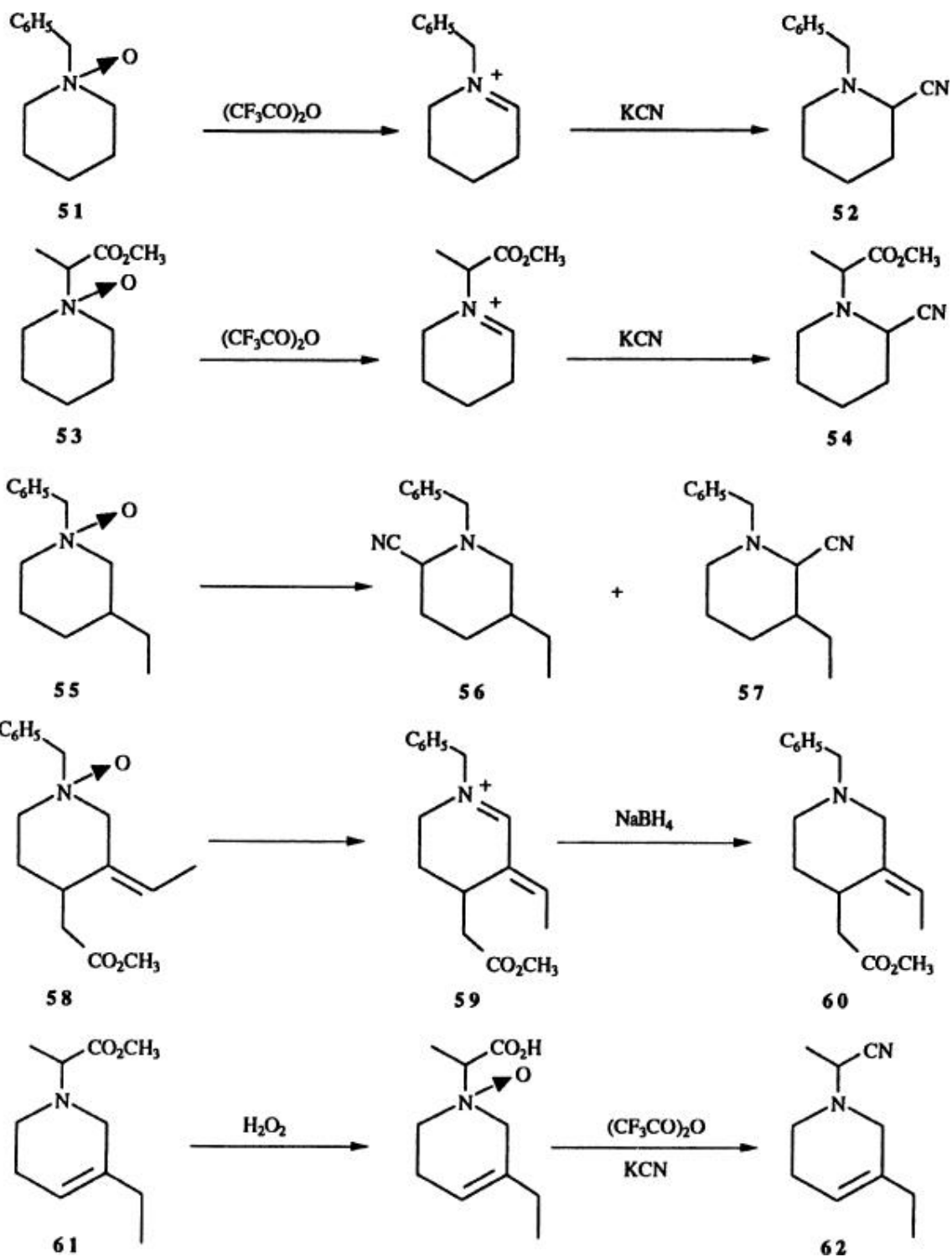
Formation of exocyclic iminium ions can be achieved under special circumstances where a functionality other than hydrogen is lost during the elimination step. One version of this technique takes advantage of the fact that carboxylic acid esters are readily hydrolyzed to the parent acids (2) during N-oxide formation with hydrogen peroxide. (107, 109) Thus on sequential treatment of the N-oxide **61** with hydrogen peroxide, trifluoroacetic acid, and potassium cyanide, the exocyclic rather than endocyclic aminonitrile **62** is produced in 48% yield.
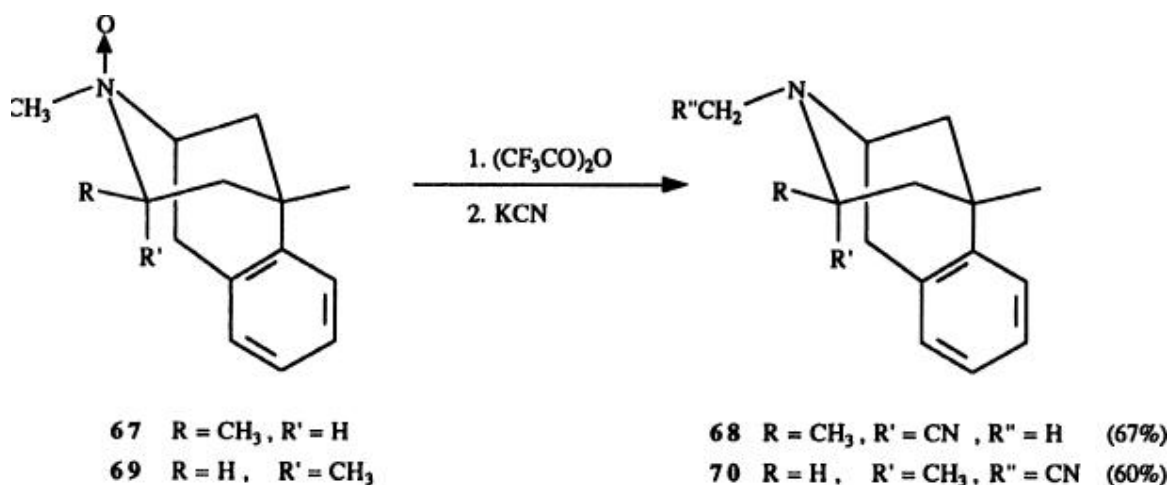
In more conformationally rigid polycyclic systems the relative stereochemistry between the N — O and neighboring C α — H bonds also becomes an important factor in determining the regiochemistry of the elimination step in the Polonovski reaction. Thus the 6 β ,7β -dideutero derivative **64** of nupharidine is converted, on reaction with acetic anhydride, into △ ^{6}-dehydrodeoxynupharidine (**66**) containing a single deuterium atom at C-6. (36)
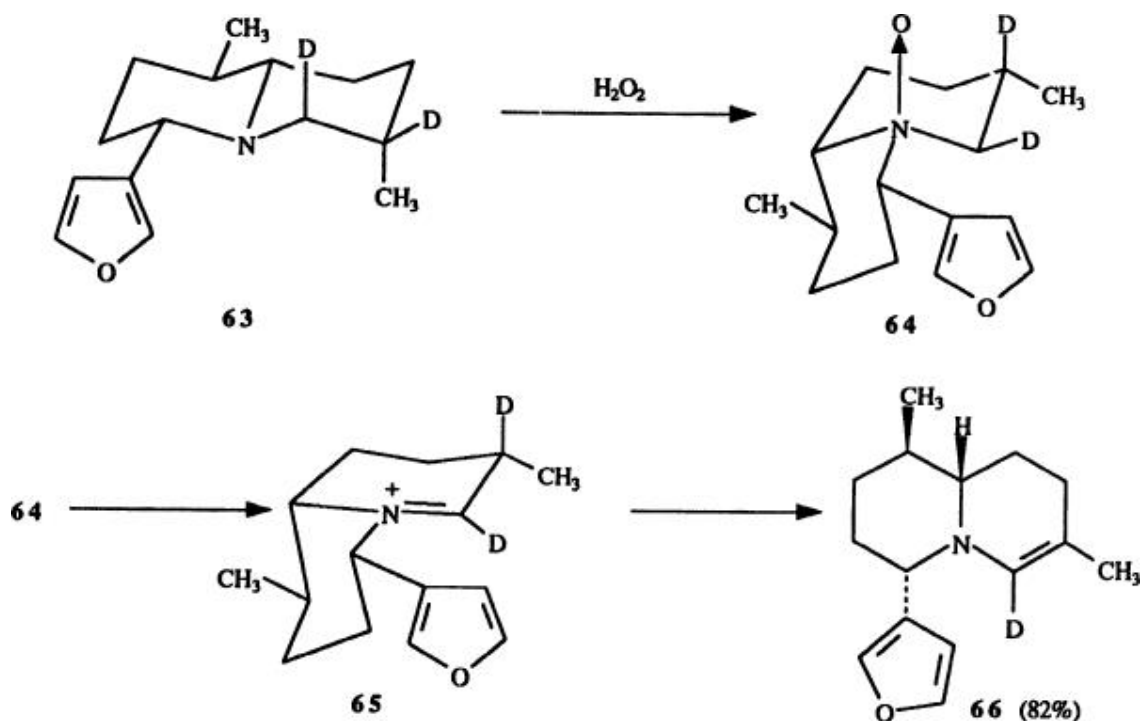

The formation of the intermediate iminium ion **65** in the reaction thus involves loss of the 6 α -H which is *trans* diaxial, that is, antiperiplanar, to the N — O bond of **64**. Although the N-oxide **64** could conceivably undergo the Polonovski reaction via its alternative *cis*-decalin conformer, this is highly improbable

because in this conformation the three ring substituents would be axially oriented. The structure of an *N*-oxide cannot always be correlated with that of the free base because of the possibility of nitrogen inversion (compare **63** with **64**).

Trans β -elimination is also observed in the transformation of the benzomorphan *N*-oxide **67** to aminonitrile **68**. (110) In contrast, compound **70** is obtained from the corresponding reaction of *N*-oxide **69** in which the *C*-methyl group is axial.

67 R = CH₃ , R' = H
69 R = H, R' = CH₃

68 R = CH₃ , R' = CN , R" = H   (67%)
70 R = H, R' = CH₃ , R" = CN (60%)

1. (CF₃CO)₂O
2. KCN

A similar high degree of stereoselectivity is observed in the Polonovski reaction of coccinelline (**71**) and its C-2 normethyl derivative **72**. (37, 111) In each reaction almost exclusive loss of the *trans* diaxial hydrogen is observed, leading to the enamines **73** and **74** in 56–60% yields.


ClCO₂CH₃ (71)
(CF₃CO)₂O (72)

71 R= CH₃
72 R= H

73   R= CH₃ (60%)
74   R= H   (56%)
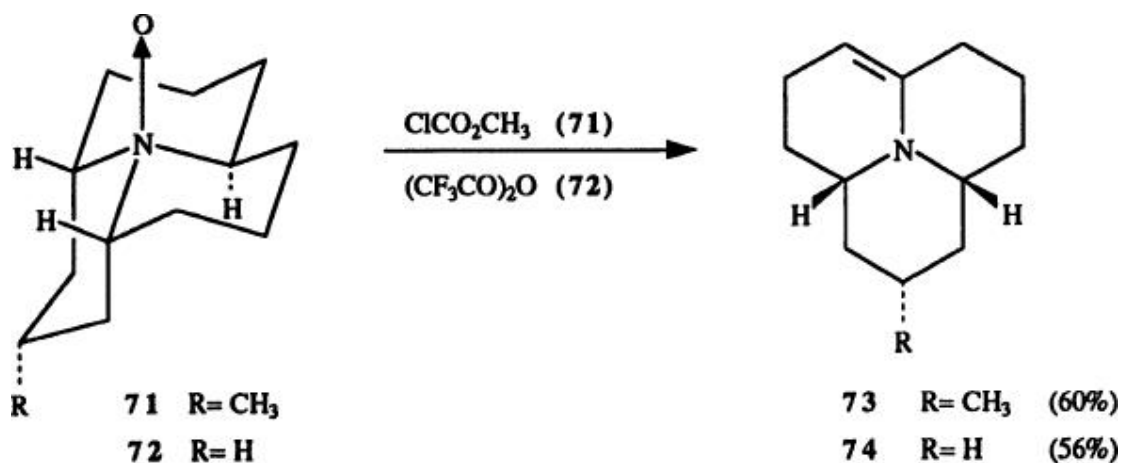
The reaction of the *N*-oxide of lupanine (**75**) under Polonovski conditions also provides a pertinent example, since the formation of $\triangle^{11}$-deoxylupanine (**76**) in this reaction was initially believed to occur by a *syn* elimination (112) from the all-chair structure **75a**. (113-115) Subsequent NMR and X-ray diffraction studies revealed that in fact lupanine *N*-oxide possesses the structure **75b**, wherein the C ring is a boat and the N — O and C(11) —H bonds are *trans* diaxial. (116-118) With mercuric acetate alone the same $\triangle^{11}$-iminium ion is obtained, whereas with mercuric acetate–ethylenediaminetetraacetic acid, *N*-bromosuccinimide, or sulfur dioxide, the less-substituted $\triangle^{17}$-iminium ion is produced, also via an *anti*-E_2 elimination. (117)
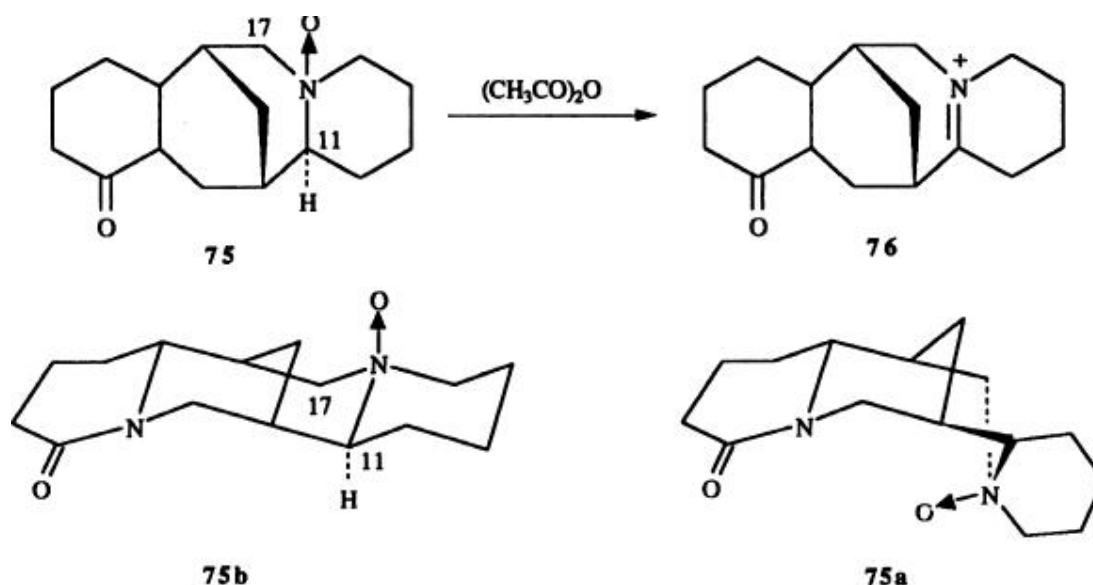

The situation is more complicated in cyclic systems such as the indoloquinolizidine *N*-oxides **77a,b** where one of the α -carbon centers is activated by the presence of an aromatic (indole) substituent. As expected, reaction of the C/D-*trans*-*N*-oxide **77a** with either acetic or trifluoroacetic anhydride leads to formation of the conjugated iminium ion product **78**. (119) More importantly, however, under the same conditions reaction of the *cis*-*N*-oxide **77b** also produces compound **78**. Since the relative rates and yields of the two reactions are comparable, it appears that *anti* elimination is not an absolute requirement for this Polonovski reaction.

Several explanations can be forwarded to account for the results obtained with **77b**. First, the combined influence of the indole ring and the electrondeficient *N*-oxide nitrogen produces an E_{1cb}-like transition state, in which case
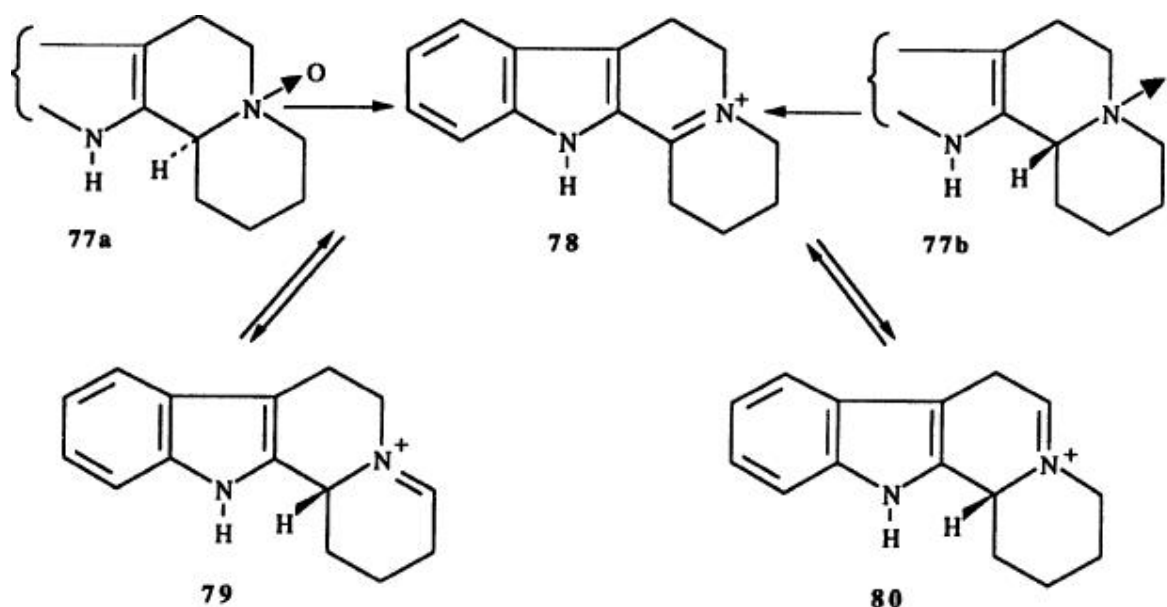
the relative stereochemistry of the α hydrogen is of lesser importance. A second possibility, also related to the enhanced acidity of the benzylic proton in these systems, is that epimerization of the C-3 center occurs prior to the elimination step. Finally, it is proposed that the reaction of **77b** produces initially iminium ions **79** and **80** via a stereochemically favored E_2-elimination, and that these intermediates then isomerize to the thermodynamically more stable product **78**. (119) A similar isomerization mechanism has been suggested to account for the change in product distribution when triethylamine is added to the reaction of the ergoline N-oxide (**81**) with acetic anhydride, (120) and a number of key steps in indole alkaloid biosynthesis are postulated to involve iminium ion isomerizations. (121, 122)

|		
81	(CH₃CO)₂O	(10%)	(24%)
	(CF₃CO)₂O	(3%)	(45-50%)
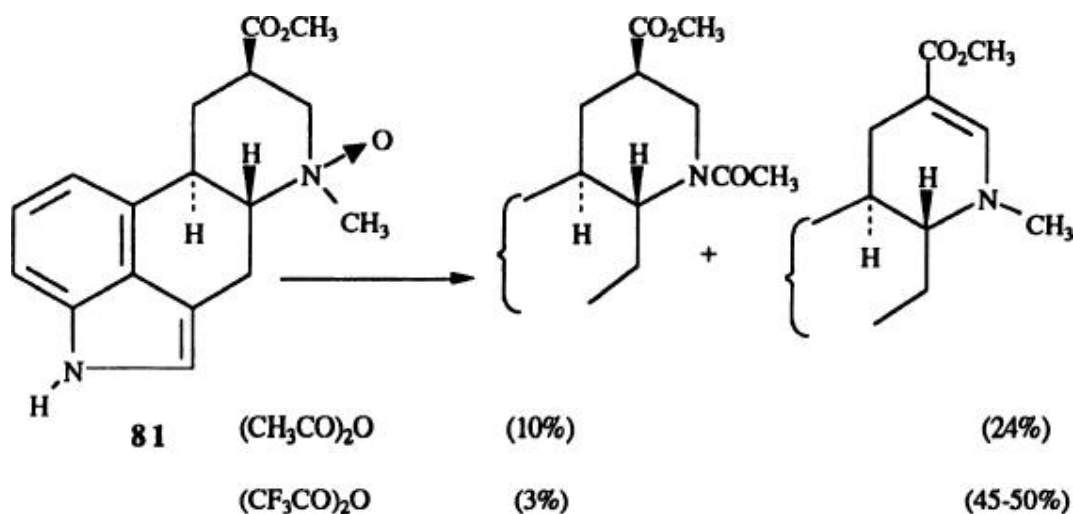
A likely mechanism for such a process involves the formation of ylides as transient intermediates which undergo reprotonation according to Eq. 19. Although at first sight the production of high-energy ylides in acidic media appears unreasonable, it has been shown that the generation of ylides such as **82** from imine derivatives of α -amino acid esters is possible in acidic media and is catalyzed by acid. (123, 124) In addition, a 1,3-dipole is formed on reaction of the *N*-oxide **83** under Polonovski conditions, as shown by trapping the intermediate **84** with dimethyl acetylenedicarboxylate. (125)

Although the mechanistic details of the reaction of *N*-oxides **77** have not been determined, the reaction of the *N*-oxide of eburnamonine (**85**) with trifluoroacetic anhydride illustrates that the Polonovski reaction of indoloquinolizidine *N*-oxides can produce either or both the thermodynamic and *anti* elimination products. When the products of this reaction are reduced in situ with sodium cyanoborohydride, *trans*-eburnamonine (**86**) is obtained in 50% yield. (126) In contrast, when a normal aqueous workup is carried out after reaction with the anhydride, the enamine **87** is obtained in yields up to 70%. (127)

The Polonovski reaction of desmethylhirsuteine *N*-oxide (**88**, R = H) is also pertinent, as the products **89** (R = H) and **90** resulting from oxidation at both C-3 and C-21 are obtained. (128) Interestingly, when this reaction is

(19)
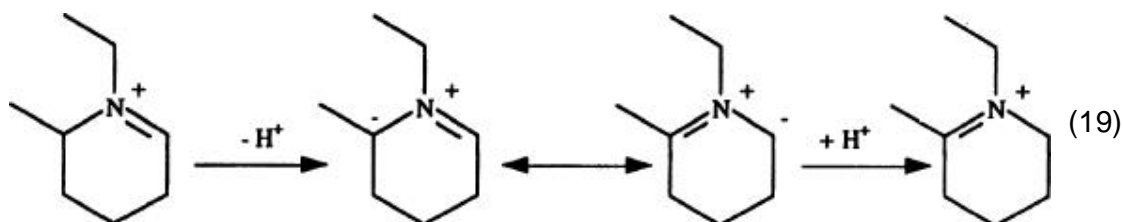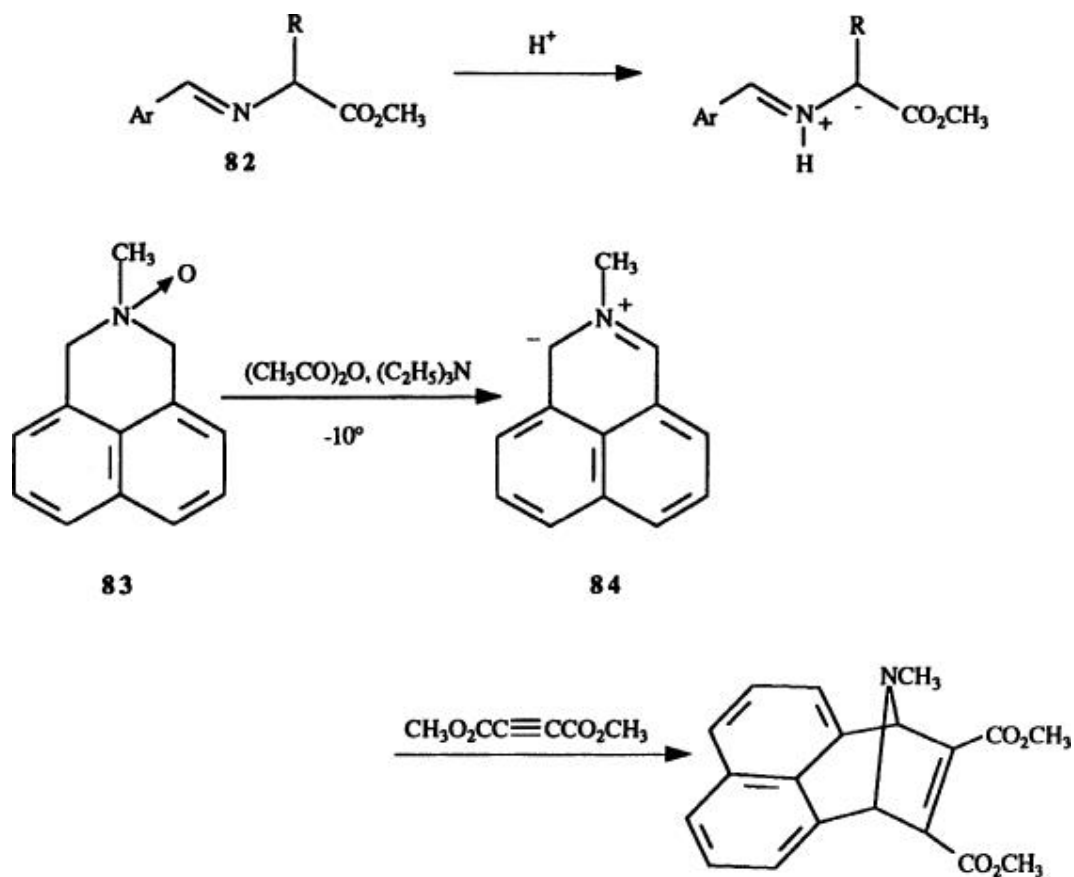
applied to hirsuteine (**88**, R = CH₃) itself, the proportion of the tetracyclic product **89** (R = CH₃) obtained after borohydride reduction is increased. It is tempting to suggest that since the intramolecular reaction with the β-dicarbonyl oxygen is excluded in this case there is a greater chance for iminium ion isomerization to occur. However, in the absence of knowledge about the structures of *N*-oxides **88** (R = H and CH₃), such an interpretation must be considered with caution. For example, the closely related alkaloid geissochizine (amine precursor to **135**) and its *O*-methyl enol ether derivative are known to adopt different conformations. (129) It may be therefore that the *N*-oxides of **88** (R = H, CH₃) are different in structure and as a consequence different in their reactivity.

85

86 (50%)

87 (70%)
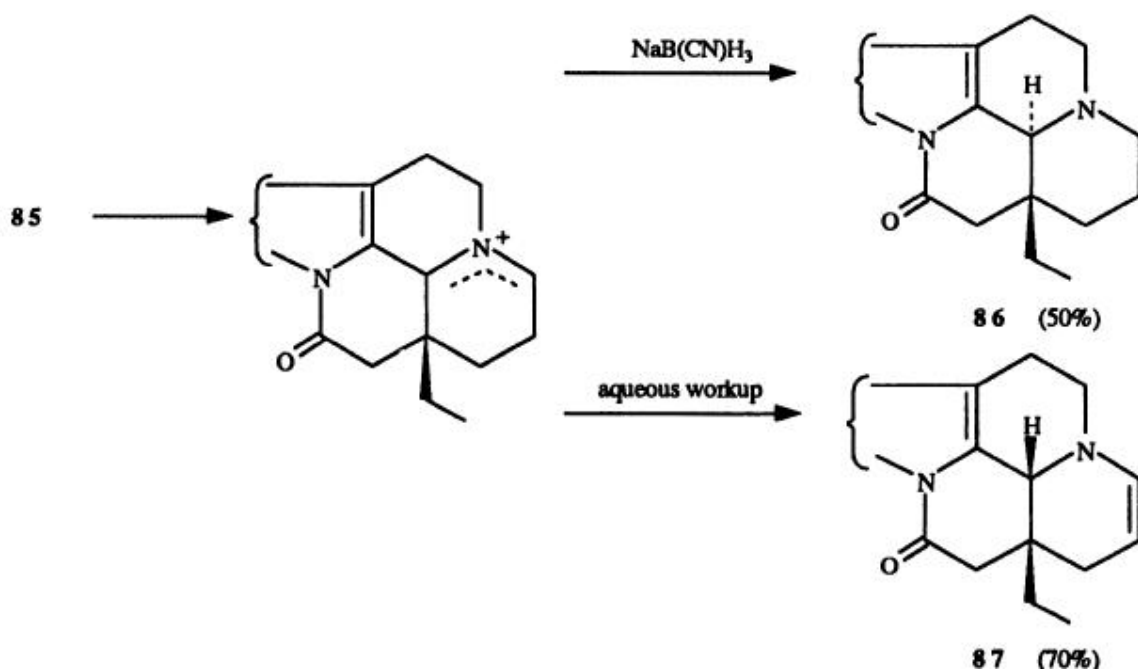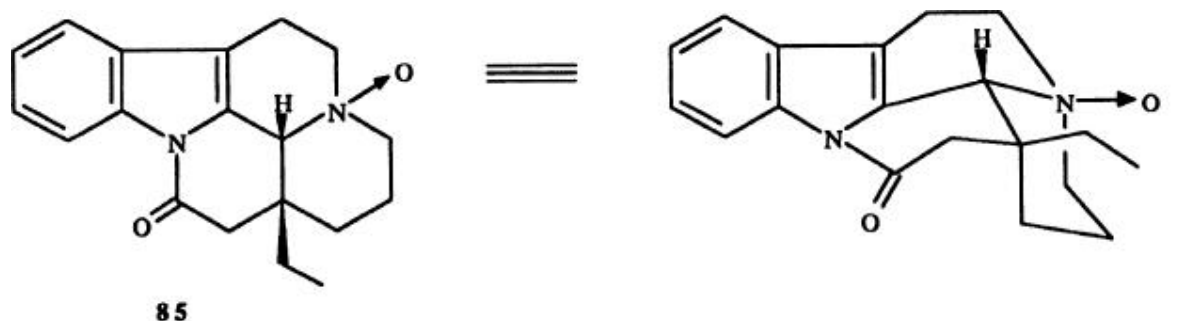
3.2.1.1.2. Five-Membered Ring Systems

For pyrrolidine *N*-oxides, one might a priori anticipate ion formation to occur by a *syn* elimination process since the N — O and adjacent C α — H bonds cannot become antiperiplanar to each other. However, the *N*-oxide **91a** of the steroid alkaloid conanine reacts with acetic and trifluoroacetic anhydride exclusively by the *anti* pathway to give the exocyclic enamine **92**. (130)

Release of steric strain between the C-16 methylene and the ring methyl substituent is undoubtedly a major driving force in this reaction. More revealing is the reaction of *N*-oxide **91b**, which would give the same enamine product if a *syn* pathway is favored. The observed formation of a mixture of compounds **93**

and **94** argues in favor of *anti* elimination in the iminium ion-forming step in five-membered ring systems.

88 R= H

1. (CF₃CO)₂O
2. NaBH₄

89 R= H (14%)   **90 (18%)**

88 R= CH₃ → **89 R= CH₃ (51%)**

1. (CF₃CO)₂O
2. NaBH₄

(22%)
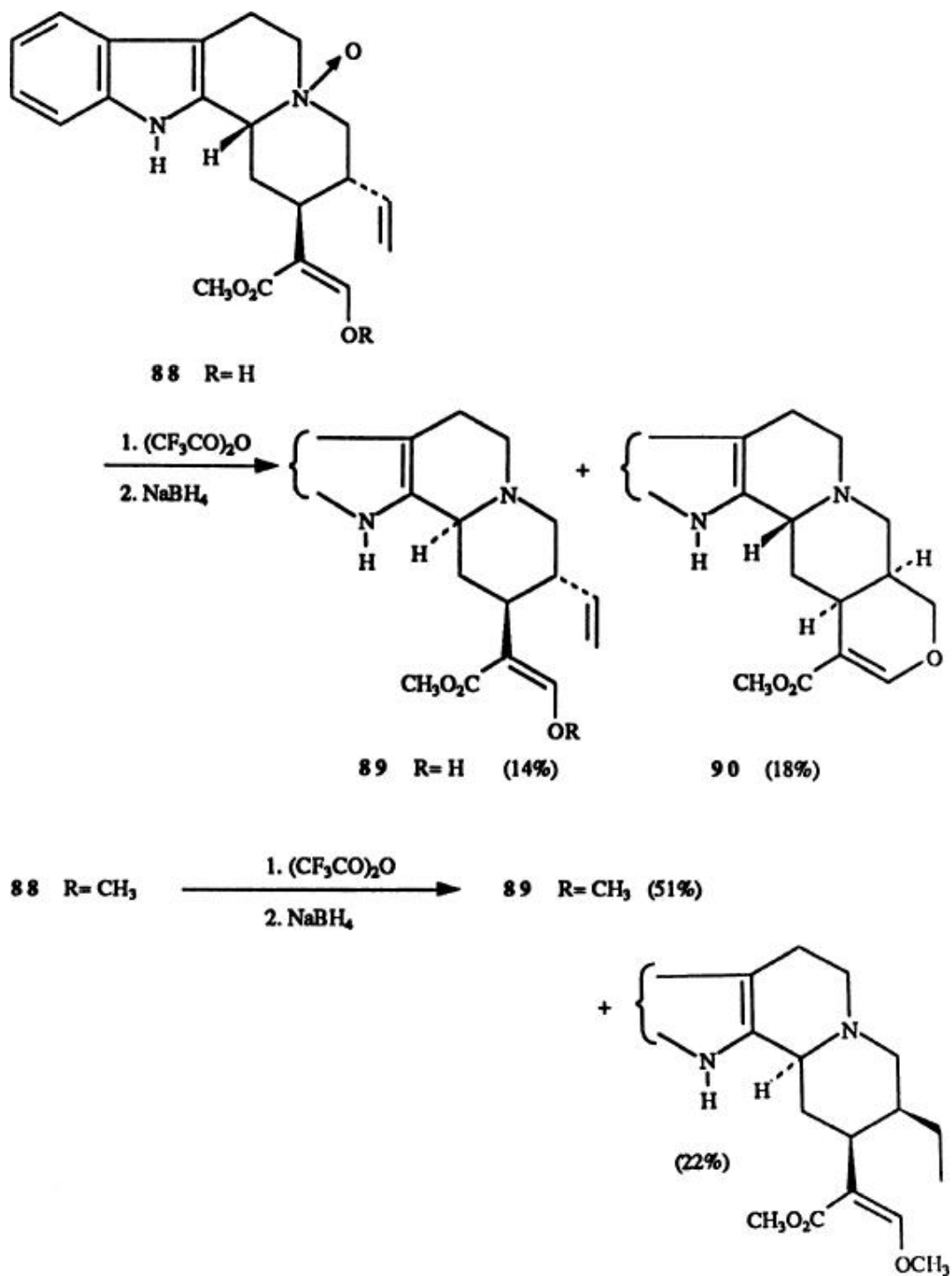
3.2.1.1.3. Three-, Four-, Seven-, and Higher-Membered Ring Systems

To date no reports of the Polonovski reaction of *N*-oxides of four- or seven- and higher-membered cyclic tertiary amines have appeared. Aziridine *N*-oxides can be prepared by ozonolysis of *N-tert*-butylaziridine; however, these compounds are unstable above 0°. At higher temperatures compound **95** undergoes first-order decomposition to ethylene and *tert*-nitrosobutane. (131)
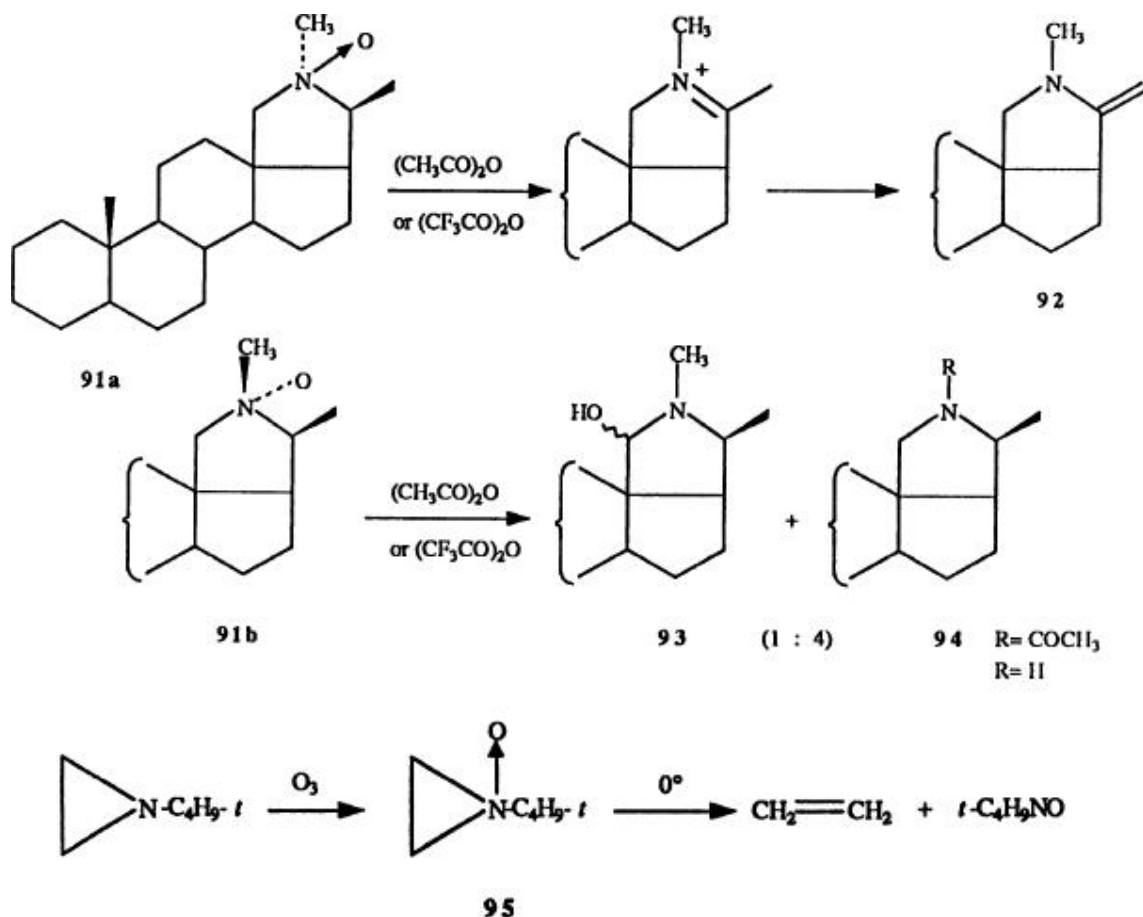
3.2.2. Synthetic Applications
3.2.2.1.1. Iminium Ion Cyclizations
Iminium ion cyclizations such as the Pictet–Spengler reaction have been widely used in alkaloid chemistry to create a carbon − carbon bond between the carbon alpha to the basic nitrogen and an aromatic ring. The intermediate iminium ions involved in this reaction are generally produced either in situ through condensation of an amine with an aldehyde or by direct oxidation of the amine. Often, mercuric acetate is employed in the latter approach. However, its use is not without drawbacks, such as the necessity for destroying amine–mercury complexes at the end of the reaction with hydrogen

sulfide. Mixtures of products epimeric at the newly created center are also obtained on many occasions, as illustrated by the reaction of the *seco*-heteroyohimbinane **96** with mercuric acetate, which produces akuammigine (**97a**) and tetrahydroalstonine (**97b**) in nearly equal proportions (combined yield 25%). (132, 133) In contrast, when this same ring closure is effected by reaction of the *N*-oxide of **96** under modified Polonovski conditions followed by brief treatment with acid, akuammigine (**97a**) is obtained in 25% yield essentially free of its 3 α –H epimer (biogenetic numbering (134)).

The stereoselectivity of this latter reaction arises from the fact that an iminium ion is formed as a discrete intermediate which cyclizes under stereoelectronic

96

97a   97b
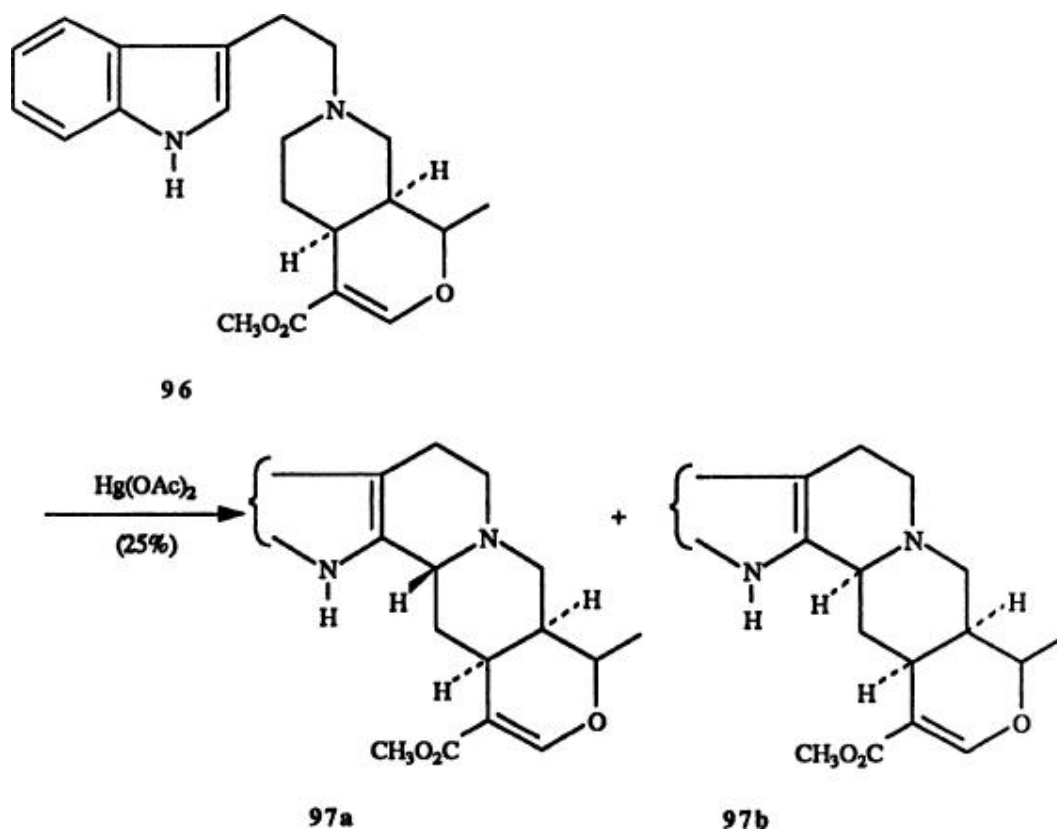
control by axial approach of indole to the α face of the iminium double bond. (135) The formation of a mixture of regioisomeric iminium ions is fortunately not observed in this example (under either set of conditions) because of conformational constraints. However, in simpler systems this can be a potential problem.

In a similar manner the Pictet–Spengler cyclization of the amine oxides **98a,b** and **99** under modified Polonovski conditions leads to selective formation of the products **100a,b** and **101**. (136) Compound **100b** is a key intermediate in the first synthesis of the alkaloid dihydroantirhine (**102**), which possesses the

uncommon 15 β -hydrogen configuration.

Use can also be made of the Polonovski reaction to readjust the stereochemistry at the C-3 center after ring closure, as illustrated for *N*-oxides **103a,b**. (137) Lower yields (8%) of compound **104a** are obtained when mercuric acetate is used as the oxidizing agent in these transformations.

In the isoquinoline alkaloid field, reaction of the *N*-oxide **105** with trifluoroacetic anhydride gives directly the tetrahydroisoquinoline derivative **106** in 33% yield. (138) What is remarkable in this reaction is that normally under modified Polonovski conditions iminium ion formation through loss of a methyl proton is only a minor pathway. Furthermore, under the same conditions the closely related *N*-oxide of dimethyltryptamine undergoes exclusive C − C bond fragmentation (see **197**). It is not surprising therefore that norcoralydine (**108**) is isolated in only 2.5% yield from the reaction of laudanosine *N*-oxide

98a   R= C₄H₉-*t*

b   R=

100a   R= C₄H₉-*t* (30%)

b   R= (25%)

99

101 (30%)

102
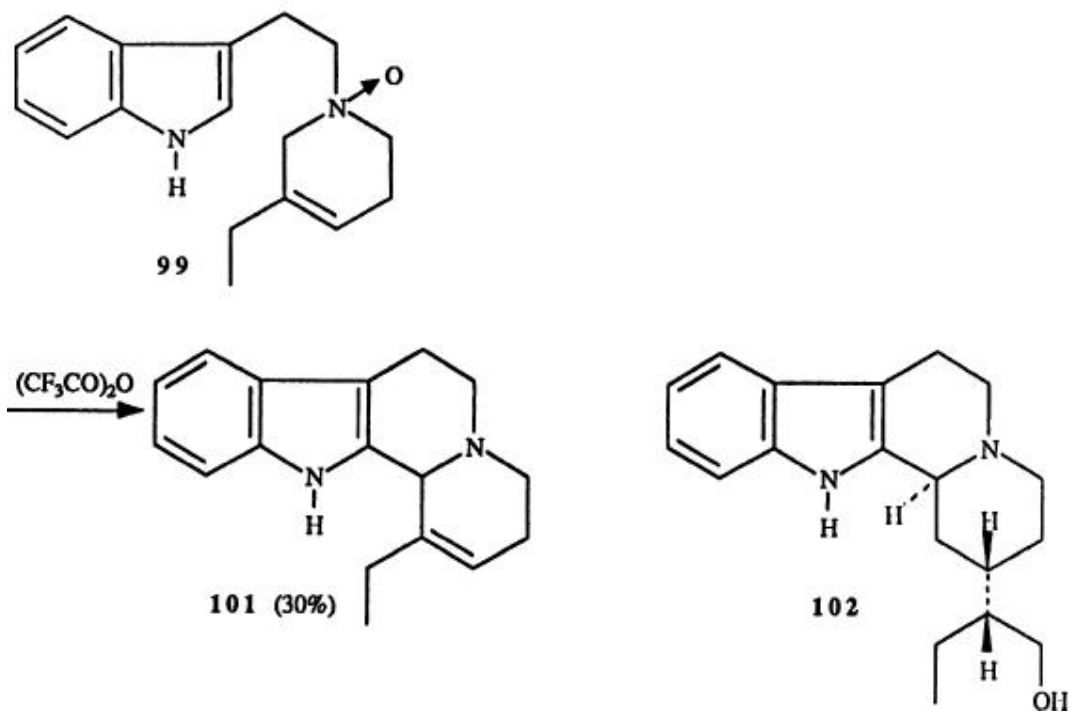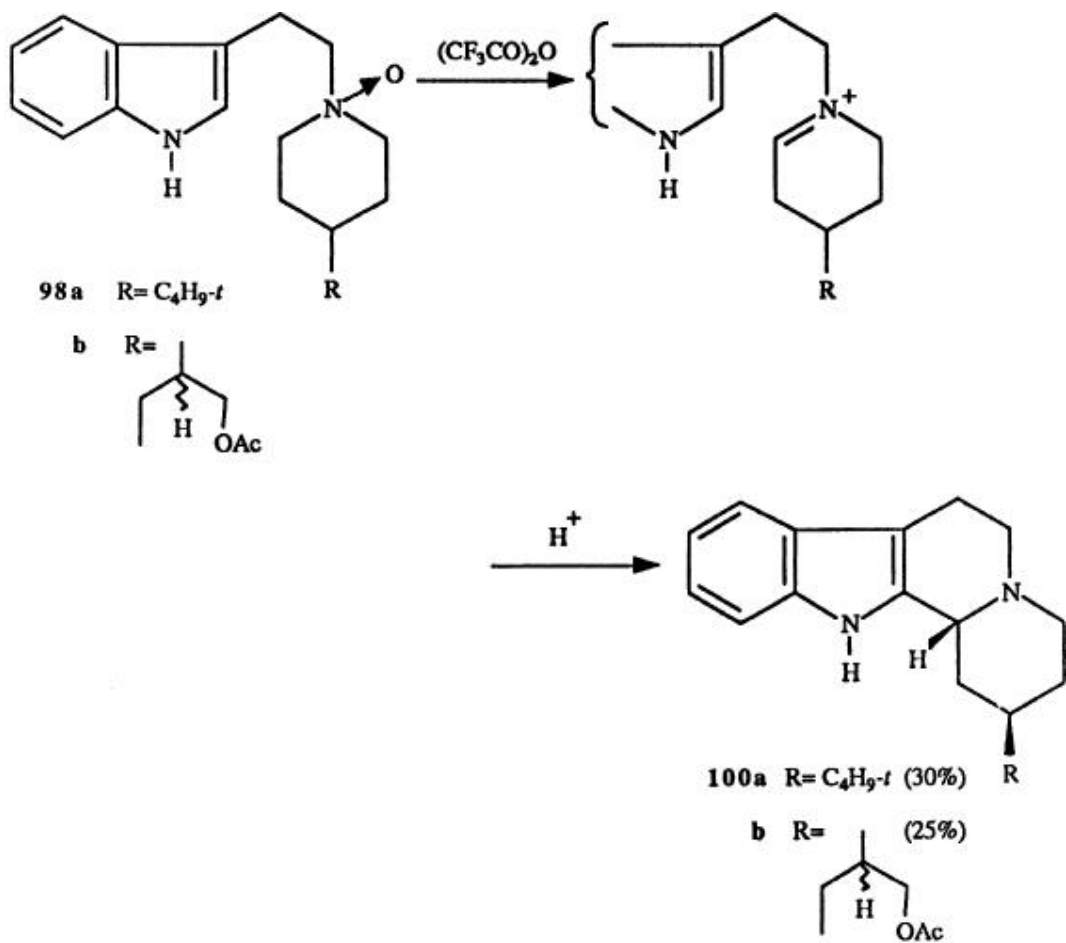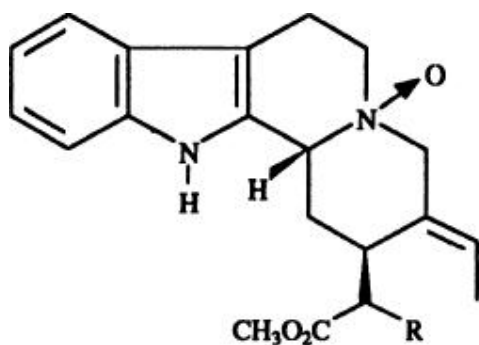
103a R= H
   b R= CH(OCH$_3$)$_2$

1. (CF$_3$CO)$_2$O
2. NaBH$_4$
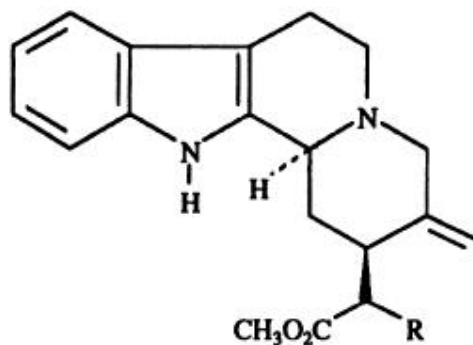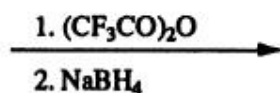
104a R= H   (40%)
   b R= CH(OCH$_3$)$_2$ (21%)

(**107**) with trifluoroacetic anhydride. (138) As discussed further on, the yield of this and similar reactions is significantly improved by using iron salts or sulfur dioxide as the activator.

Transannular cyclization between the carbon α to nitrogen and the C-7 position of indole is also achieved under modified Polonovski conditions in the synthesis of the strychnos alkaloid derivative **110** from *N*-oxide **109**. (139) This result contrasts with the analogous reaction of stemmadenine *N*-oxide with trifluoroacetic anhydride (see **200**   **201**), and is probably a consequence of different stereochemical relationships between the N — O bond and the adjacent centers in the two molecules.

105   106 (33%)

107   108 (2.5%)

109

110 (-)
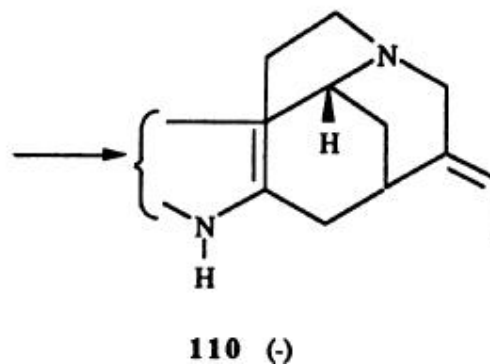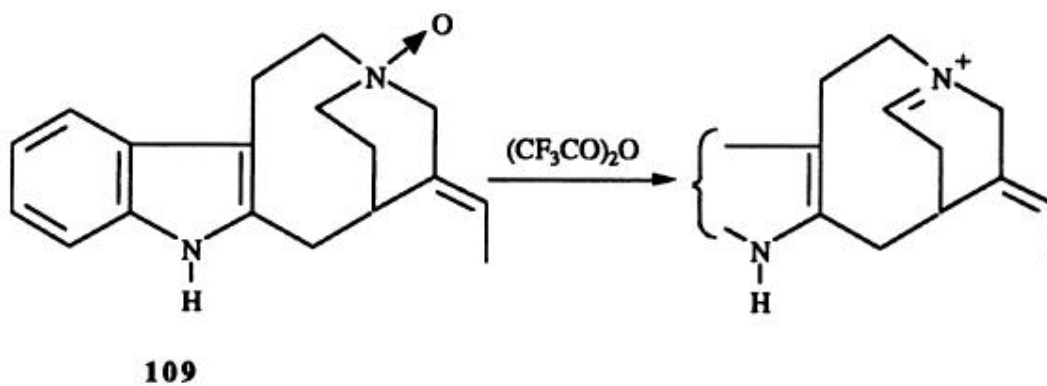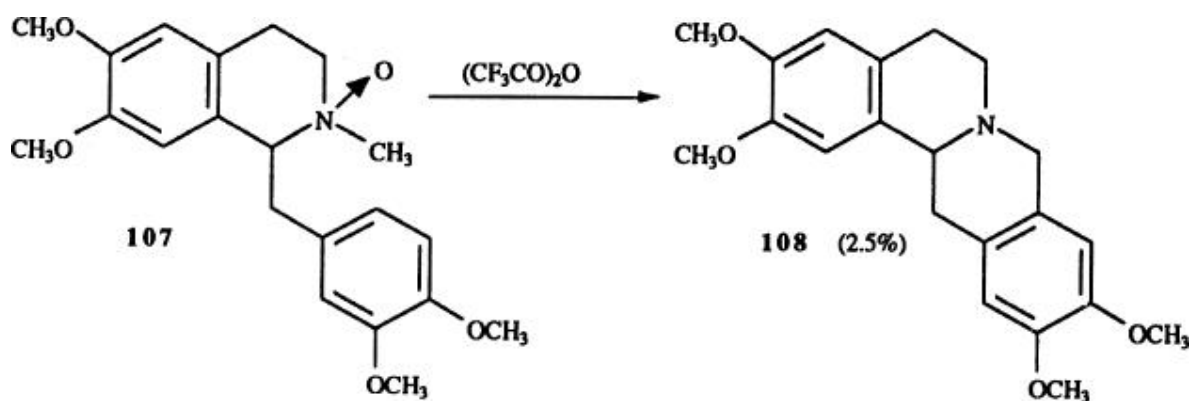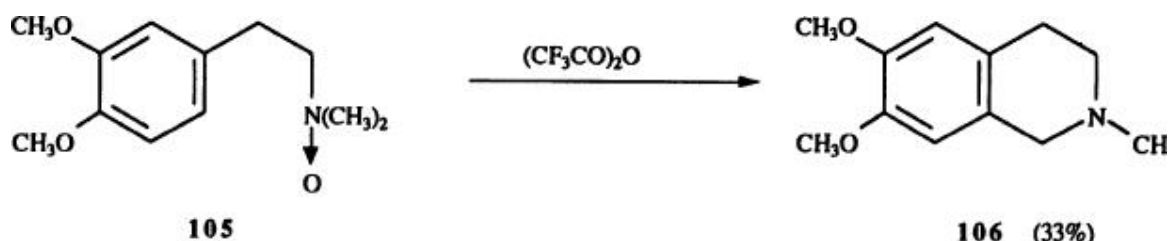
Carbon — carbon bond formation by intramolecular cyclization of conjugated iminium ions is also possible, as illustrated by the transformation of amine oxide **111** to **112**. (140) In another example intramolecular condensation of the

conjugated iminium intermediate **113** with the indole ring is achieved in an efficient and elegant biomimetic approach to the synthesis of the pyridocarbazole alkaloid ellipticine (**114**). (141)

3.2.2.1.2. Formation of α -Cyanoamines and Related Iminium Ion Reactions In a number of instances the iminium ion intermediates formed under Polonovski conditions are too reactive or labile to be employed as such in projected syntheses. The acidity of the Polonovski reaction medium is sometimes a further problem when considering in situ reactions with organometallic reagents and other carbon nucleophiles. One technique that can circumvent this problem is to convert these labile iminium ion intermediates into their

111

112 (50%)

113

114

(92%)
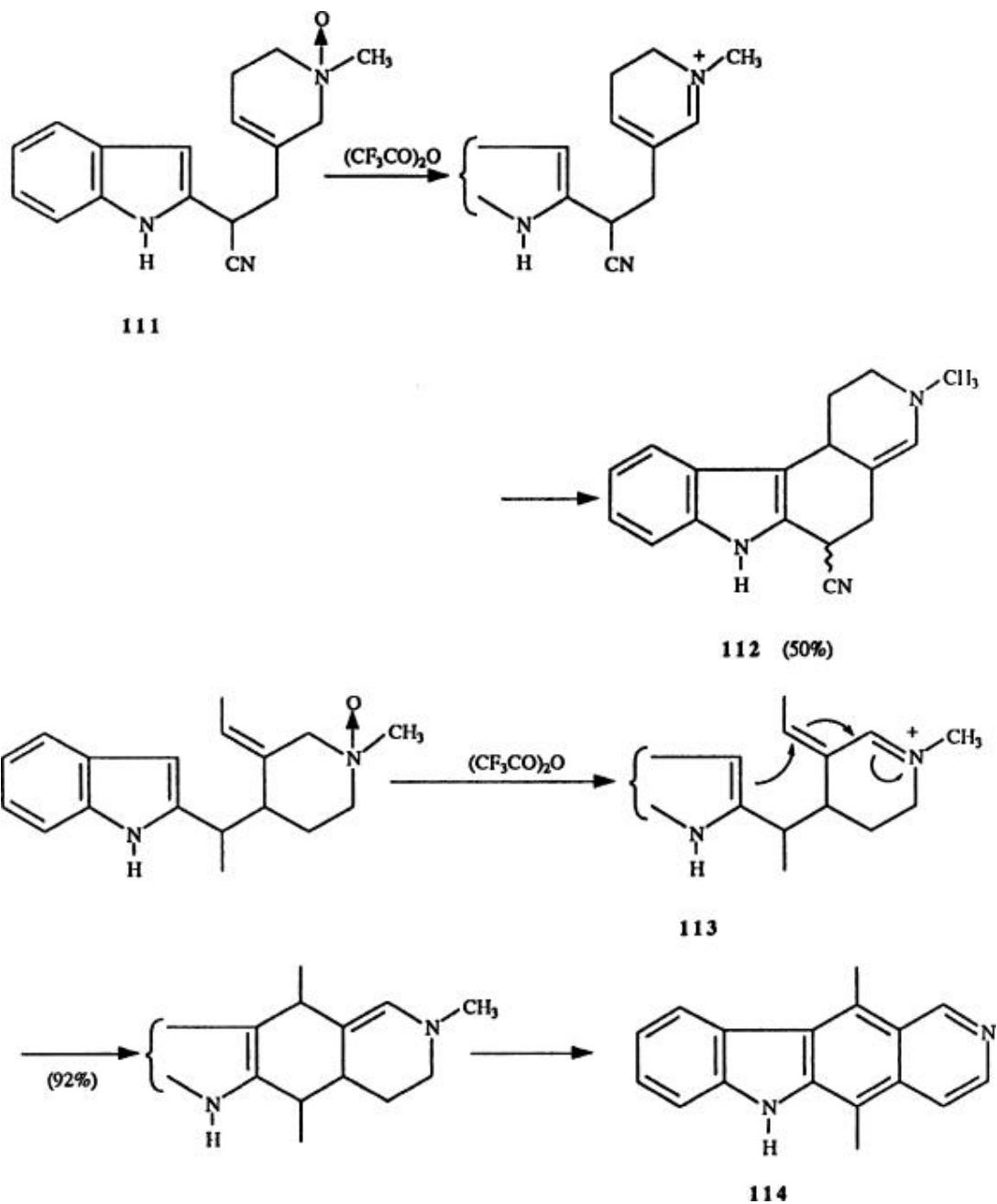
more stable α -cyanoamine derivatives. There are two advantages to this approach. First, the reaction of cyanide ion with iminium salts generally gives high yields, and second, the resultant α -cyanoamines react efficiently as "iminium ion equivalents" with a wide range of nucleophilic reagents. An additional gain is the possibility of effecting an "Umpolung" of the normal reactivity of iminium ions via the reaction of α -cyanoamine anions with electrophiles. The dual reactivity of these cyanide adducts thus broadens considerably the scope of application of iminium ions in synthetic chemistry.
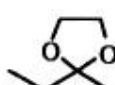
The use of α -cyanoamines in place of their less-stable iminium ion precursors often results in considerable improvement in product yields in the Pictet–Spengler and other ring-closure reactions. In this manner, the indole **116** is obtained in 65% yield on treatment of **115** with acid, whereas reaction of the iminium ion derived from *N*-oxide **117** with hydrogen chloride in methanol gives the chloro-substituted product **118** in only 42% yield. (142) Similarly, the Polonovski-derived α-cyanoamine **119** cyclizes to **120** in 84% yield. (143) In contrast, attempted reaction of the tertiary amine **121** with mercuric acetate is unsuccessful.
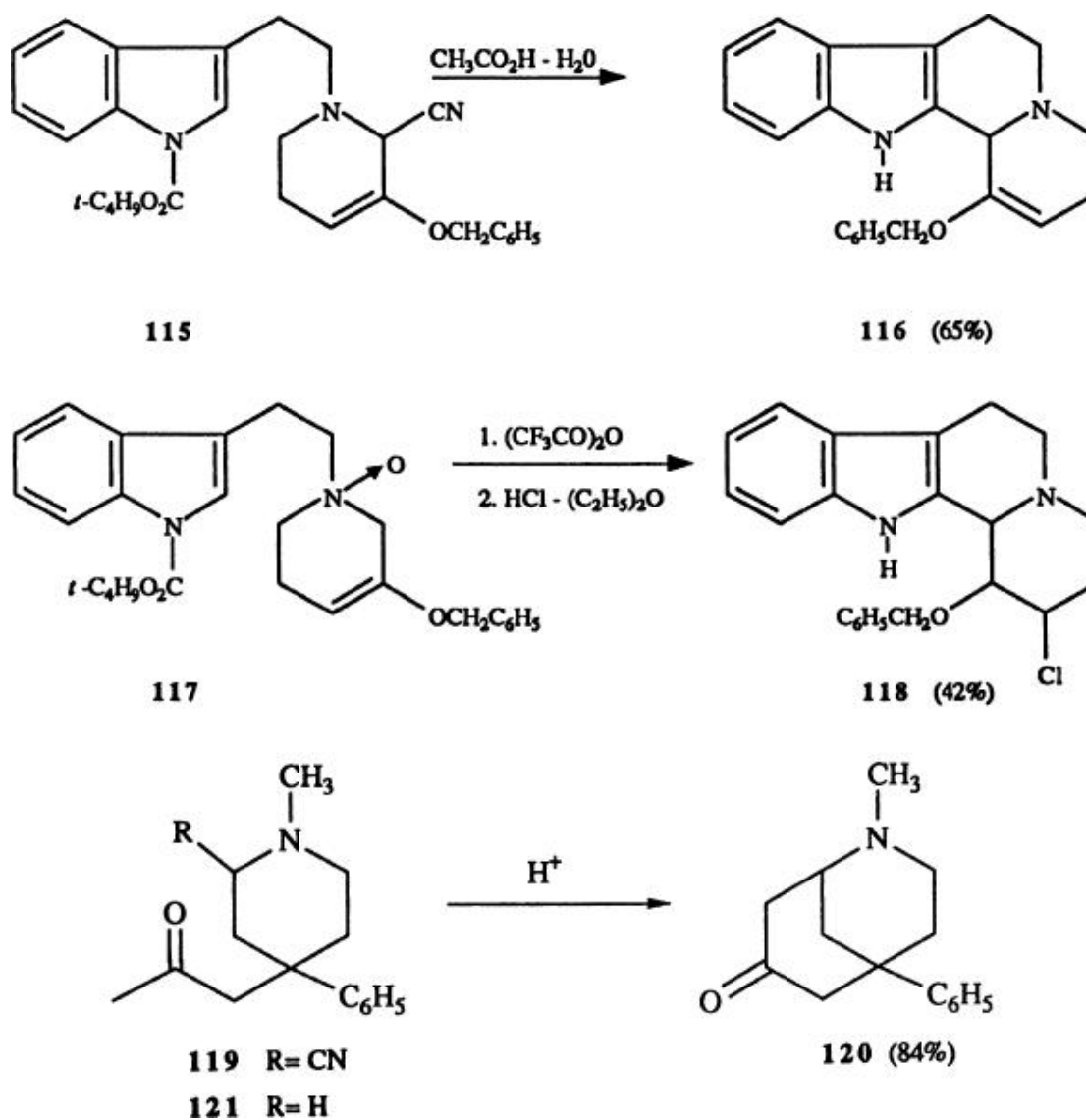
Another area in which use of this methodology has met with particular success is in the conversion of the 5,6-dihydropyridinium salts **122a–e**, formed by

reaction of the appropriate tetrahydropyridine *N*-oxides with trifluoroacetic anhydride, into the 2-cyano- $\triangle^3$-piperideines **123a–e**. (144) These stable allylic α -aminonitriles are employed as piperidine synthons in the construction of a variety of alkaloids, including adaline (**124**) from **123d** and 20-epiuleine (**125**) and olivacine (**126**) from **123e**. (145-147) Strategies for the synthesis of C-1 substituted benzomorphans **127**, corynanthé indole, 2-acylindole, and decahydroquinoline (pumiliotoxin-C) alkaloids from these versatile synthons are also reported. (148-152)

	R	R'	R"	R'''
a	H	H	H	CH₃
b	C₂H₅	H	H	CH₃
c	CH₃	CH₃	H	CH₃
d	H	H	(dioxolane)	CH₂C₆H₅
e	H	(dioxolane)	H	CH₂C₆H₅

The reaction of iminium salts with cyanide ion is similarly used to prepare the C-3 cyanobenzomorphans **129** from the *N*-oxide **128**. (153) By hydrolysis of the cyano group and coupling of the resultant carboxylic acid with a tetrapeptide fragment the novel enkephalin analog **130** is prepared.

128 → (CF₃CO)₂O / KCN → **129** (86%)

130
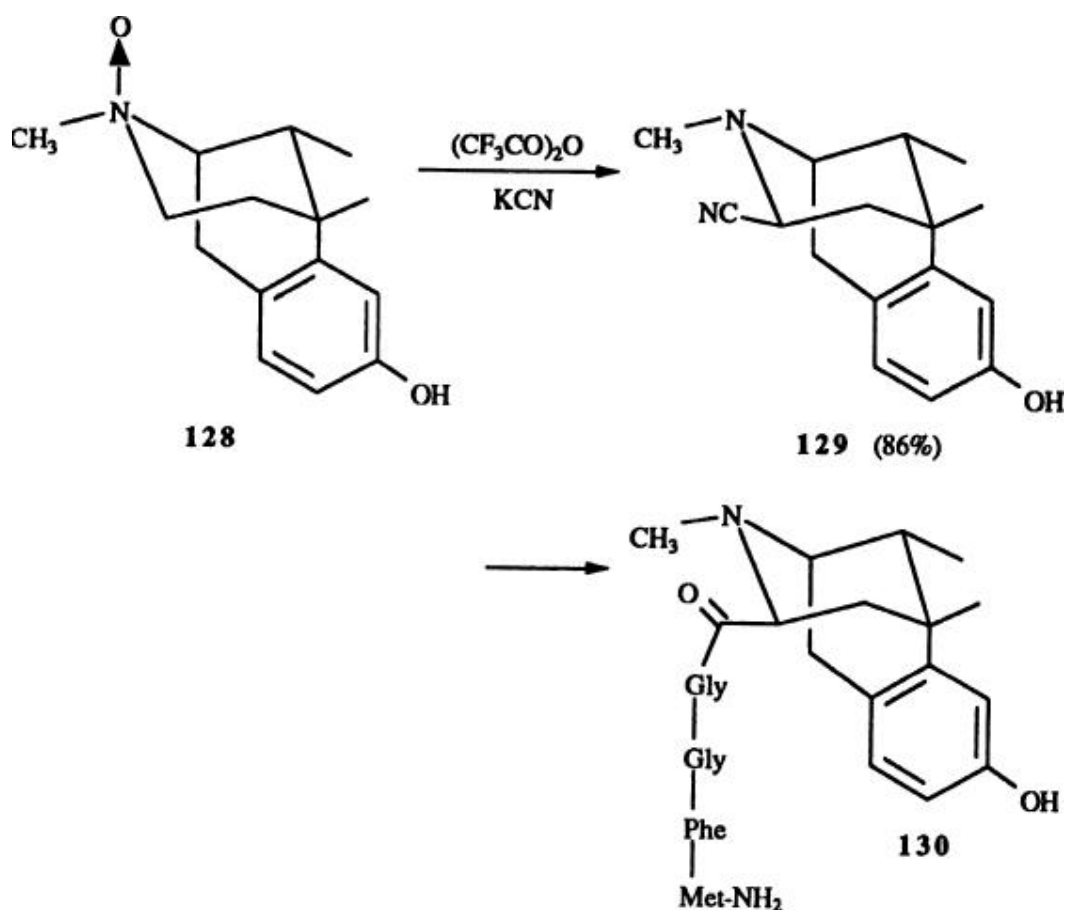
In a further application of this methodology, the sensitive iminium ion **132**, generated from the reaction of epipandoline N-oxide (**131**) with trifluoroacetic anhydride, is isolated as its stable α -aminonitrile adduct **133** (30% yield). (154) On reaction of **133** with N-methyldescarbomethoxytabersonine (**134**) in the presence of silver fluoroborate, a coupled product **135** is formed (20% yield) which possesses two of the crucial bonds that link the monomeric units of the ervafoline alkaloids (see ervafoline **136**). This experiment both mimics and lends strong support to the proposed biogenesis of alkaloids of the ervafoline series.

Interception of dihydropyridinium ions through reaction with an internal oxygen nucleophile forms the basis for the correlation of the structures and absolute configurations of the alkaloids vincine (**137**) with craspidospermine (**138**) (140) and of desacetylvindorosine (**139**) with desacetylcathovaline (**140**). (155)

Intramolecular trapping of the iminium ion formed on reaction of desmethylhirsutine N-oxide (**141**) with trifluoroacetic anhydride also provides a

131

(CF₃CO)₂O

132

KCN

133 (30%)

133 +

134

AgBF₄

135 (20%)

136
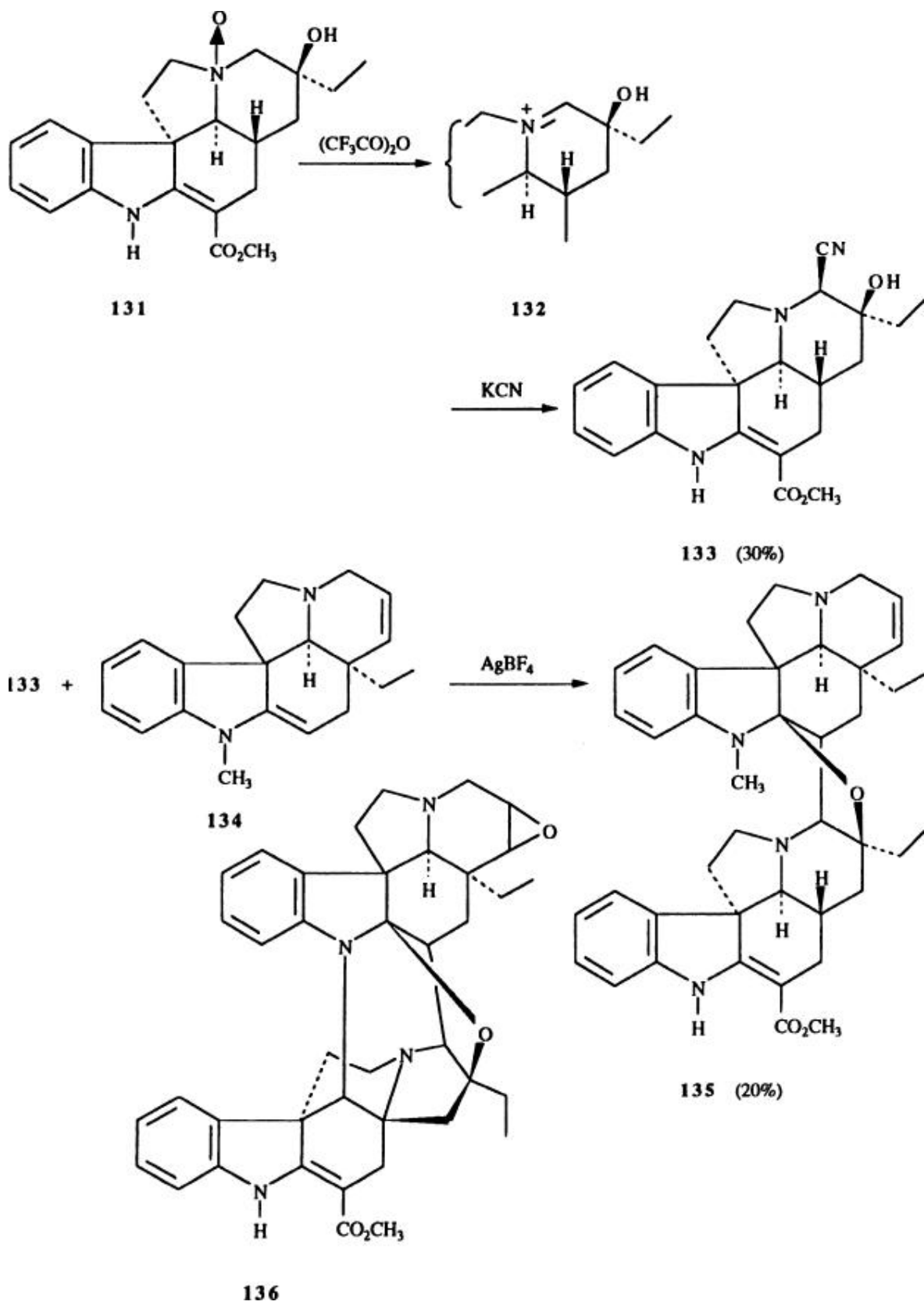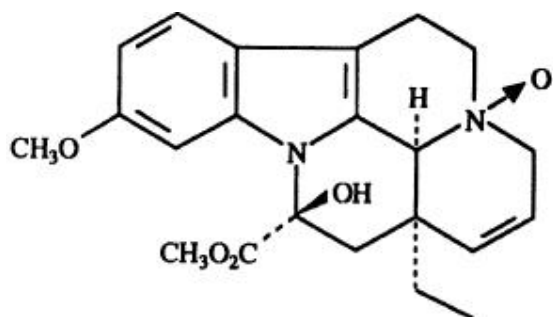
137
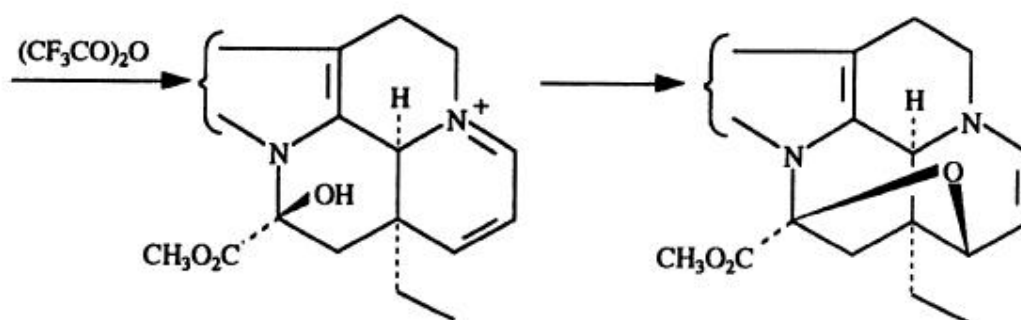
138 (20%)
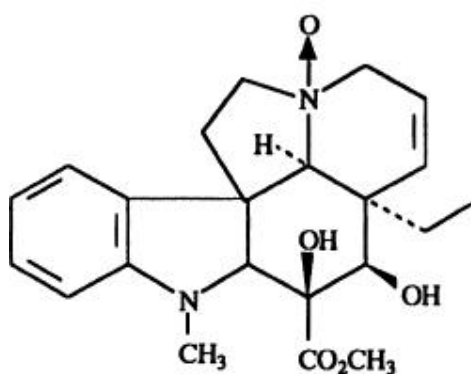
139
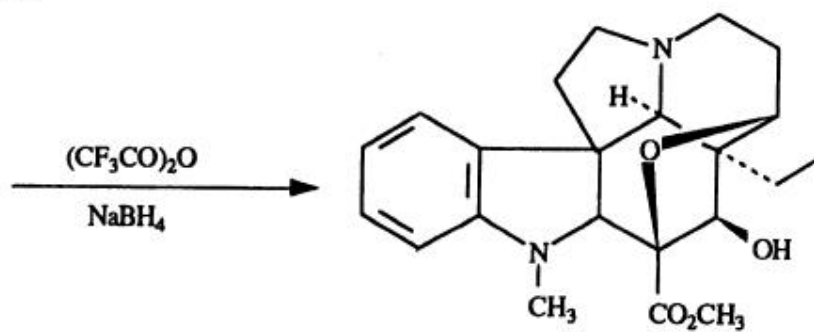
140 (50%)

direct route to the dihydro derivative **142** of mancunine (**143**). (128)
Cathenamine (**146**), a key intermediate in the biosynthesis of heteroyohimbine
indole alkaloids, (156, 157) is similarly produced via 1,4 addition of oxygen to
the conjugated iminium ion **145** derived from geissochizine *N*-oxide (**144**).
(158)

141

(CF₃CO)₂O

142   R= C₂H₅
143   R= CH=CH₂

144   145   146
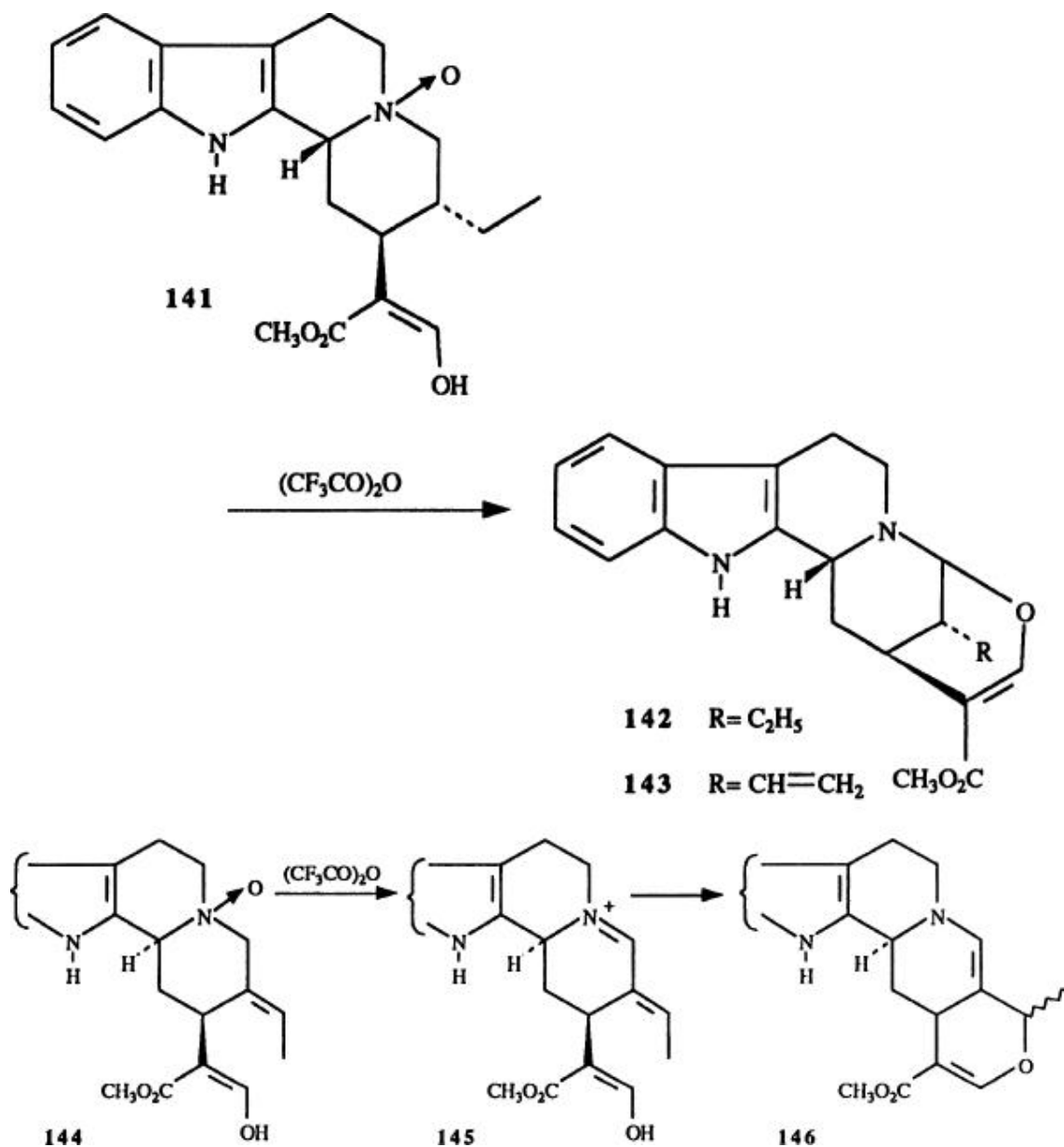
3.2.2.1.3. Enamines

Enamines can be obtained as the products of the Polonovski reaction of amine oxides, and in particular by reaction of piperidine *N*-oxides with acetic anhydride. This is primarily due to the fact that when acetate is the counterion the intermediate iminium ions are labile and readily tautomerize. The formation of enamines during the Polonovski reaction is also favored by the presence of a base. In fact, enamines are often obtained in high yield from the reaction of an *N*-oxide with trifluoroacetic anhydride in the presence of triethylamine or pyridine. Conversion of intermediate iminium ions generated under modified Polonovski conditions to enamine products can also occur during hydrolytic workup (**85** **87**).

147

(CH₃CO)₂O

C₅H₅N

148

149 (12%)

150

151 (-)
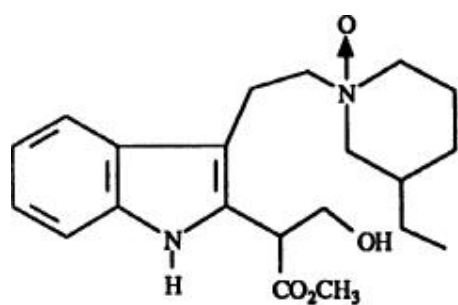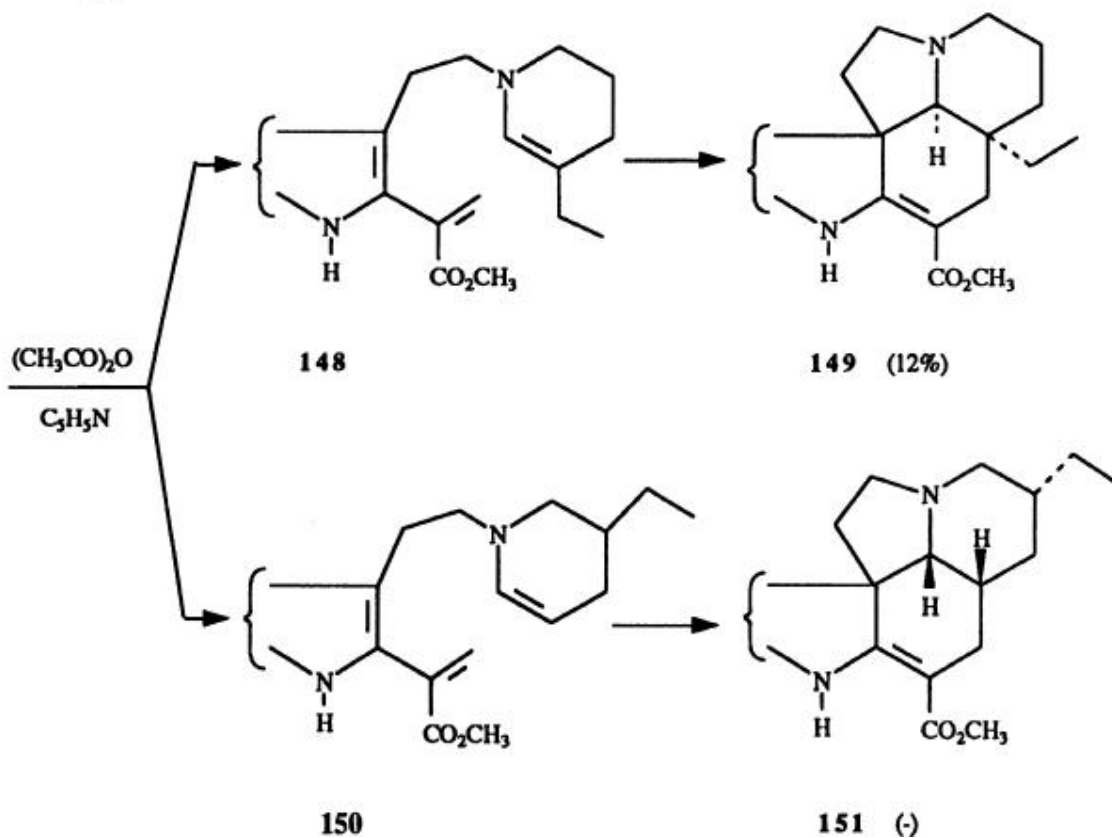
Synthetic applications wherein the Polonovski reaction has been employed to generate enamine intermediates include a biomimetic approach to the aspidosperma indole alkaloids. Reaction of the *N*-oxide **147** with acetic anhydride–pyridine provides a direct means for the in situ generation of the highly reactive dehydrosecodine intermediate **148**. (159) This species undergoes spontaneous cyclization to give vincadifformine **149** (12%) via an intramolecular Michael reaction followed by B/C ring closure. Ψ -Vincadifformine (**151**) is also produced in this reaction via enamine **150**, since a simple ethyl side chain in the starting *N*-oxide does not induce any appreciable directing effect on the iminium ion-forming step.

152   **153**

154   **(52%)**
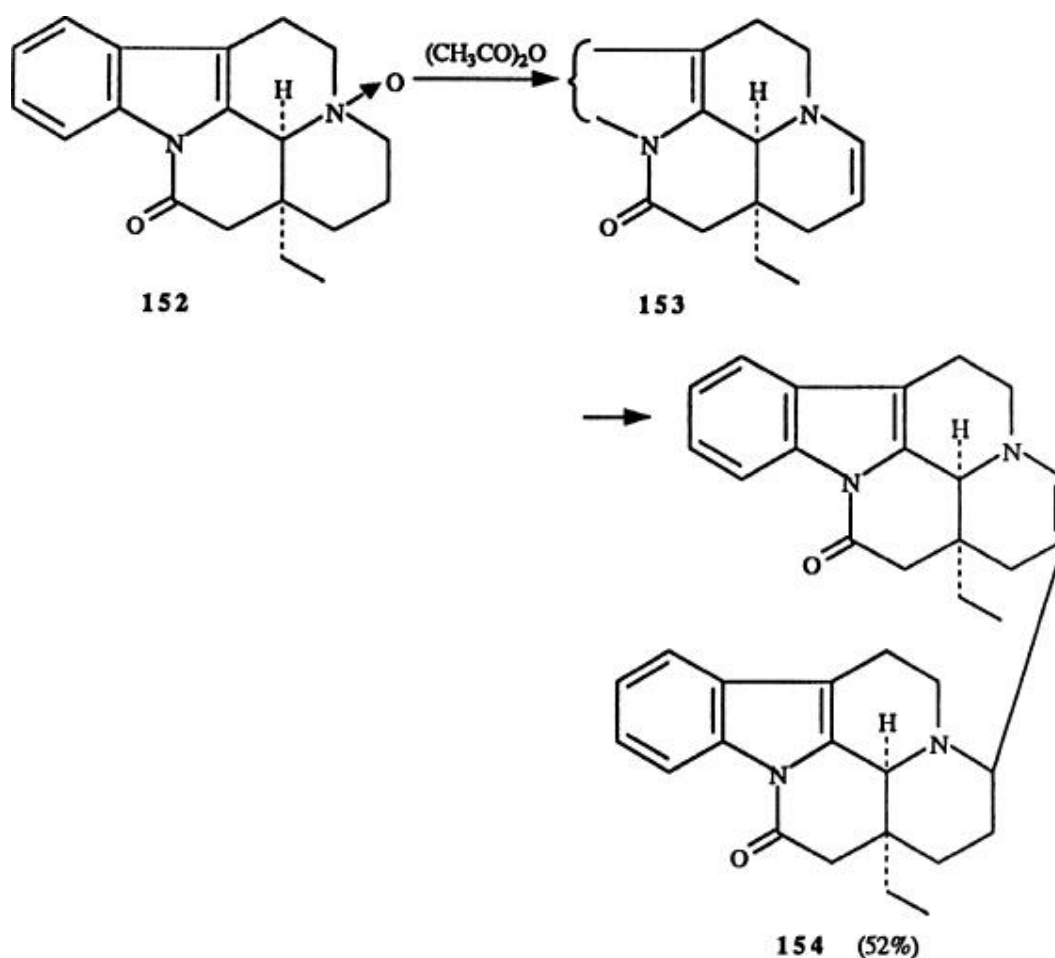
Reaction of vincaminone *N*-oxide (**152**) with acetic anhydride leads to formation of the enamine **153**. Under the mild acid conditions of the reaction this sensitive intermediate undergoes self-condensation to the crystalline

dimer **154** in 52% yield. (160) The reaction of the vobasine N-oxide derivatives **155** and **156** under Polonovski conditions is also oriented toward formation of the enamine product **157** when acetic anhydride or a mixture of acetyl chloride and sodium hydroxide is employed. (161) As is discussed later, the reaction of these two N-oxides with trifluoroacetic anhydride proceeds exclusively by cleavage of the C(5) $-$ C(6) bond. Formation of an enamine is similarly favored in a key step leading to the anticancer agent vinblastine by a judicious choice of acetic anhydride as the activating agent (see **220** **221**).

The Polonovski reaction solves the difficult problem of cleaving the glycoside bond linking an amino sugar to the 16-membered macrolide aglycones in leucomycin A_3 (**158**), carbomycin (**159**), tylosin (**160**), and rosaramicin (**161**). The idea is to generate an endocyclic enamine **162** under Polonovski

155 (20S)

156 (20R)

157 R= C_2H_5 (80-88%)

conditions (Eq. 20) so that the lone pair of electrons on nitrogen can assist in breaking the glycoside bond through a vinylogous β -elimination reaction.

The reaction of leucomycin A_3 N-oxide with acetic anhydride in refluxing chloroform leads to formation of the desired aglycone hemiacetal **163** in 10% yield, along with the secondary amide **164** (15%) and ketone **165** (30%). (162, 163) However, if aqueous workup is avoided, equal amounts of both the ketone

158 R= (MYCAM)

(MYCAR)

X= H, OH

159 R= MYCAM-MYCAR

X= O

160 R= MYCAM-MYCAR

161 R=

(20)

162

165 and enamine **166** are isolated. (164) Both of these products can be converted into hemiacetal **163** without difficulty.

(N-Oxide) **158** $\xrightarrow[\text{CHCl}_3,\text{ heat}]{(CH_3CO)_2O}$

163 (10%)

164 (15%)

166

165 (30%)

Likewise, the hemiacetal **167** is isolated in 10% yield by reacting tylosin *N*-oxide (**160**) with acetic anhydride in hot chloroform. (165) It is not surprising that formation of the amide and ketone products is suppressed and the yield of **167** significantly increased (65%) under modified Polonovski conditions (trifluoroacetic anhydride–pyridine). (166) Even higher yields (76%) of **167** are obtained by reacting the *N*-oxide of the desmycarose derivative of tylosin under these conditions. Remarkably, the yield for the cleavage reaction increases to 80% in the reaction of the tylosin *N*-oxide derivative **168** where the C-9 aldehyde function is replaced by a methyl group. (165)
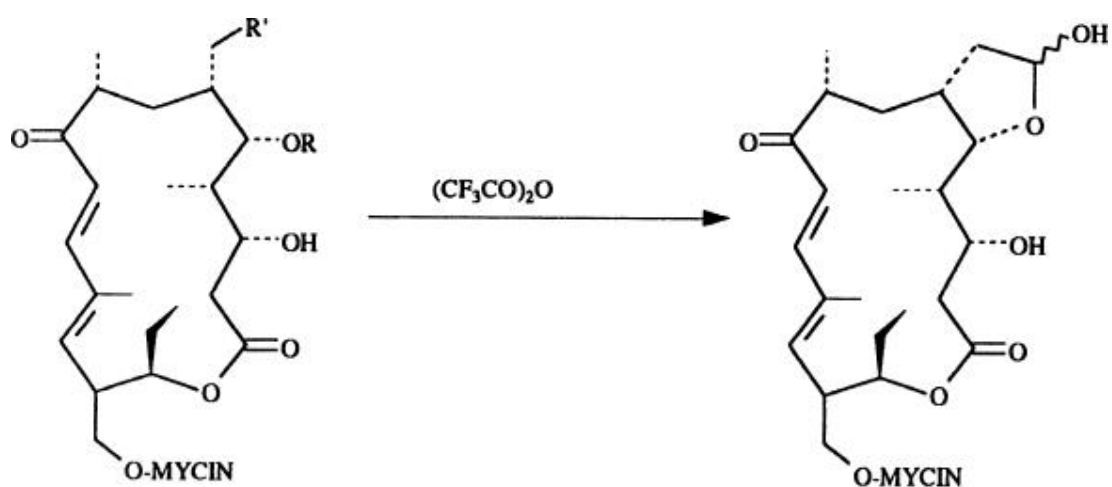
160 R = MYCAM(*N*-Oxide)-MYCAR

R' = CHO

167 (65%)

168 R = MYCAM(*N*-Oxide)

R'= CH$_3$
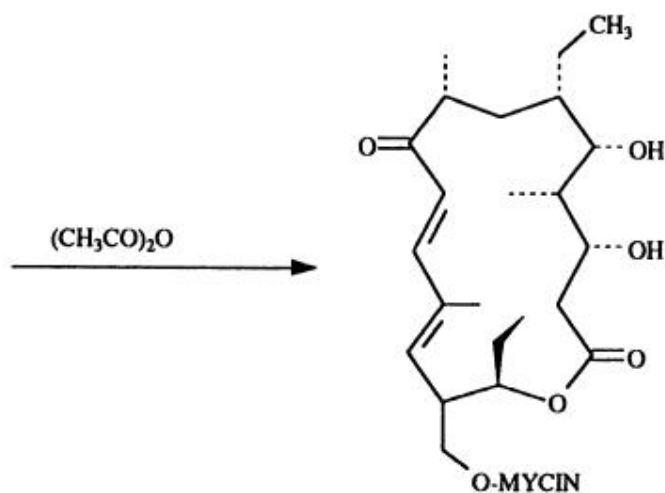
(80%)

Other examples of the Polonovski reaction in which enamines are obtained as products include the reactions of coccinelline (**71**) with trifluoroacetic anhydride followed by base, nupharidine (**66**) in acetic anhydride, morphine *N*-oxide (**69**) with acetyl chloride, and finally, *N*-oxide **91** of the steroid alkaloid conanine with either acetic or trifluoroacetic anhydride.

The enaminoketone **171** can also be prepared by a Polonovski approach involving either sequential addition of *m*-chloroperbenzoic acid, acetic anhydride, and triethylamine to a cooled solution of **169** in methylene chloride (120) or reaction of the *N*-oxide of enol silyl ether derivative **170** with trifluoroacetic anhydride. (167) Although the latter approach involves three distinct steps, the overall yield of **171** is markedly higher. Enaminones of this type can be employed in a variety of ways in synthesis. One technique for enhancing their reactivity toward Grignard and organocuprate additions is to convert them into the corresponding dihydropyridinium intermediates **172** by reaction with acetyl chloride at low temperature. (167-169)
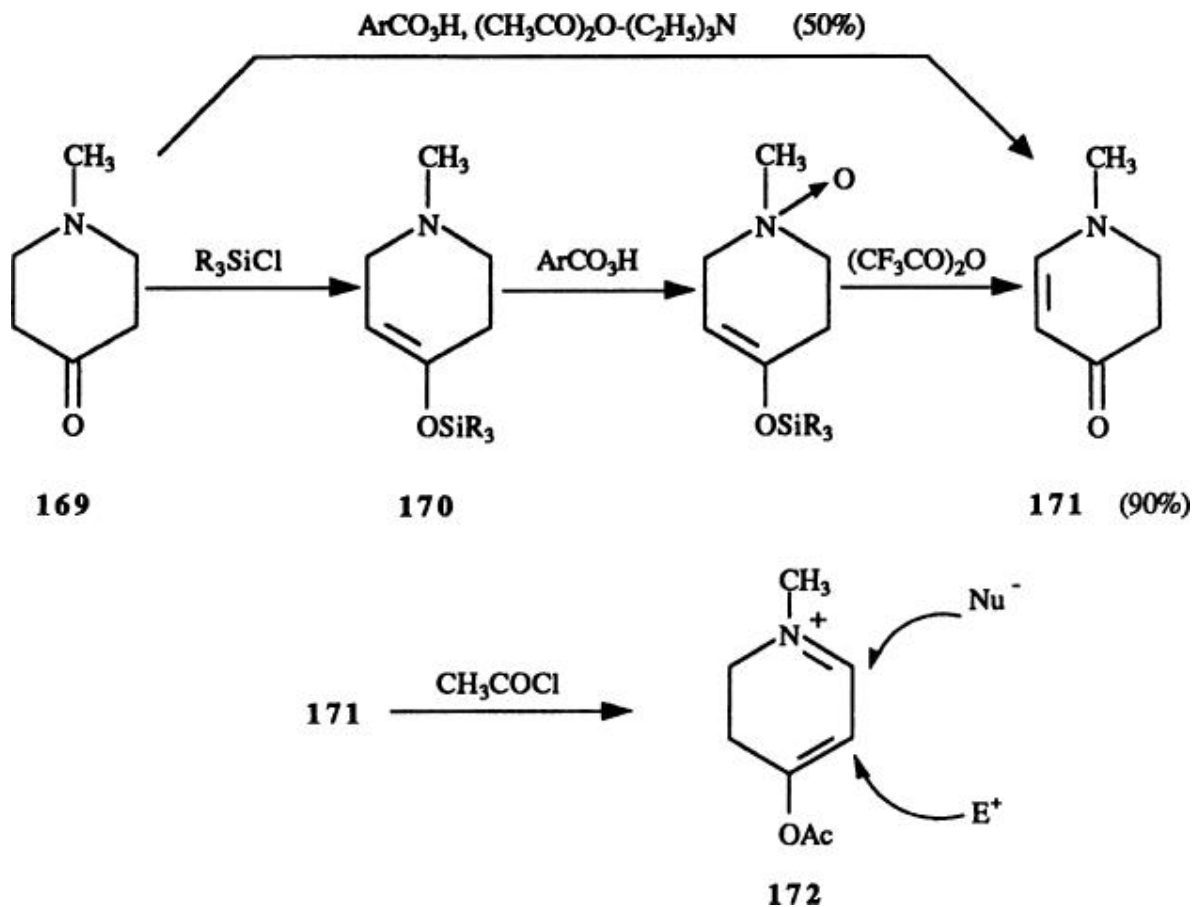
3.2.2.1.4. Pyrrole Ring Formation and Other Reactions of Five-Membered Rings

Although in cyclic systems studied to date the *N*-oxide function is for the most part incorporated into a six-membered ring system, there are several examples where pyrrolidine or dihydropyrrole *N*-oxides are the substrates. For instance, the reaction of amine oxides **173** and **174** with acetic anhydride at 0° provides a convenient route to the *N*-alkylpyrroles and *N*-alkylisoindoles **175** and **176**. (170, 171)
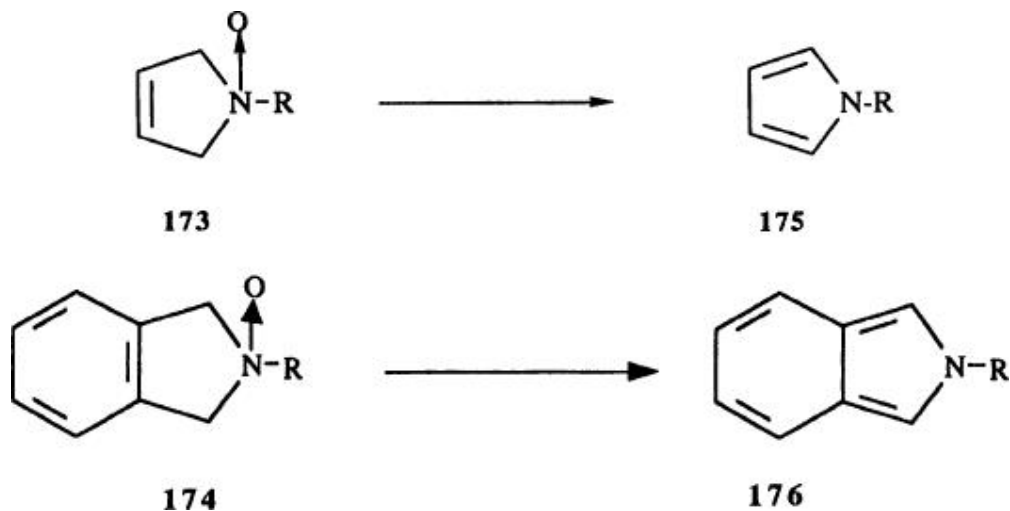
The mitosane *N*-oxide derivative **177** is similarily converted into the pyrroloindole derivative **178** in high yield upon reaction with acetic anhydride in chloroform. (172) The corresponding reaction of the 1,2-diacetoxy derivative **179** is more complex however, producing a mixture of compounds **180–185** (in addition to the parent tertiary amine), which apparently arise from iminium ion formation in all three possible directions. Indeed, in order to explain the formation of compound **185** it is necessary to invoke participation of the

177

(CH₃CO)₂O →

178 (73%)

179

$$\frac{(CH_3CO)_2O}{CH_3OH - CDCl_3}$$

180   R= OAc, R'= H   (9%)

181   R= H   R'= OAc (2%)

182   (25%)

183   R= CH₃ (20%)

184   R= H   (6%)

185   (18%)

186

187
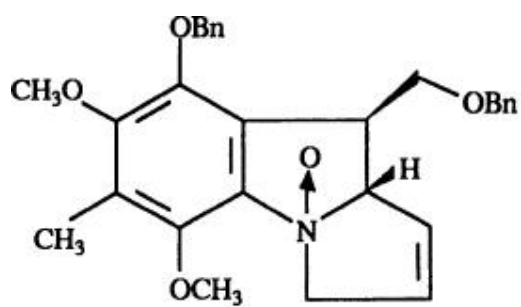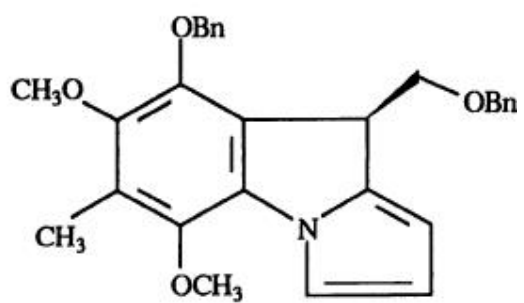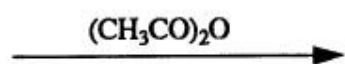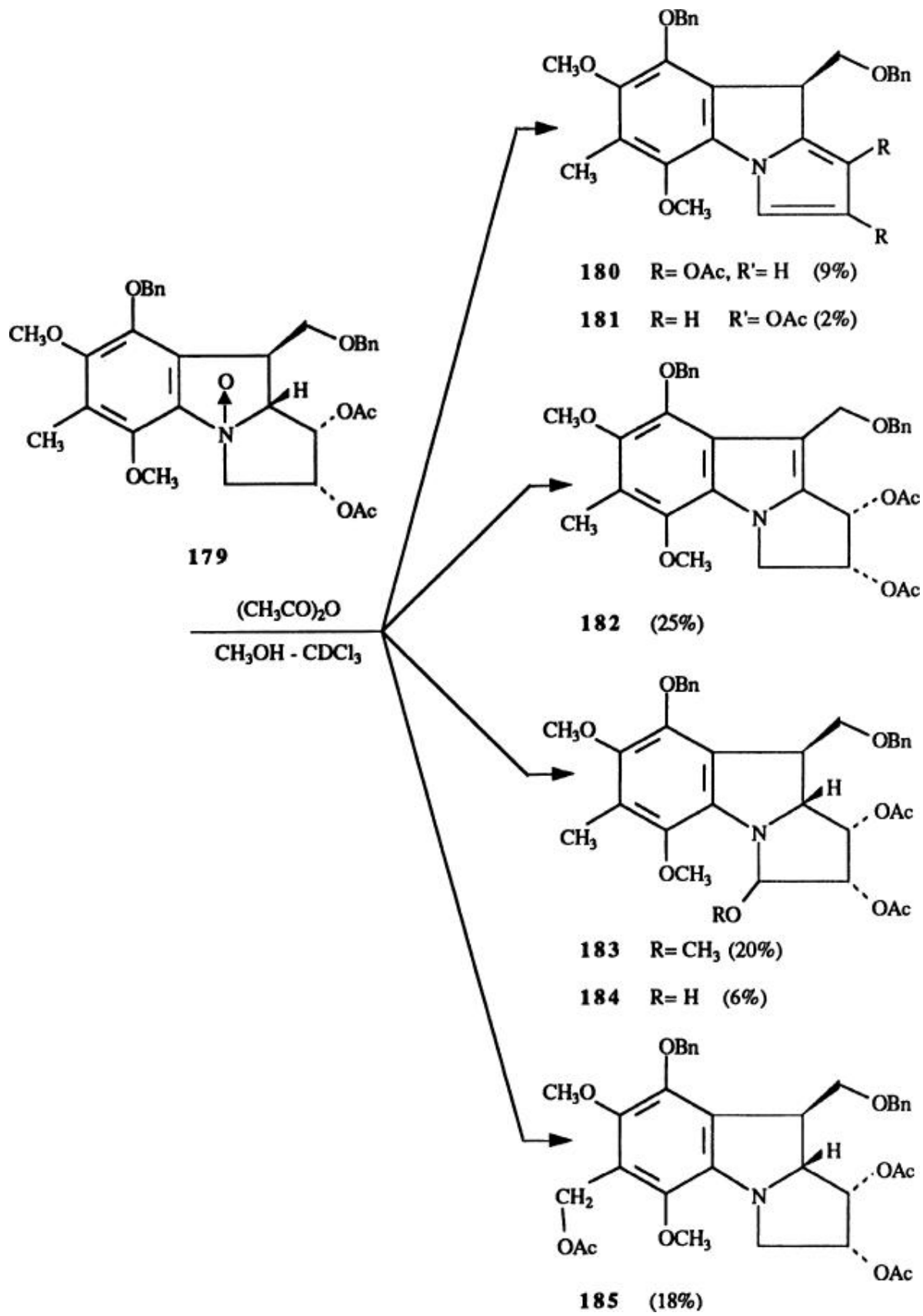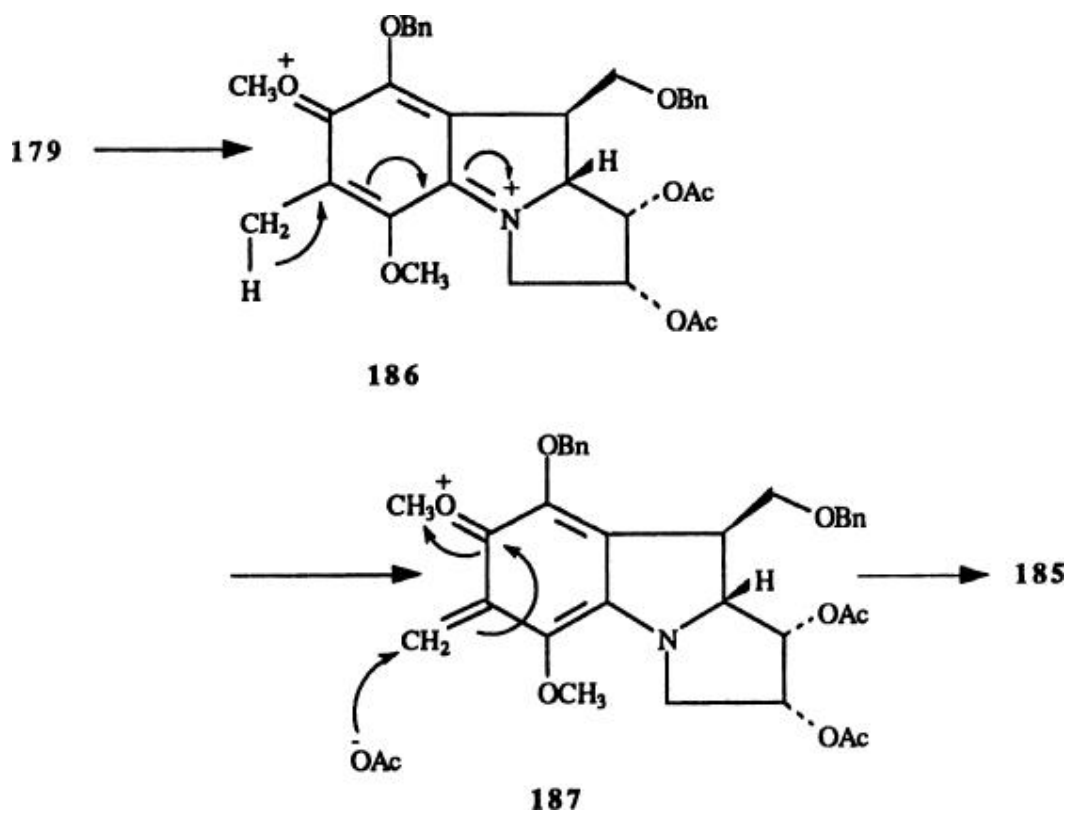
electrons on one of the methoxy groups in the cleavage of the N $-$ O bond of **179** and formation of the *p*-quinoid dication intermediate **186**. Rapid neutralization of the positive charge on nitrogen through loss of a C-11 methyl proton would then give **187**, which can rearomatize on reaction with acetate ion to yield the observed product **185**. If this mechanistic rationale is correct, the transformation of **179** to **185** represents the first example of a new manifestation of the Polonovski reaction.

The Polonovski reaction of a series of tropane *N*-oxide derivatives gives the norsecondary amides resulting from *N*-demethylation (Eq. 21). (2) Nicotine *N*-oxide (**188**) also gives the *N*-demethylated amide **189** in unspecified yield. (2)

3.3. Carbon–Carbon Fragmentation Reactions

As outlined in the section on mechanism, Polonovski reactions in which intermediate iminium ions are produced by fragmentation of the C α -carbon bond (Grob reaction; (46) Eqs. 3 and 8) are of considerable interest in synthesis since extensive modification in structure is achieved in a single operation. Not every *N*-oxide, however, can react in this manner. In fact, for this reaction mode to become operative, the C α -carbon bond to be broken must be both activated toward cleavage by an adjacent electron-donating center (double bond, aromatic ring, or heteroatom), and be oriented antiperiplanar to the N $-$ O bond.

(21)

188   189
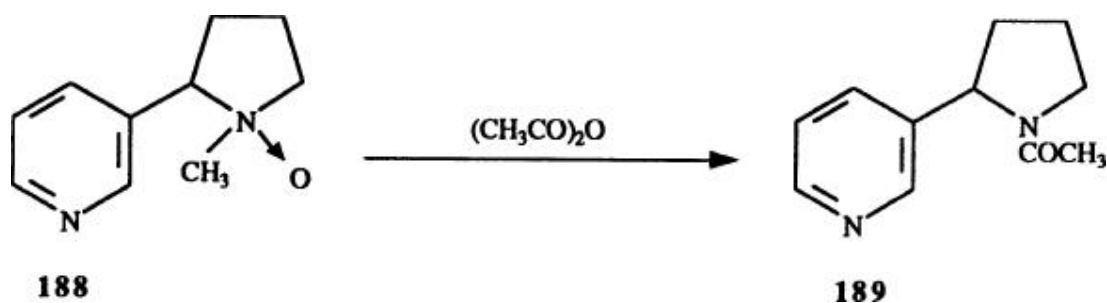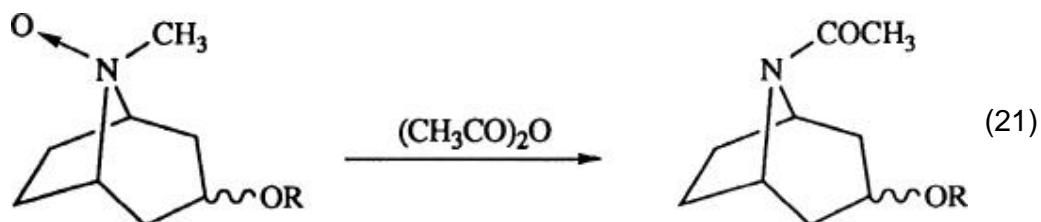
3.3.1.1. Synthetic Applications

The first example of this fragmentation reaction to be described is the conversion of the *N*-oxide **190** into the 17-oxa-D-homoandrostane derivative **192**. (173) The crucial step in this transformation involves the participation of the lone pair of electrons on oxygen in the departure of trifluoroacetate ion from the *O*-acylimonium salt intermediate **191**. The decarboxylation of the *N*-oxide acid derivative of **61** mentioned earlier is also an example of this heteroatom-assisted fragmentation reaction.

190   X = O

191   X = O$_2$CCF$_3$ | (CF$_3$CO)$_2$O

192
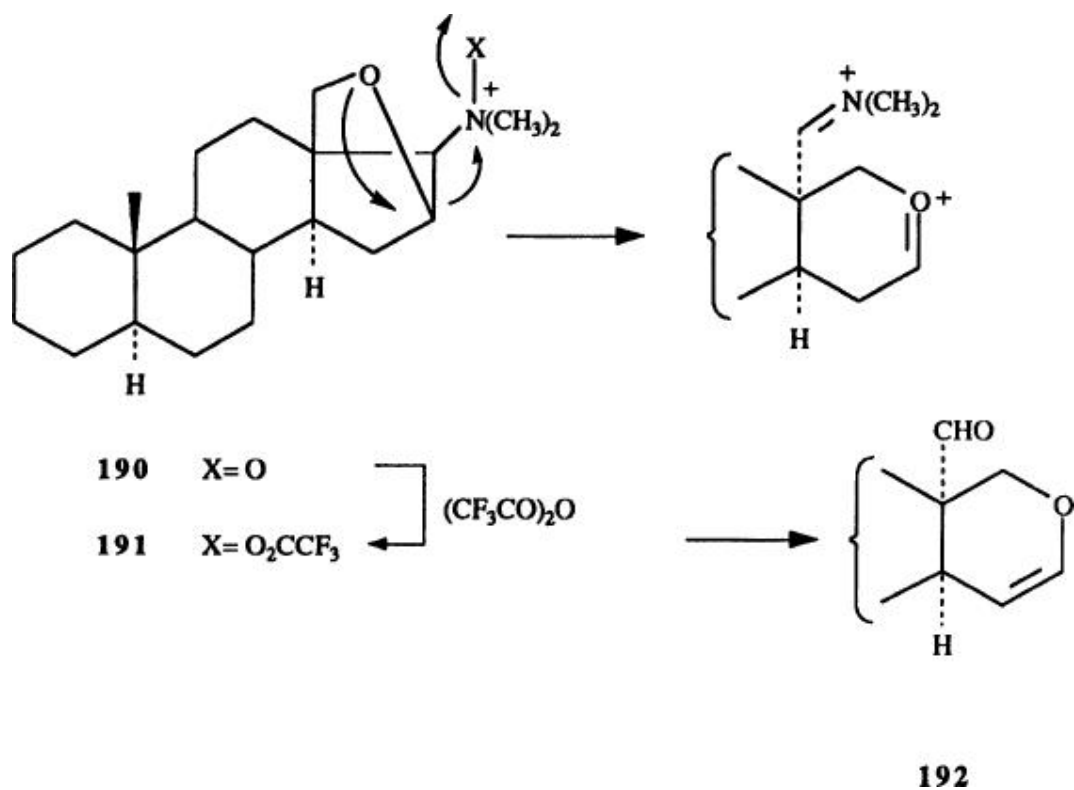
In certain substrates such as the $\triangle^{5,6}$,-steroidal *N*–oxide **193**, carbon $-$ carbon and carbon $-$ hydrogen bond-breaking processes occur competitively (compare with the reaction of **44**). (34) It is important to note that whereas the elimination reaction leading to iminium ions **194** and **195** (detected by NMR) is base-dependent $(CF_3CO_2^-)$, the carbon–carbon fragmentation reaction producing **196** is not. This latter transformation can thus be made to predominate if one carries out the reaction in acidic media.
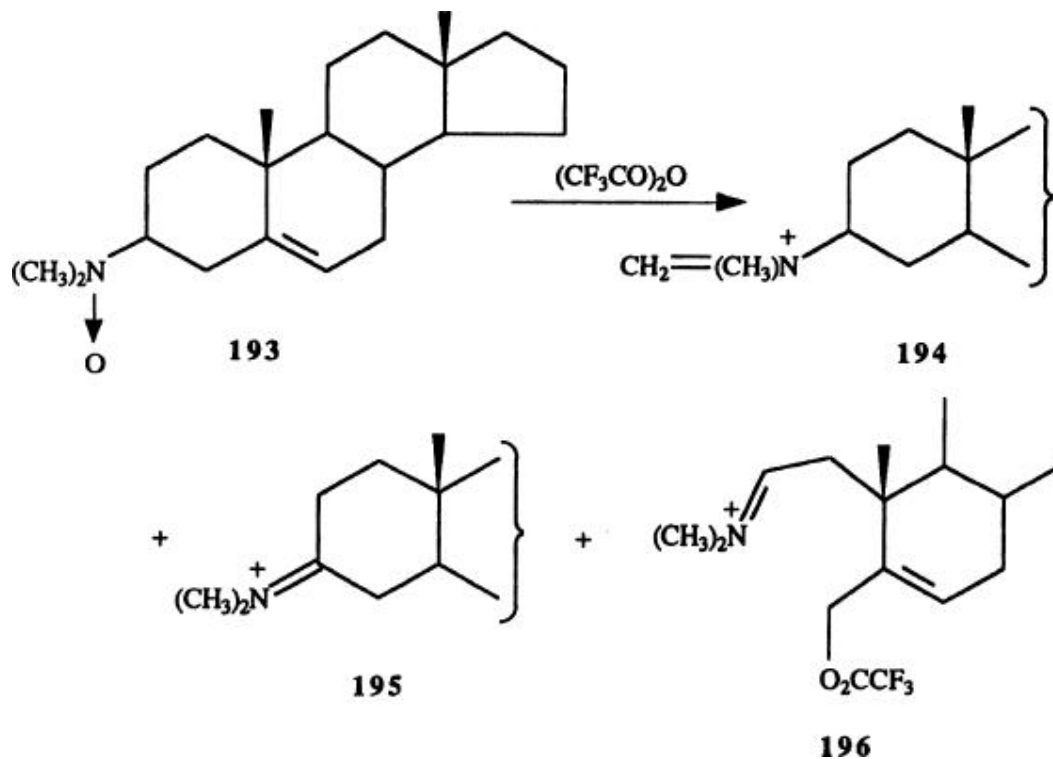
Structurally flexible phenethylamine-type *N*-oxides also undergo carbon —
carbon bond fragmentation under Polonovski–Potier conditions as illustrated
by the reaction of *N,N*-dimethyltryptamine *N*-oxide (**197**), wherein cleavage of
the side chain is facilitated through participation of the electrons on the indole
nitrogen. (174)

The ease with which *N*-oxide **197** undergoes fragmentation implies that the in
vivo equivalent of this reaction may be important in the biosynthesis of certain
indole alkaloids including uleine (**198**), apparicine (**199**), ellipticine (**114**), and
olivacine (**126**), whose derivation from tryptophan is not immediately obvious.
(122) The transformation of stemmadenine *N*-oxide (**200**) to vallesamine (**201**),
a prototype alkaloid to apparicine, suppports this hypothesis. (175)

Another example of this rearrangement, which may also mimic in vivo
processes, involves transformation of the vobasine derivatives **155**, **156**, and
202 to the ervatamine-type indole alkaloids **203–205**. (176) Indeed, reaction of
dregamine *N*-oxide (**155**) with trifluoroacetic anhydride followed by
borohydride

197

$+\quad CH_2 = \overset{+}{N}(CH_3)_2$
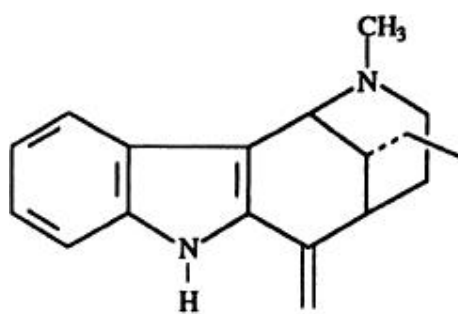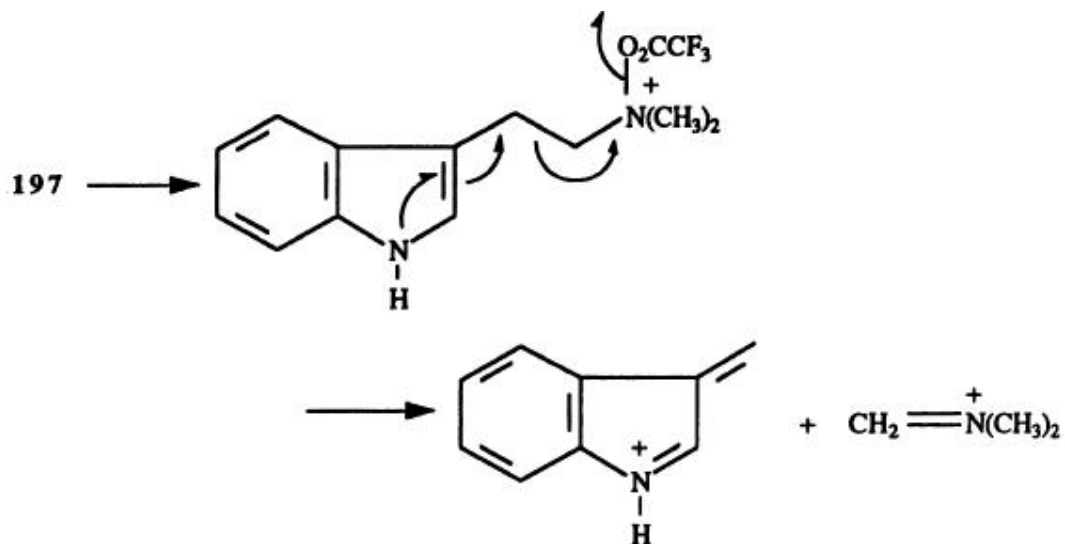
198
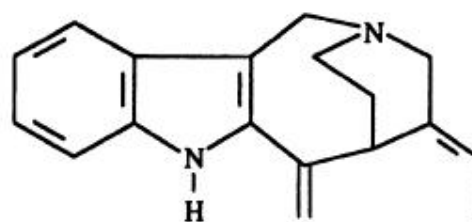
199
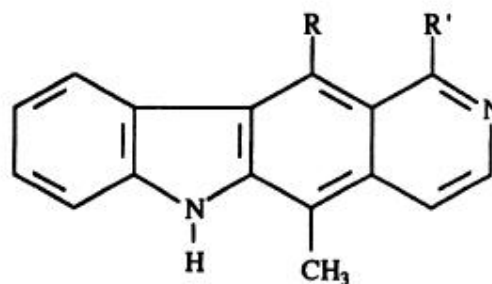
114   R = CH$_3$, R'= H

126   R = H   R'= CH$_3$

reduction produces (20S)-epiervatamine (**203**) in 90% yield. Tabernaemontanine N-oxide (**156**) is likewise converted to ervatamine (**204**) in good yield (50%). Unfortunately, dehydroervatamine (**205**) is obtained in only low yield from N-oxide of **202** as a result of iminium ion formation in the direction of the C-20 ethylidene side chain.

That fragmentation of the C(5) — C(6) bond, as opposed to competitive

200

201 (37%)
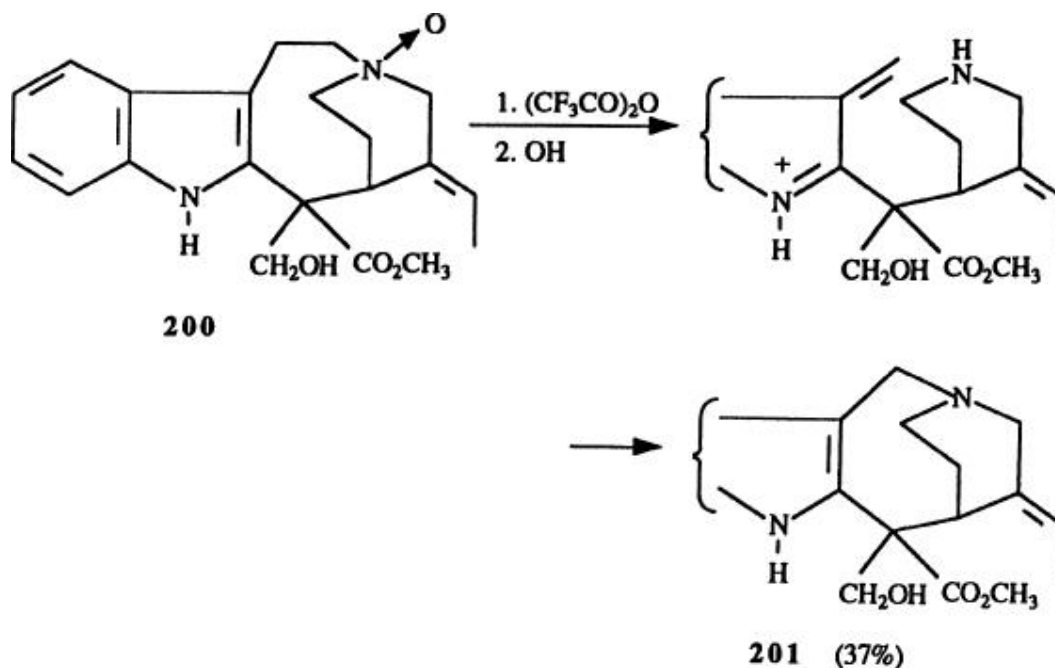
elimination of a β hydrogen, in these *N*-oxide reactions is primarily dependent on the nature of the leaving group on nitrogen is elegantly demonstrated by comparison of the reaction of **155** with trifluoroacetic anhydride, which produces **203**, and with that using trifluoroacetic–acetic anhydride, which gives **157**. In both reactions trifluoroacetate is liberated as the counterion in the initial reaction of the *N*-oxide with the anhydride.

Without doubt the most relevant and spectacular application of the modified Polonovski reaction is the development of the first successful method for the preparation of the dimeric indole antitumor agent vinblastine (**206**) and its congeners leurosine (**207**), vincristine (**208**), and leurosidine (**209**). These clinically important compounds have been employed with considerable success over the last 30 years in the treatment of various forms of leukemia, Hodgkin's disease, and solid tumors.

The problem presented in the synthesis of these compounds is to couple the two monomeric units in such a way that the lower vindoline moiety approaches a precursor to the upper iboga unit from the correct, that is, alpha direction. This is achieved under Polonovski–Potier conditions by choosing catharanthine *N*-oxide (**211**) as the precursor to the top portion of the molecule. Thus, on reaction of *N*-oxide **211** with trifluoroacetic anhydride at >–50° in the presence of vindoline (**210**) followed by treatment with sodium borohydride, the natural configuration-coupled product **212** is obtained in 50% yield along

with only minor amounts of **213**. (177-181)

Although the precise mechanism of the coupling reaction is not thoroughly established, one can visualize the formation of dimer **212** as arising by initial fragmentation of the C(16) — C(21) bond of **211** followed by condensation of vindoline with the more accessible alpha face of the iminium ion **214**. The impact of the Polonovski approach in this area is emphasized by the fact that

MCPBA
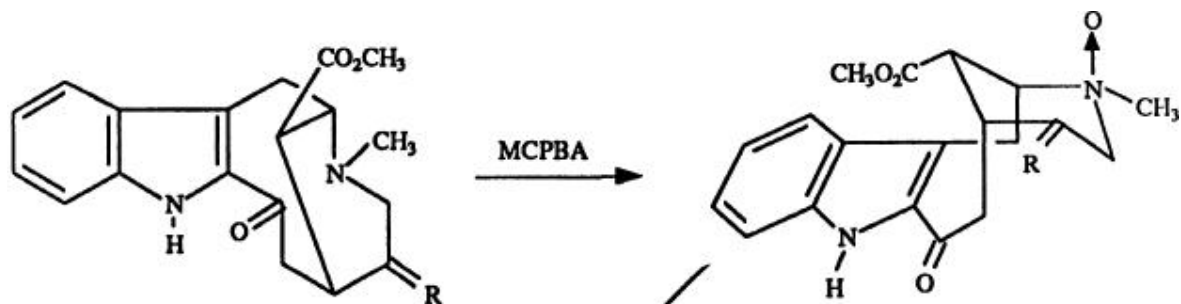
$(CF_3CO)_2O$

$(CF_3CO)_2O$

155   R = H, C_2H_5 (20S)

156   R = H, C_2H_5 (20R)

202   R= CHCH_3

$OCOCF_3$

NaBH_4

157
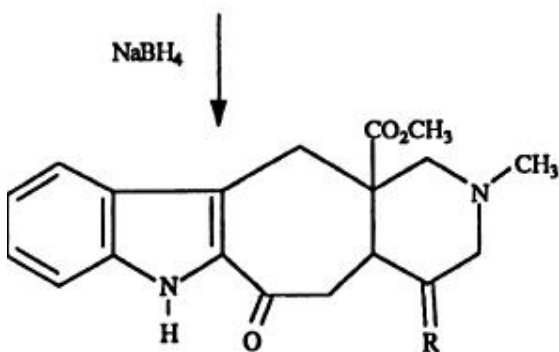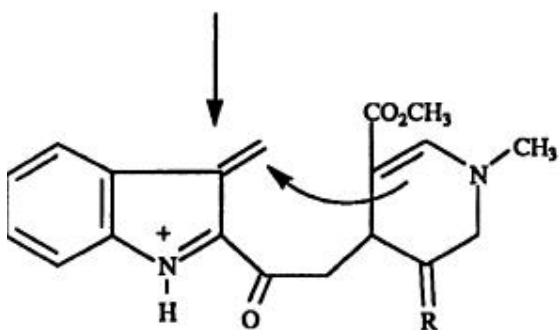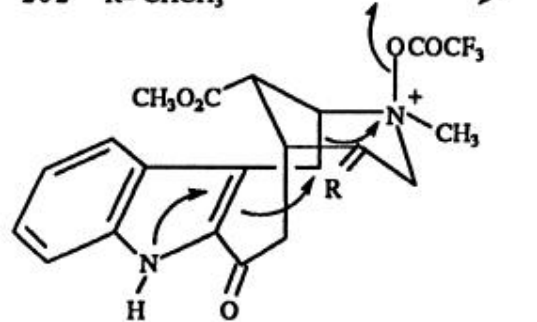
203   R= H, C_2H_5 (20S)

204   R= H, C_2H_5 (20R)

205   R= CHCH_3

		R	R'	R"	R'''
	206	H	C_2H_5	OH	CH_3
	207	—O—		C_2H_5	CH_3
	208	H	C_2H_5	OH	CHO
	209	H	OH	C_2H_5	CH_3

211

214

210 (VIND)

212 (50%)

213 (10%)
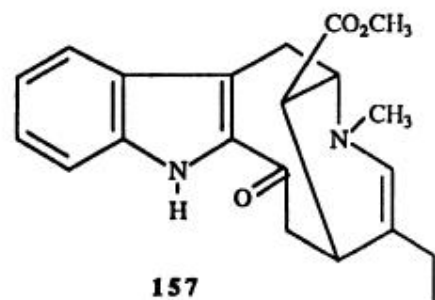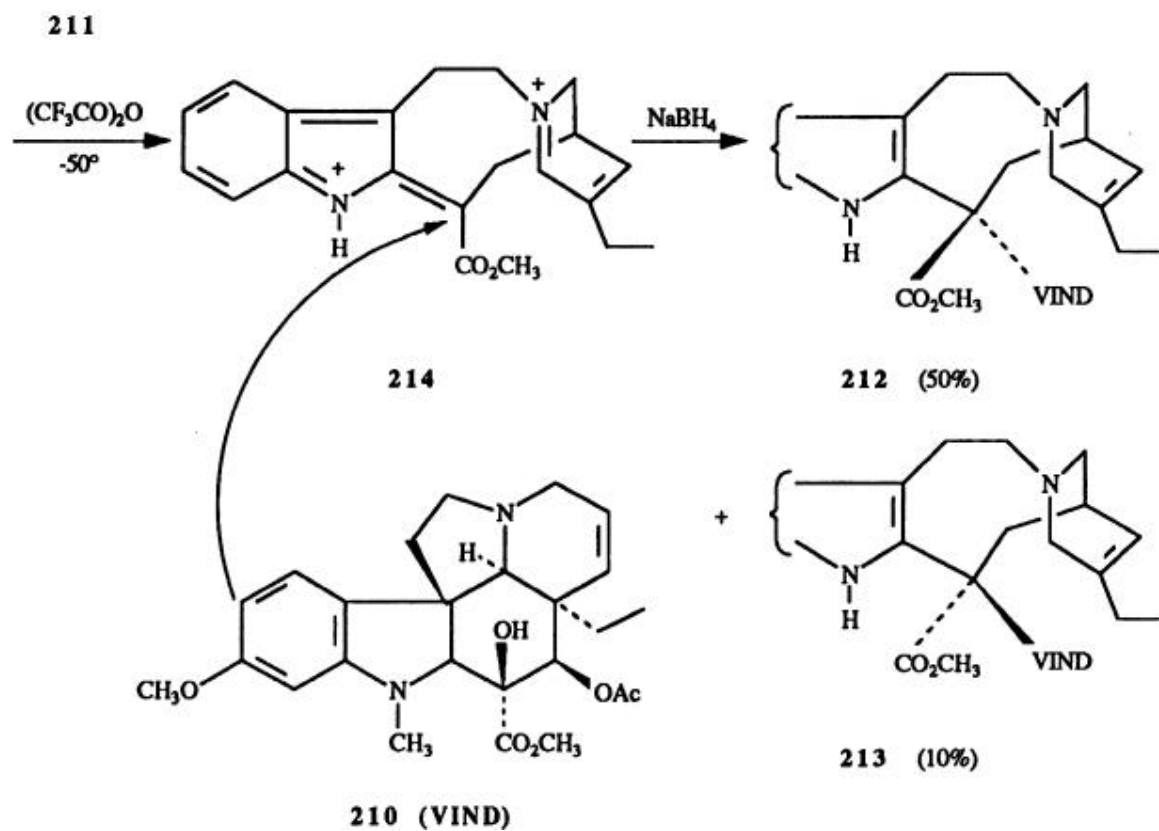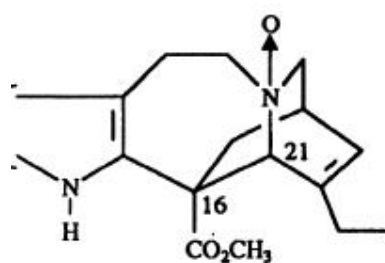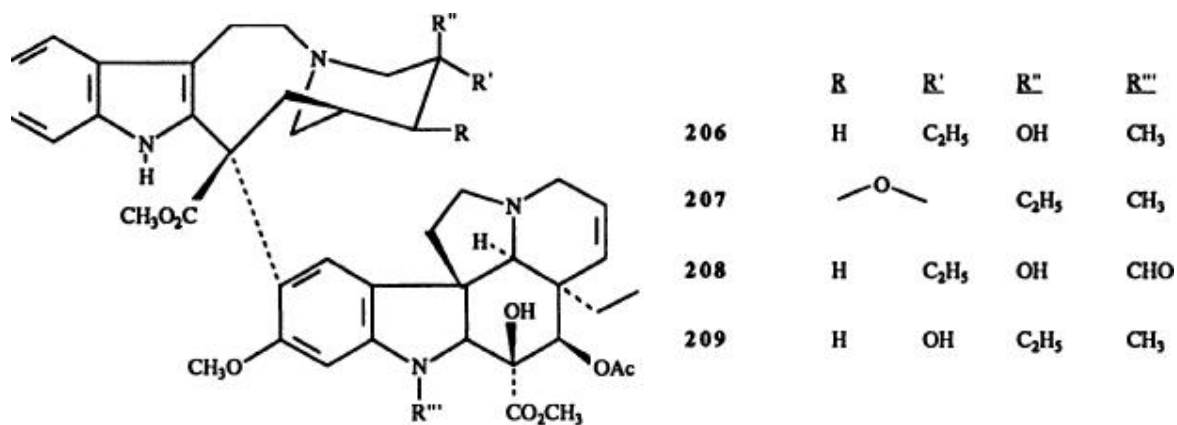
all other attempts to couple vindoline with *seco*-16,21-derivatives of catharanthine lead invariably to formation of the unnatural dimer **213**. (182-187) The biomimetric Polonovski approach (186, 187) was subsequently demonstrated in vivo. (188-194)

Since the C-15 and C-20 positions are functionalized in the natural compounds **206–209**, coupling studies have also been made with the appropriately functionalized catharanthine *N*-oxide derivatives **215–218**. (187, 195-202) The yields of the natural products are poor, however, because of a competing reaction involving fragmentation of the C(5) $-$ C(6) bond and formation of compounds such as **219**. The presence of the double bond in the piperidine ring is thus

215

216

217

218   219 (62%)
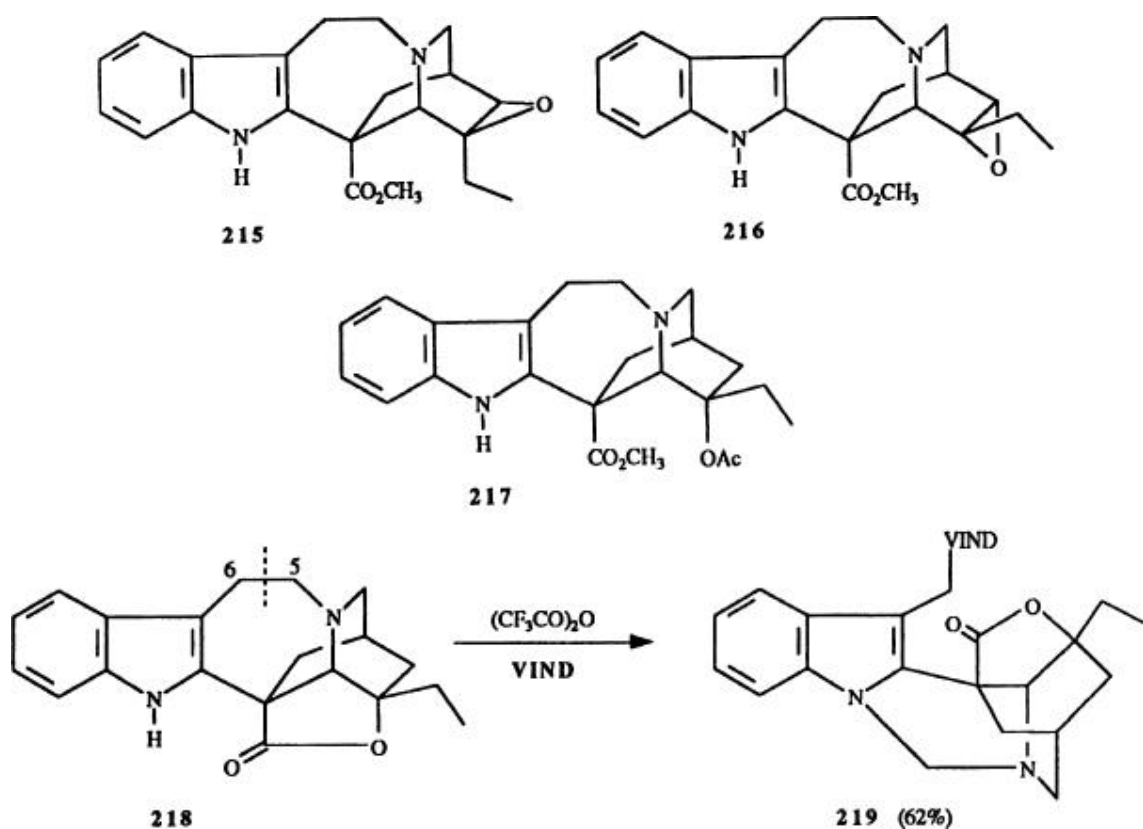
seen to be important in directing the reaction to the desired result. The subtle nature of these reactions is further emphasized by the fact that fragmentation of the C(5) $-$ C(6) bond of **211** is also favored under conventional Polonovski conditions with acetic anhydride. (203)

Elaboration of anhydrovinblastine (**212**) to the vinblastine alkaloids is the most efficient approach for accessing those materials. (204, 205) To arrive at vinblastine a second Polonovski reaction is performed with the *N*-oxide **220**. In this instance acetic anhydride is used to favor formation of the enamine **221**.

Treatment of this fragile intermediate with thallium (Tl-III) acetate followed by borohydride reduction gives **206**, whereas reaction with osmium tetroxide gives leurosidine (**209**).

212 → 1. H₂/Pd-C 2. ArCO₃H

220

1. OsO₄
2. NaBH₄

209

(CH₃CO)₂O →

221

1. Tl(OAc)₃
2. NaBH₄

206
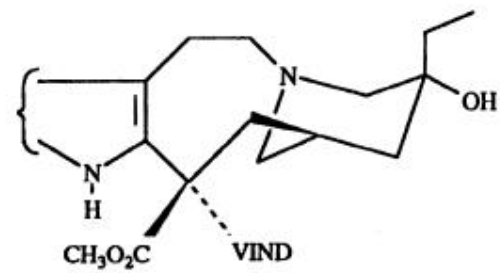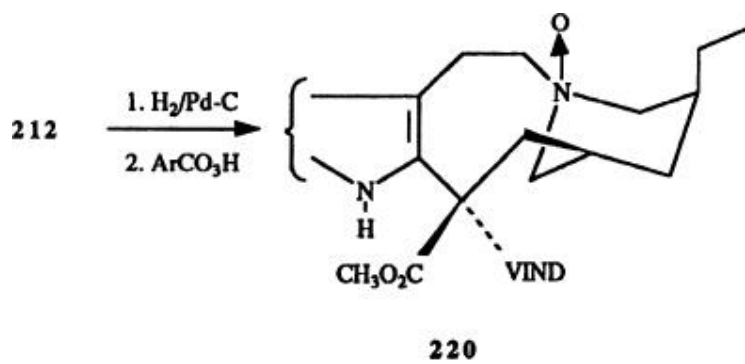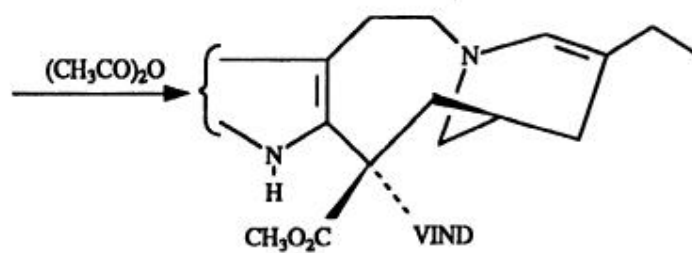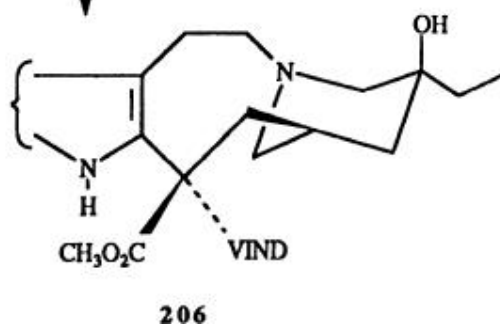
The synthetic antitumor agent *nor*-anhydrovinblastine (**222**) (Navelbine) is also prepared from anhydrovinblastine by reaction of its *N*-oxide under modified Polonovski conditions. (206, 207)

222 (27%)
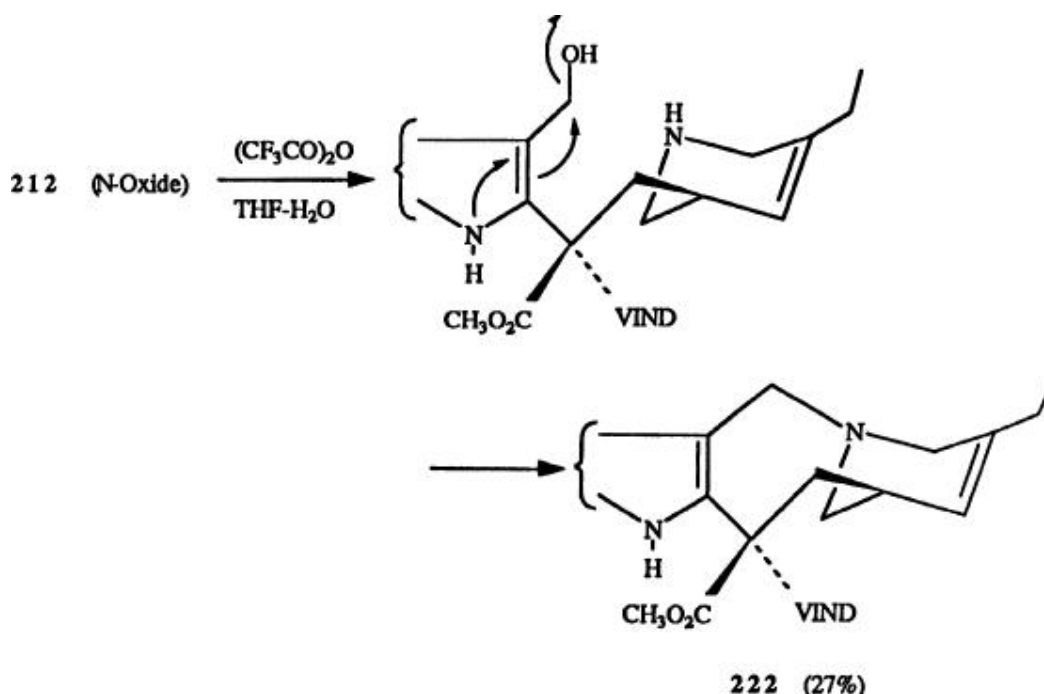
3.4. Other Reactions

In two instances reaction of an amine oxide with acetic anhydride triggers a process in which the amine oxide nitrogen acts as a leaving group and the C α — N bond is cleaved (Eqs. 22 and 23). (208, 209) Interestingly, these reactions occur to the exclusion of the Polonovski pathways, that is, elimination of the benzylic α hydrogen or fragmentation of the phenethylamine chain.

Quinuclidine *N*-oxide **223** undergoes an anomalous reaction on treatment with trifluoroacetic anhydride since formation of the bridgehead iminium ion is precluded (210) (see also ref. 29). Although the key step in the formation of **225** is viewed by the authors to involve transfer of the *N*-oxide oxygen in **223** to the C-2 carbon of indole via an intramolecular S_N2-like displacement of the quaternary nitrogen center from oxygen, the possibility that this transformation occurs by an intermolecular mechanism should not be neglected.

In the reaction of dimethylaniline *N*-oxide (**226**) with acetic anhydride in

chloroform a mixture of compounds **227** and **228** is formed. (33) The ratio of the rearranged phenol **227** to dimethylated product **228** varies with solvent polarity, compound **227** being formed preferentially (84%) in water, and **228** (85–95%) in tetrahydrofuran. Ionic mechanisms are involved in both these processes, (33, 211) although at higher temperatures radical species are also generated. (27, 28, 50-56)

In a number of reactions the Polonovski products are obtained directly on reaction of a tertiary amine with peracids. This can happen when the peracid

(22)

(23)

223

$(CF_3CO)_2O$

OAc

224

225 (40%)

226

1. $(CH_3CO)_2O$
2. OH^-
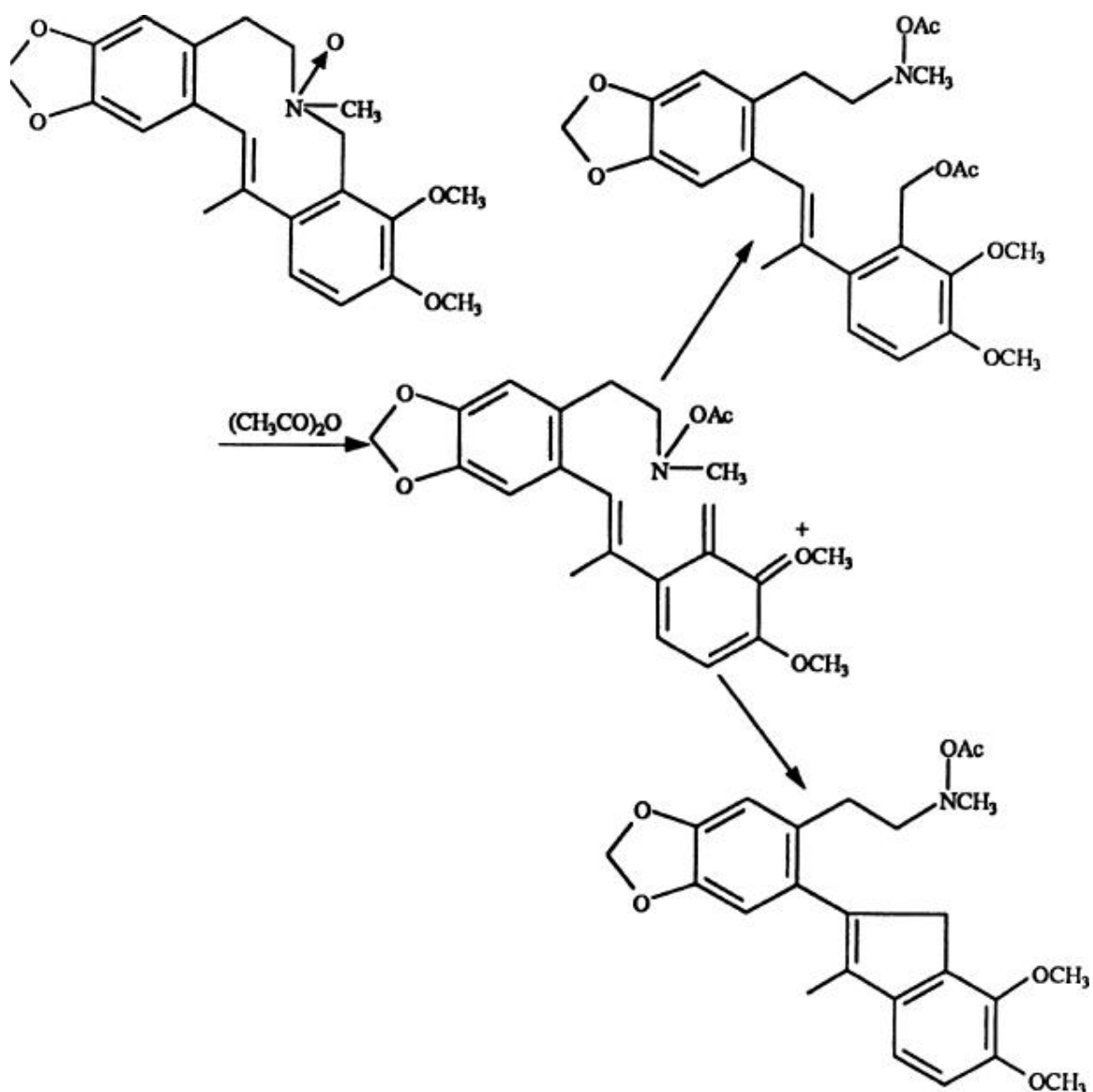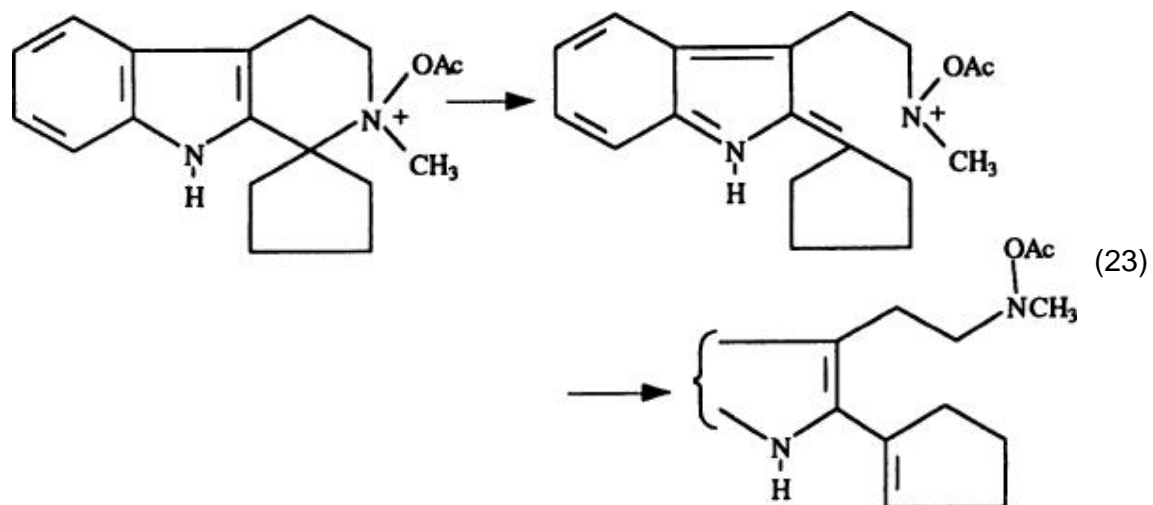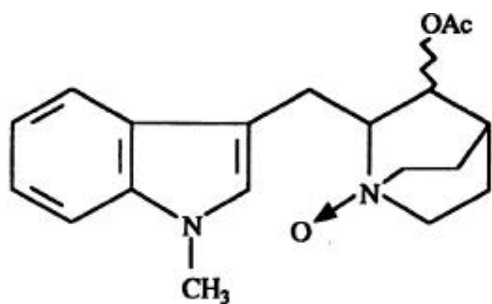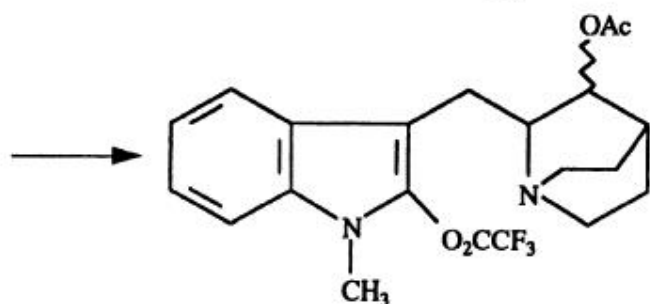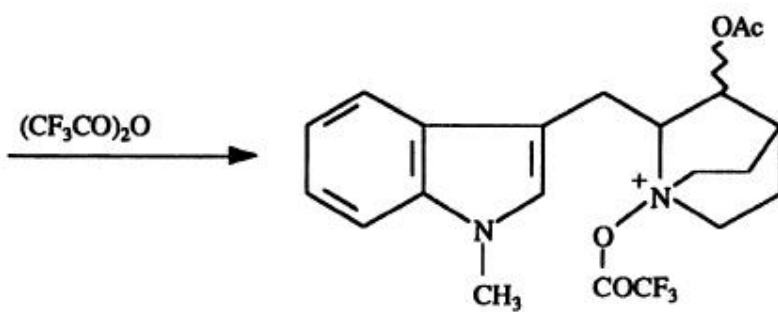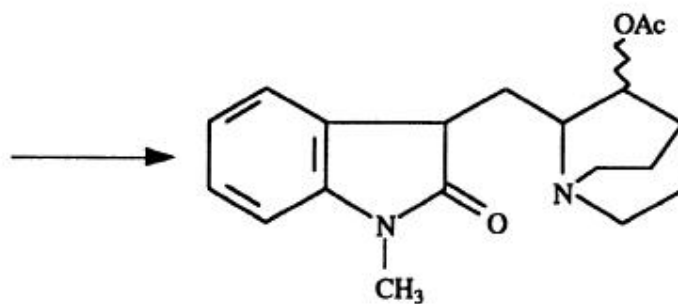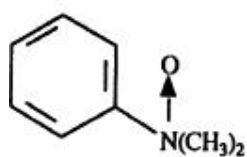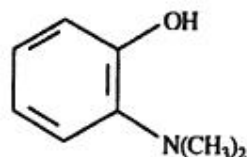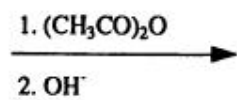
227

+
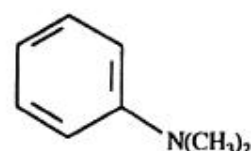
228

is present in excess, in which case it acts as both the oxidizing and activating agent, or when an appropriately positioned acid or amide group which can act as an internal activator is present in the *N*-oxide. The latter situation is illustrated by the efficient conversion of compound **229** to the benzimidazole **230**. (212) Support for the intramolecular mechanism of this reaction comes from the observed formation of the unusually stable cyclic lactone **232** from **231**.
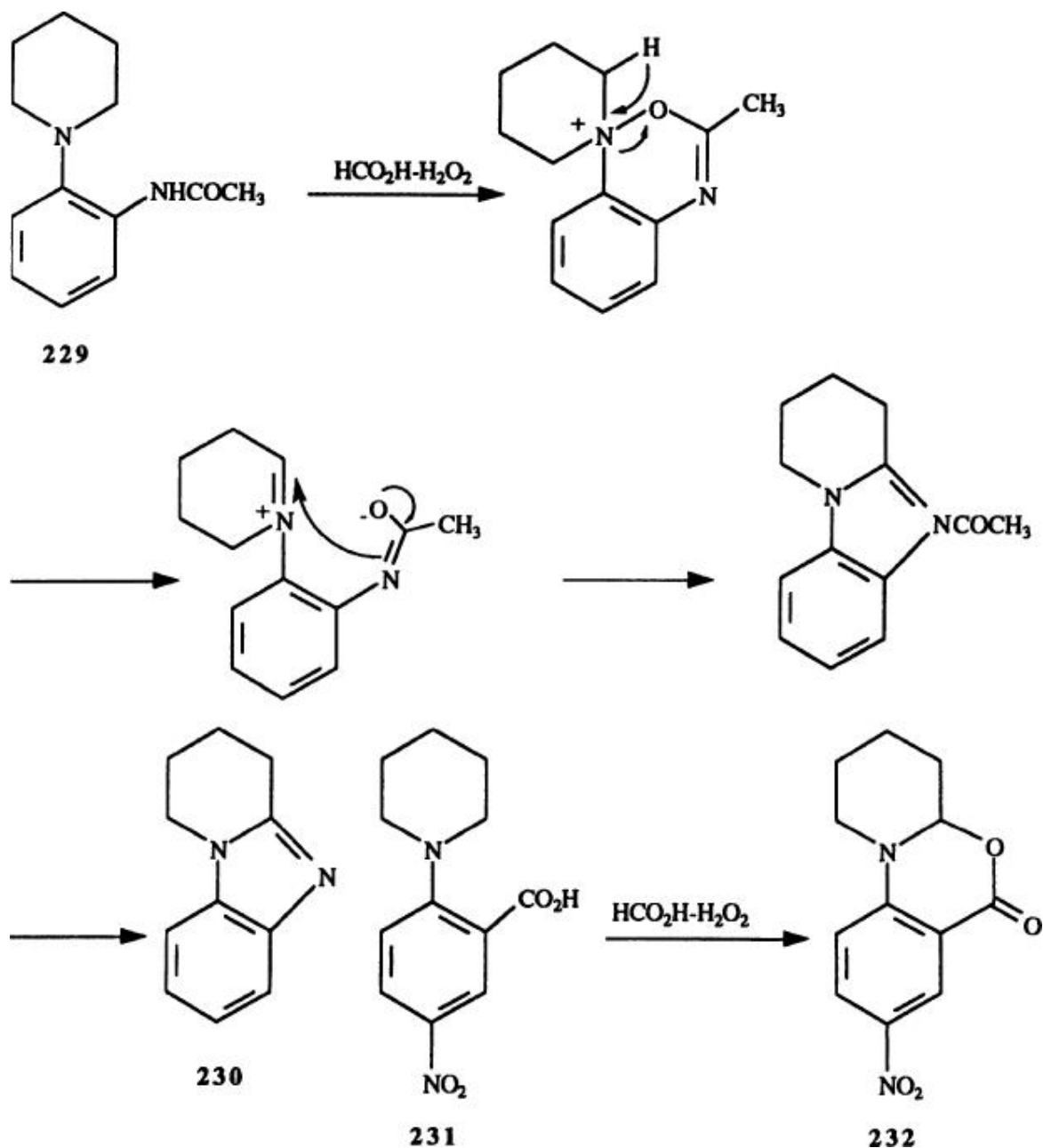
Excess peracid transforms dehydroaspidospermine (**233**) and vincadifformine (**234**) to the pentacyclic products **235** and **236**. (213, 214) These deep-seated rearrangements are believed to involve an initial Polonovski reaction, which generates the iminium ion **237**, followed by fragmentation of **237** ® **238** and subsequent intramolecular cyclization. In support of this mechanism, the *N*-oxide of **233** is converted into **235** in 8% yield on reaction with trifluoroacetic anhydride and dilute hydrochloric acid. (213) The 1,3 dipoles **240a,b**, precursors to the tropolones **241**, are similarly obtained on reaction of the tetrahydropyridines **239a,b** with *m*-chloroperbenzoic acid, (215, 216) and the $\triangle$ ^{2}-piperideines **242a–c** are obtained from the piperidine derivatives **243a–c**. (217) The yields of these reactions are good since a considerable driving force exists for product formation.

Disubstituted nitrones, like heteroaromatic *N*-oxides, react with acetic anhydride to produce *O*-acetyl imidates by an addition–elimination mechanism (Eq. 24). Hydrolysis of the product **245** provides ready access to the corresponding amide **246**. Although there are certain resemblances between the mechanism of the nitrone reaction and that for the Polonovski reaction, they

233

237

238

235

234

236

239 a R = OCH$_3$

240

b R = C$_3$H$_7$-i

HC≡CCO$_2$CH$_3$

241

ArCO$_3$H

242 a R = (CH$_2$)$_2$COCH$_3$

243

b R = CH$_3$

c R = (CH$_2$)$_2$CCOCH$_3$
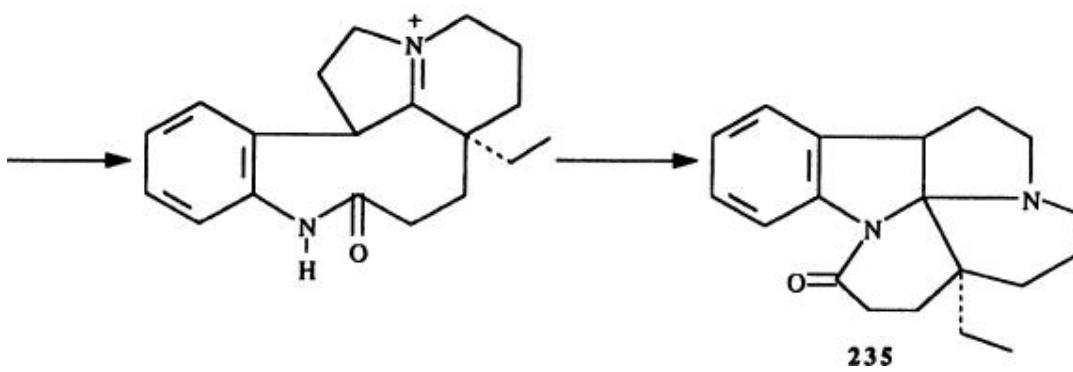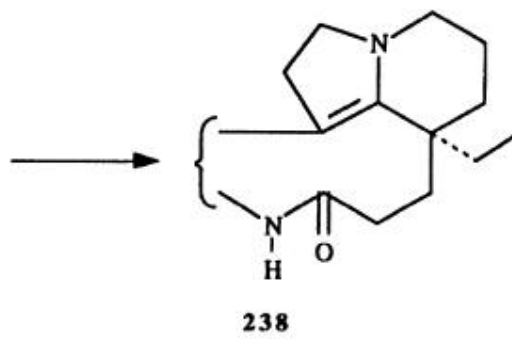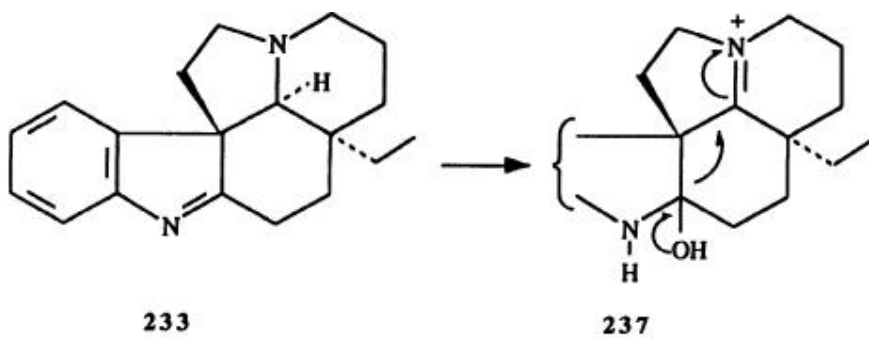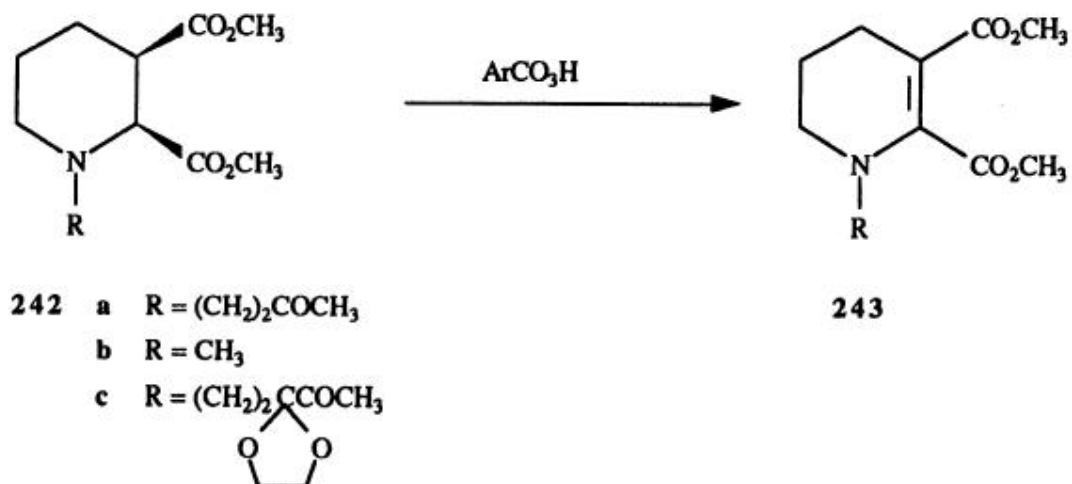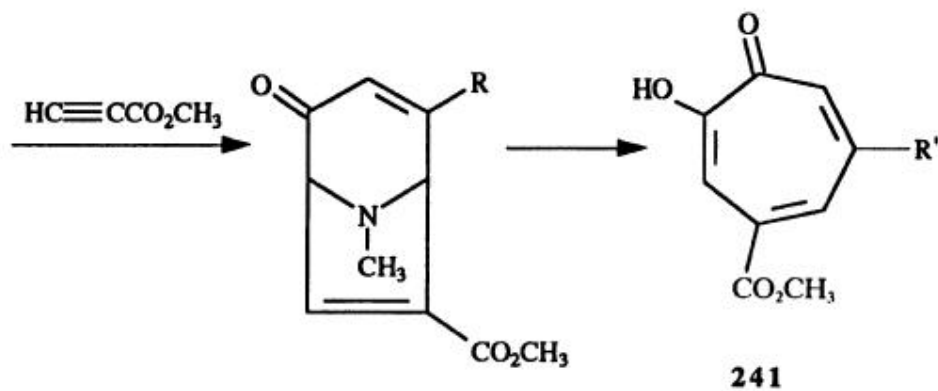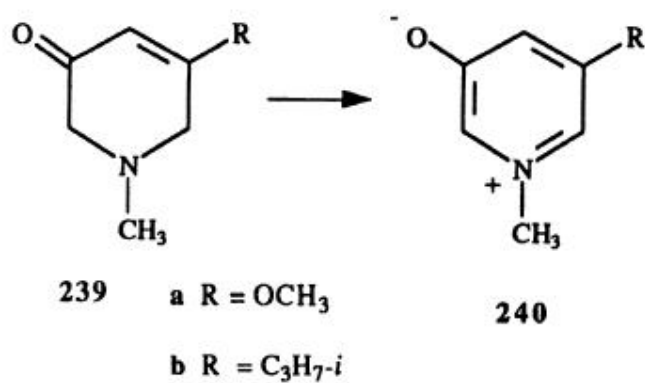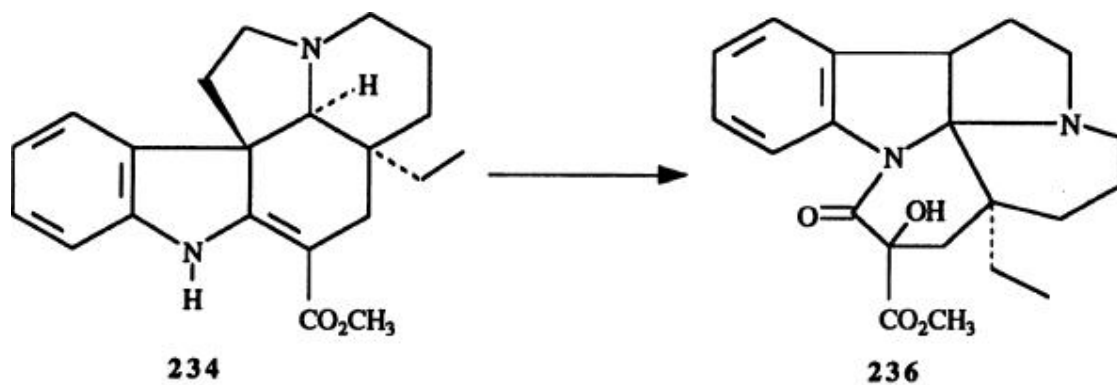
are in reality fundamentally different. In the reaction of nitrones with acetic anhydride the product-determining step is the addition of acetate ion to the electron-deficient carbon center of the nitronium salt **244**, and one of the nitrogen substituents is not lost in the secondary amide products.

$$
\underset{}{RCH=N\begin{smallmatrix}R'\\ \\O\end{smallmatrix}} \xrightarrow{(CH_3CO)_2O} \underset{\textbf{244}}{RCH=\overset{+}{N}\begin{smallmatrix}R'\\ \\OAc\end{smallmatrix}} \longrightarrow \underset{OAc}{RC}-N\begin{smallmatrix}R'\\ \\OAc\end{smallmatrix}
$$

(24)

$$
\longrightarrow \underset{\underset{\textbf{245}}{OAc}}{RC=N}^{R'} \longrightarrow \underset{\textbf{246}}{RCONHR'}
$$
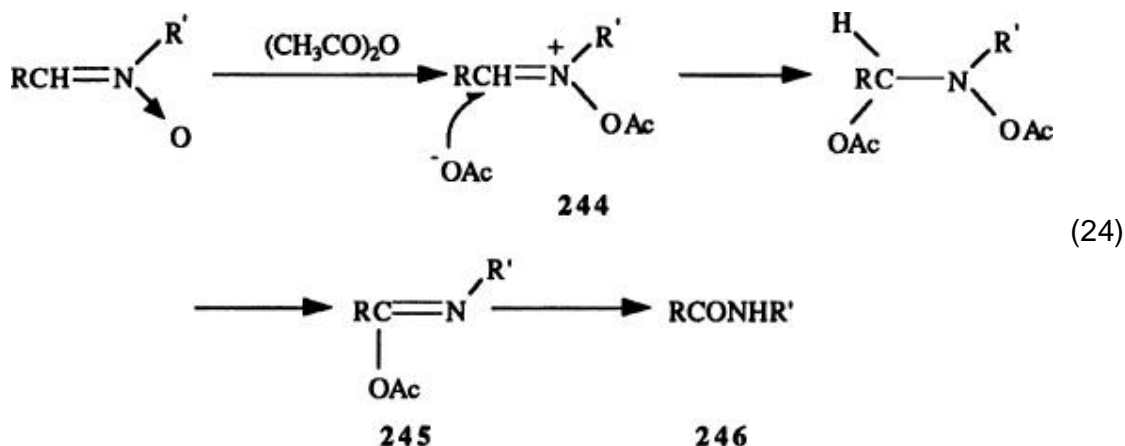
There is one special example involving the reaction of 1,4-diazepine *N*-oxides such as **247** (a trisubstituted nitrone) with acetic anhydride which has repeatedly been referred to as a Polonovski reaction because the acetate group is introduced at the saturated C-3 carbon position in the product **248**. (218-227)
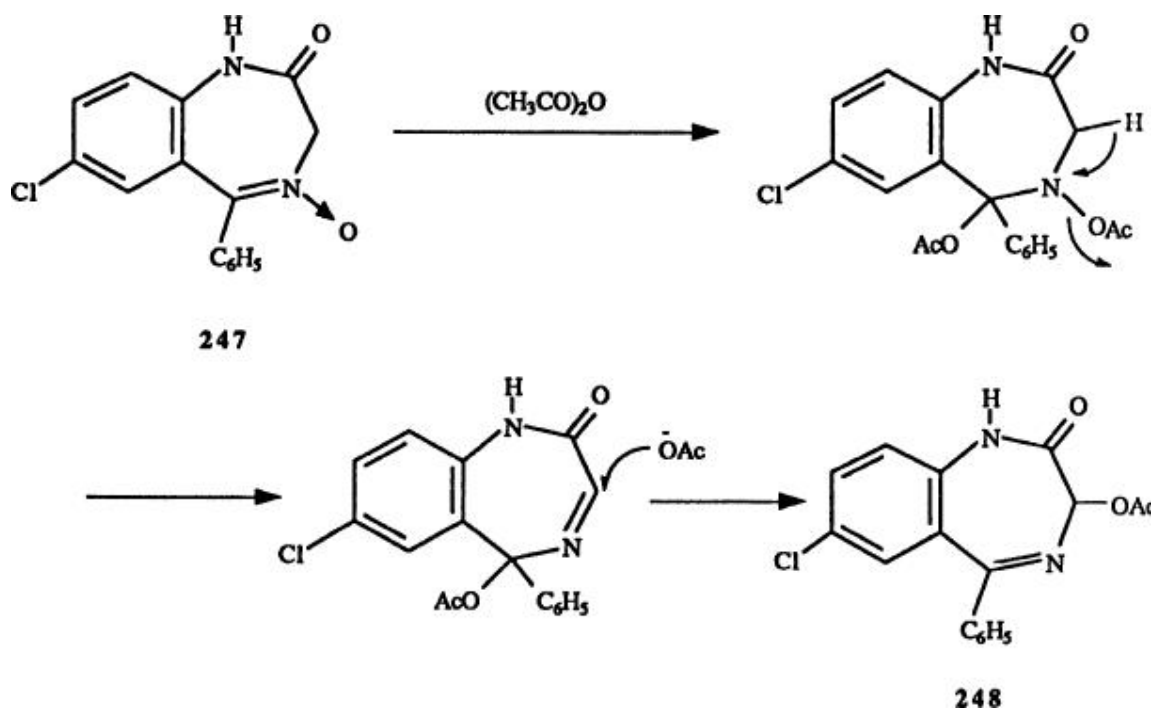
As for the Polonovski reaction itself, an ylide mechanism has been proposed to account for the migration of the acetoxy group from nitrogen to carbon. (221, 222) A more likely mechanism, which does not invoke the formation of high-energy intermediates, and for which there is literature precedent, has also been forwarded. (225) This alternative mechanism conserves all the aspects of the chemistry of nitrones with the slight variation that the elements of acetic acid are eliminated through loss of the C-3 proton. The formation of compound **248** from "*N*-oxide" **247** should therefore not be looked upon as resulting from a Polonovski reaction.

3.5. Iron Salts and Sulfur Dioxide

3.5.1.1. General Characteristics

An important feature that distinguishes the iron salt and sulfur dioxide initiated Polonovski reactions from their acid anhydride counterpart is the pronounced sensitivity of these reagents to the steric bulk of the substituents of the *N*-oxide substrate and to the relative acidities of the α hydrogens. This is manifested by a marked preference for oxidation at the methyl carbon center of *N*-methyl-substituted amine oxides. Selective conversion of such *N*-oxides to the *N*-demethylated secondary amines or intramolecular cyclization reactions involving the formaldiminium ion generated at the methyl carbon center are thus typically observed.

The yields of these reactions are generally moderate, however, as reduction of

the *N*-oxide to the tertiary amine is a competing side reaction. In fact, both iron salts and sulfur dioxide (at elevated temperatures) can be employed as reagents to selectively deoxygenate amine oxides. (228-230) Attention must therefore be paid to experimental conditions (temperature, solvent, pH, and concentration of reactants) in order to optimize the formation of the desired Polonovski products. (63, 138)

Little is known concerning the influence of α -hydrogen stereochemistry on the regiochemistry of the elimination step in these Polonovski reactions. Where aminium ion cations are involved, as in the iron salt reaction, the alignment of the C_α — H bond (either eclipsed or antiperiplanar) to the singly occupied orbital on nitrogen is important. (74-77) In the sulfur dioxide initiated reaction a cyclic transition state *A* is evoked for the elimination step, and a *syn*-elimination mechanism is thus considered to be operative. (138) The transformation of lupanine *N*-oxide (75) to the $\triangle^{17}$-iminium ion 249, rather than to the $\triangle^{11}$-iminium ion as observed with acetic anhydride, is suggested to result from a *syn*-elimination. (114)

Mention should be made that attention currently centers on the use of iron porphyrins as catalysts in the Polonovski reaction. (79-84, 91-93, 231-233) An added feature of this approach is that the *N*-oxide can act as an oxygen source for other synthetically useful iron porphyrin catalyzed transformations. (79, 94-93)
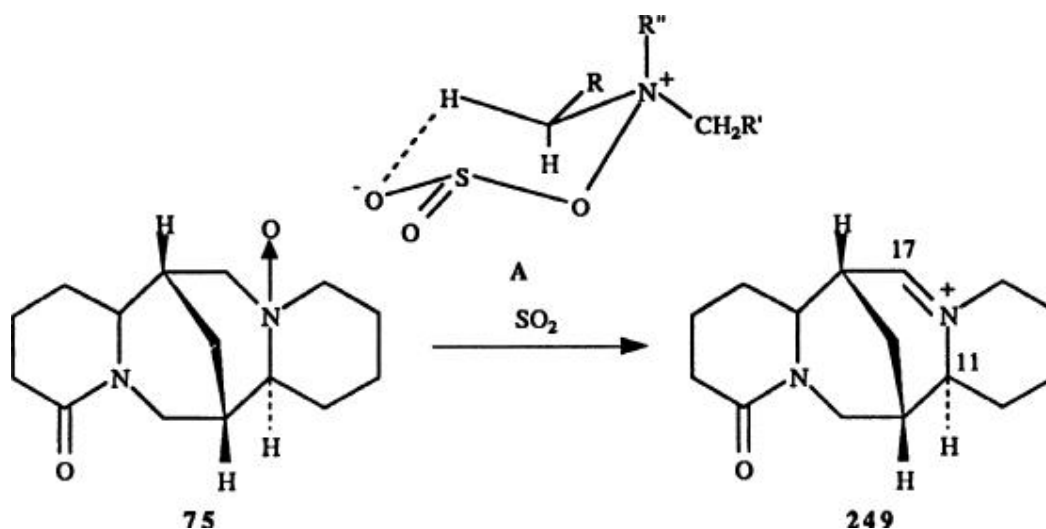
3.5.2. Synthetic Applications
3.5.2.1.1. Dealkylation Reactions

On the reaction of simple acyclic amine oxides with iron salts the ease of alkyl group conversion to the corresponding carbonyl compound decreases in the order $C_6H_5CH_2 > CH_3 > RCH_2 > R_2CH$, which suggests that product formation depends primarily upon the kinetic acidities of the α hydrogens. (63) Thus on reaction of benzyldimethylamine *N*-oxide with ferrous sulfate in dilute sulphuric acid (pH 1), benzaldehyde is the only observed product (Eq. 25). Similarly, formaldehyde is the only product obtained from the reaction of butyldimethylamine *N*-oxide. The acidity of the medium is important, however, as at higher pH (6.3) a mixture of aldehyde products is obtained in both reactions. The statistical number of α hydrogens also plays a role, since in the reaction of dibutylmethylamine *N*-oxide at pH 1 a 1:2 mixture of butyraldehyde and formaldehyde is produced (Eq. 26).

$$C_6H_5CH_2\overset{\overset{\displaystyle O}{\uparrow}}{N}(CH_3)_2 \xrightarrow{\text{FeSO}_4\,,\,0.49\text{ N H}_2\text{SO}_4} C_6H_5CHO \tag{25}$$

$$n\text{-}C_4H_9\overset{\overset{\displaystyle O}{\uparrow}}{N}(CH_3)_2 \xrightarrow{\text{FeSO}_4\,,\,0.49\text{ N H}_2\text{SO}_4} H_2CO \;+\; n\text{-}C_4H_9NHCH_3$$

$$(n\text{-}C_4H_9)_2\overset{\overset{\displaystyle O}{\uparrow}}{N}CH_3 \xrightarrow[\text{(pH 6.3)}]{\text{FeSO}_4\,,\,\text{tartaric acid}} \underset{2\,:\,1}{H_2CO \;+\; n\text{-}C_3H_7CHO} \tag{26}$$
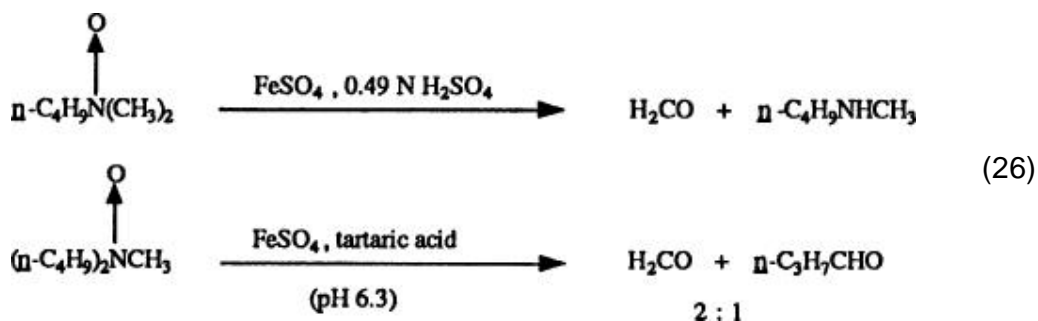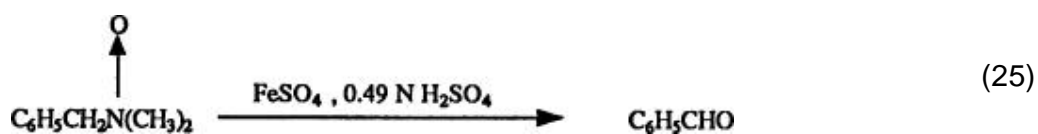
The corresponding reaction of benzyldimethylamine *N*-oxide with sulfur dioxide is not as clear-cut, as the literature data are conflicting. In one study (96) compound **250** is obtained as the major product in 52% yield (a precipitate which decomposes quantitatively to benzaldehyde on treatment with 95% ethanol), whereas in another study (138) a 1:4 mixture of benzaldehyde and benzylmethylamine is formed. As the former reaction is conducted at 0° and the latter at 20°, temperature may be a factor influencing these results.

$$\text{[benzyl-N(CH}_3)_2\text{ N-oxide]} \xrightarrow{\text{SO}_2} \text{[intermediate 250 (52%)]} \xrightarrow{95\% \text{ C}_2\text{H}_5\text{OH}} \text{C}_6\text{H}_5\text{CHO} \ (100\%)$$

250 (52%)
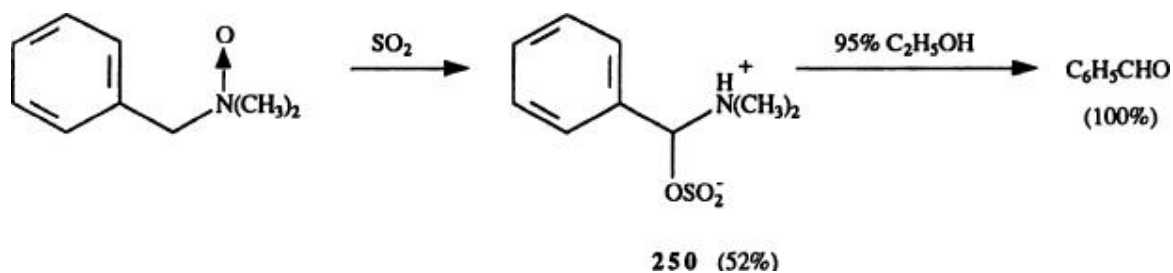
Selective transformation of the aporphine alkaloids *N*-methylovigerine and nuciferine to their nor-methyl derivatives **253** and **254** is possible by reaction of their *N*-oxides **251** and **252** with sulfur dioxide in water followed by hydrolysis with hydrochloric acid. (234) These conditions are sufficiently mild to also allow conversion of the phenolic aporphine *N*-oxide (**255**) to the normethyl compound **256**. The yields of these reactions are moderate, but

251 R,R' = CH₂

255 R= CH₃ , R' = H

1. SO₂
2. HCl - H₂O

253 (28%)

256 (18%)

252

254 (34%)

257
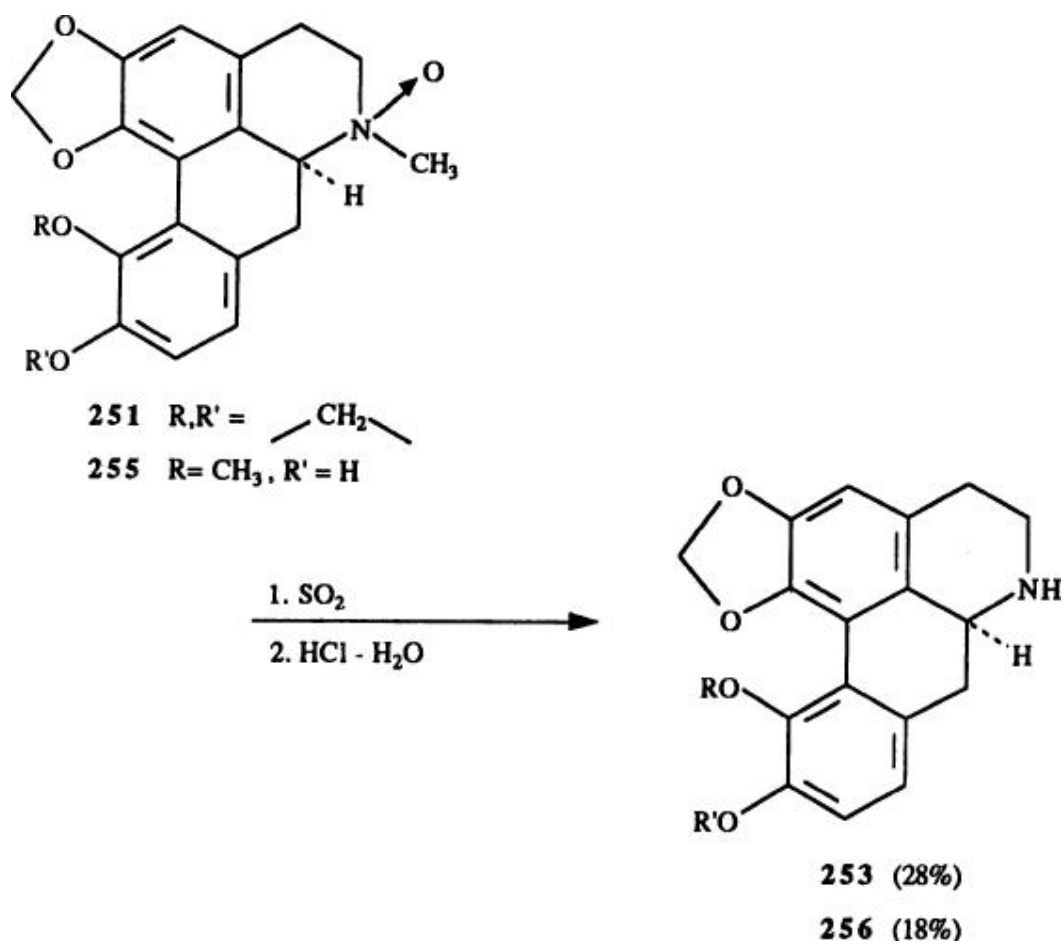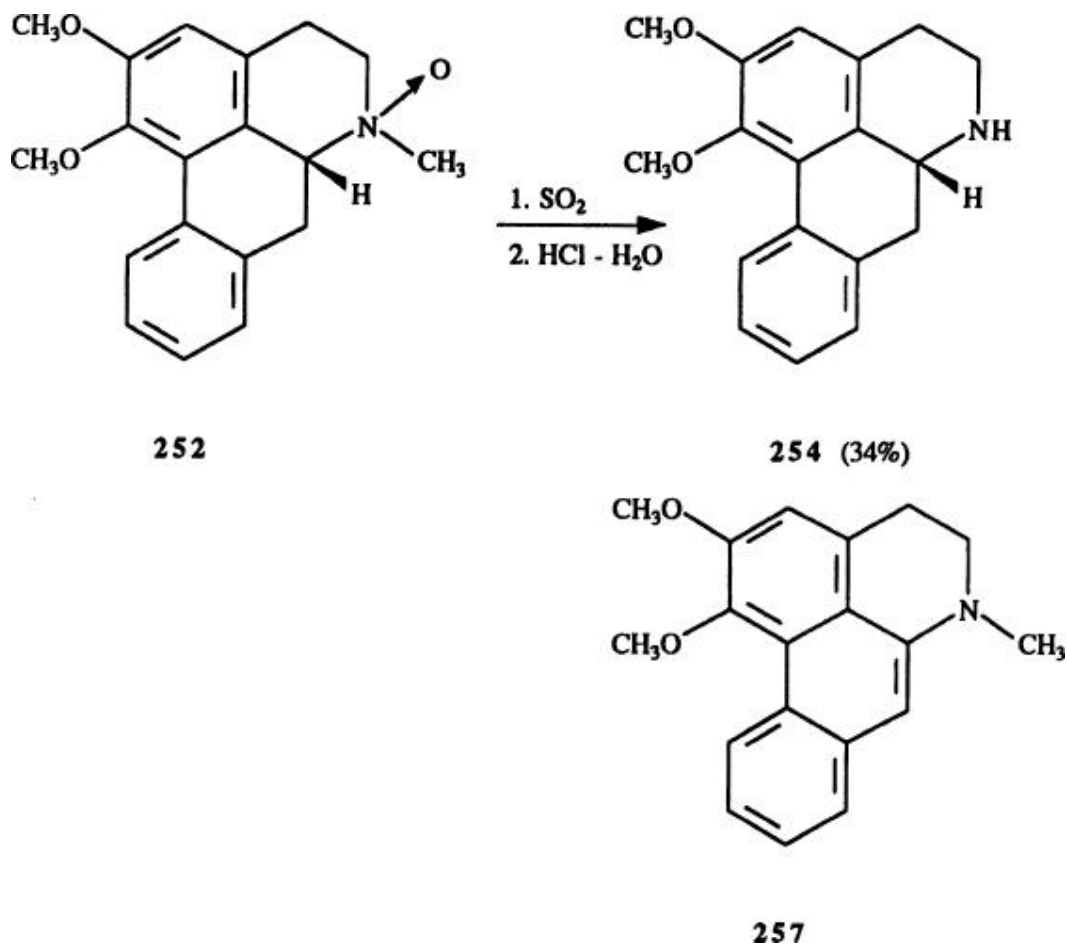
acceptable in view of the difficulty normally encountered in *N*-demethylations. Interestingly, when the reaction of nuciferine *N*-oxide with sulfur dioxide is carried out in methanol–benzene, and the mixture treated with base, the major Polonovski product is the enamine **257** (**254:257**, 2:5).

The reaction of *N*-oxides with catalytic amounts of ferrous chloride in water at –10° to room temperature shows promise of being an effective way for dealkylating tertiary amines. (235) For example, using this procedure the secondary amines **260** and **261** are obtained in over 80% yields from *N*-oxides **258** and **259**, and demethylation of *N*-oxides **262** and **263** is achieved in 56 and 63% yields, respectively. An additional advantage is that a number of functional groups, ketone, amide, primary amino, and hydroxy, are compatible with the essentially neutral conditions of this reaction. Note also that for the cyclic *N*-oxides **258**, **259**, and **262**, the exocyclic substituent is lost. This result contrasts with those obtained using trifluoroacetic anhydride, and shows a much higher selectivity than one would expect using acetic anhydride.

Dimethylaniline *N*-oxide (**226**) is not a good substrate in either the iron or sulfur dioxide Polonovski reactions. In the sulfur dioxide reaction a competing

free-radical process occurs, leading to formation of a mixture of the *ortho* and *para*-substituted sulfonic acid derivatives **264** and **265**. (96)

258   X = CH₂, R = $\square$

259   X = O , R = $\triangle$

FeCl₂ (cat.)
-10°

260   X = CH₂   (80%)

261   X = O   (89%)

262

263

226

264 (60%)

+

265 (20%)
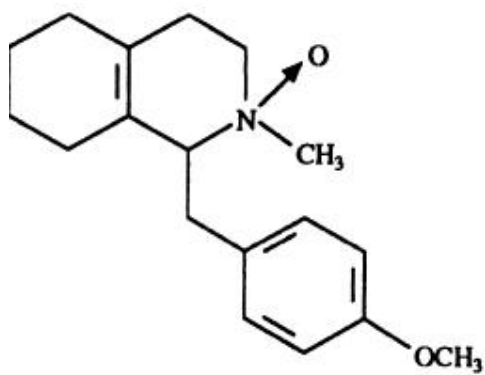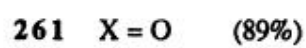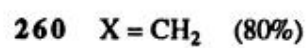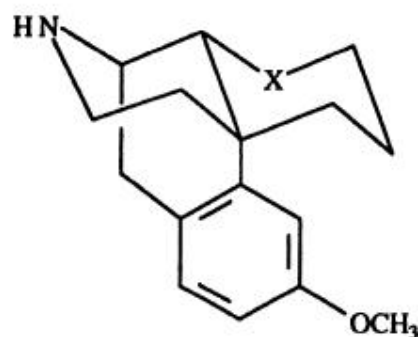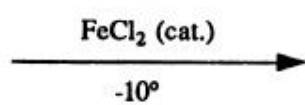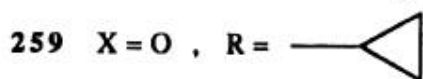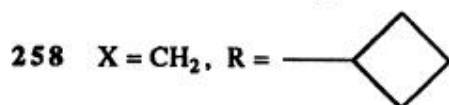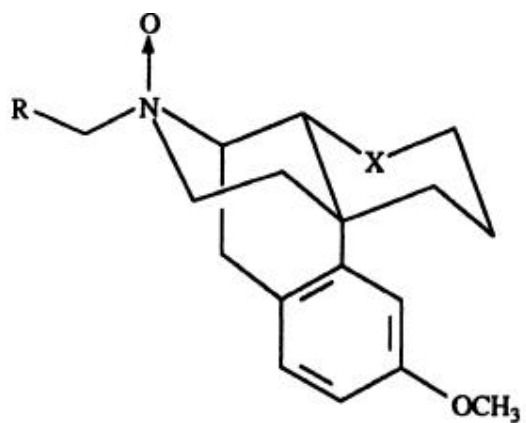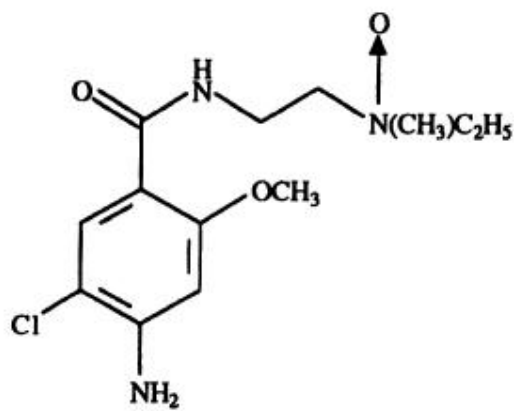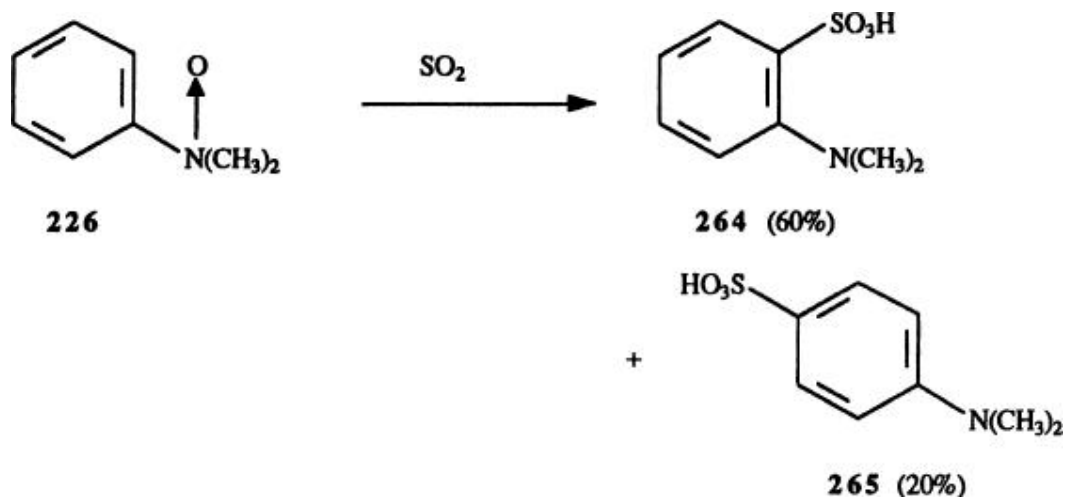
3.5.2.1.2. Intramolecular Ring-Closure Reactions

As a result of the selective reaction of iron salts and sulfur dioxide at the methyl group of N-methyl substituted N-oxides a variety of intramolecular ring-closure reactions can be achieved which are either unsuccessful or low yielding using acetic and trifluoroacetic anhydrides. The Pictet–Spengler cyclization of dimethyltryptamine N-oxide (**197**) to the carboline **266** using sulfur dioxide in anhydrous formic acid illustrates this point. (138) Reaction of this N-oxide with trifluoroacetic anhydride results exclusively in fragmentation of the C(5) − C(6) bond. (174)

197

SO$_2$, HCO$_2$H

266 (58%)
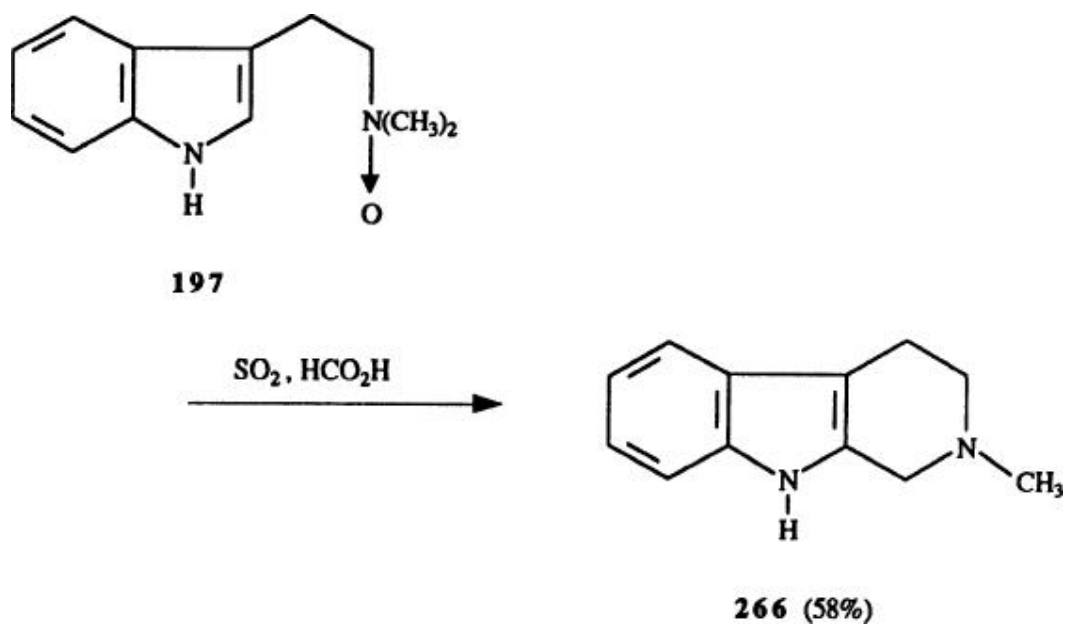
Similarly, 3-4-dimethoxy-*N-N*-dimethylphenethylamine *N*-oxide (**105**) is cyclized to the tetrahydroisoquinoline derivative **106** in 61% yield. (138, 236) Using trifluoroacetic anhydride compound, **106** is obtained in 33% yield (which in itself is surprising, see page 112). In contrast, when the reaction is conducted in water using sulfur dioxide or with ferrous sulfate in dilute sulfuric acid containing pyridine, (64) practically none of the cyclized product is formed. The principal Polonovski product in these reactions is the demethylated secondary amine **268**. This result arises from the fact that hydrolysis of the iminium ion intermediate **267** to the secondary amine is faster than its cyclization.
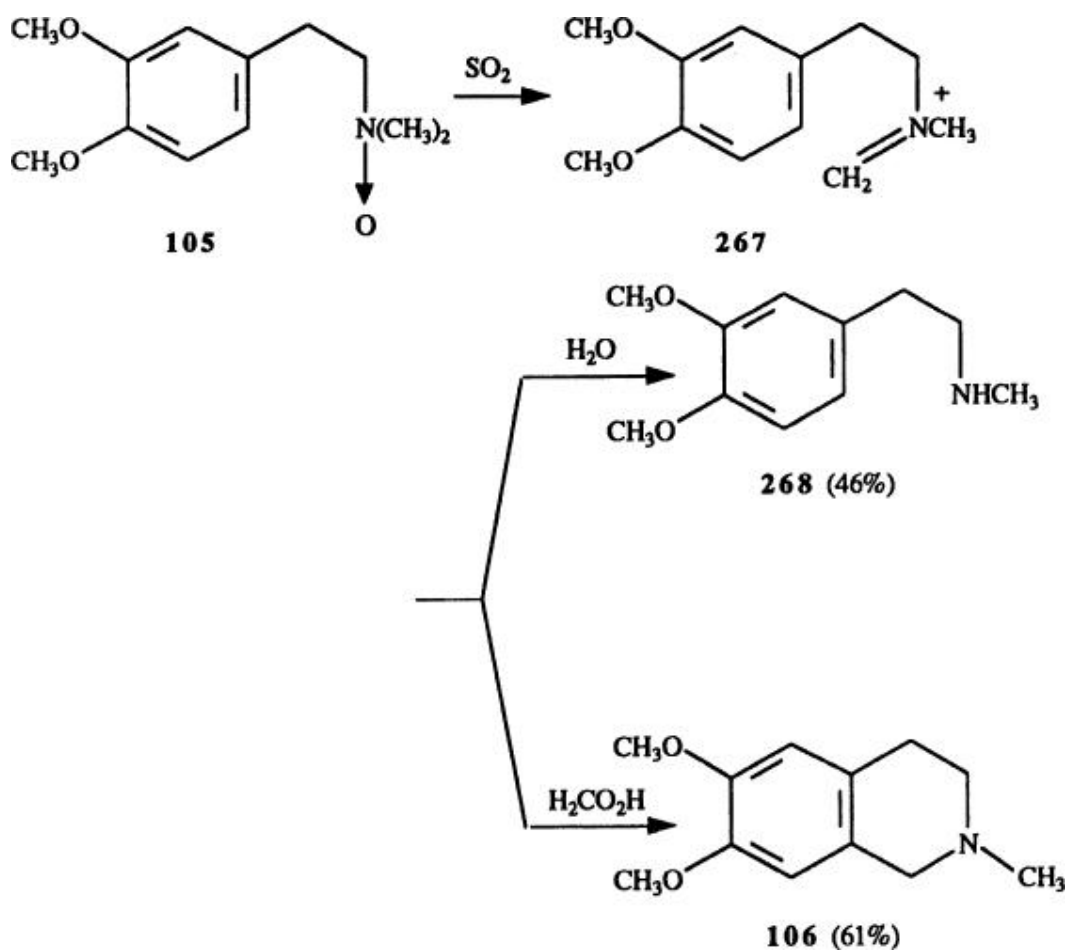
The ring closure of *N*-oxide **270** on treatment with sulfur dioxide in formic acid, which gives compound **269** in 40% yield, is also illustrative. (138) Laudanosine **271**, whose formation by the alternative cyclization may be expected on statistical grounds, is not observed in this reaction.

A biomimetic synthesis of the protoberberine alkaloids corexine (**273**) and scoulerine (**274**) has been developed involving reaction of reticuline *N*-oxide (**272**) with excess ferrous sulfate in methanol. (237, 238) The closely related *N*-oxide **275** does not cyclize under these conditions. However, a clean reaction is observed in acidic media giving **276** in 55% yield. In an analogous way homoprotoberberine systems can be constructed. (239)

3.5.2.1.3. Other Reactions

Perhaps the most remarkable example of the iron-initiated Polonovski reaction involves the ring opening of dehydroaspidospermine *N*-oxide

271

270

$$\xrightarrow{SO_2 - H_2O}$$

269 (40%)

$$\xrightarrow[CH_3OH]{FeSO_4}$$
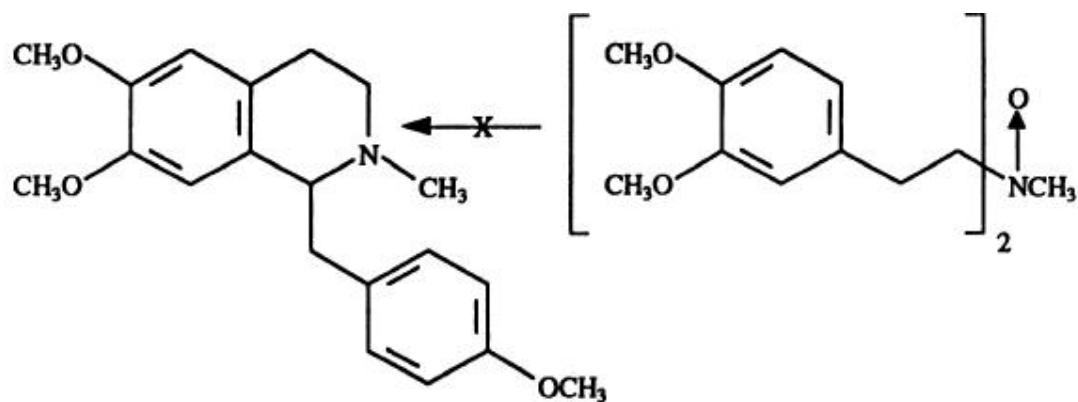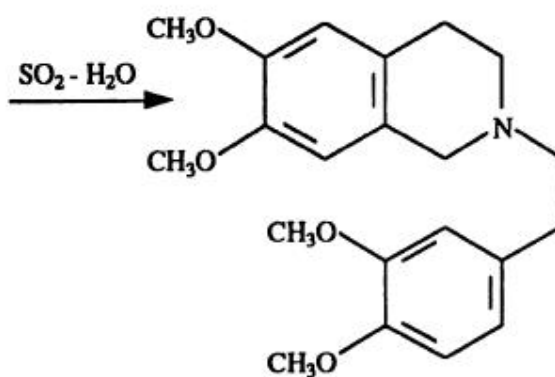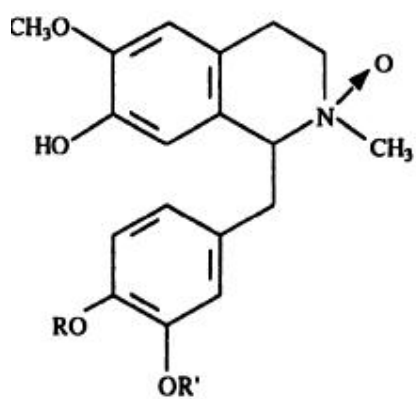
272 R = CH₃ , R' = H
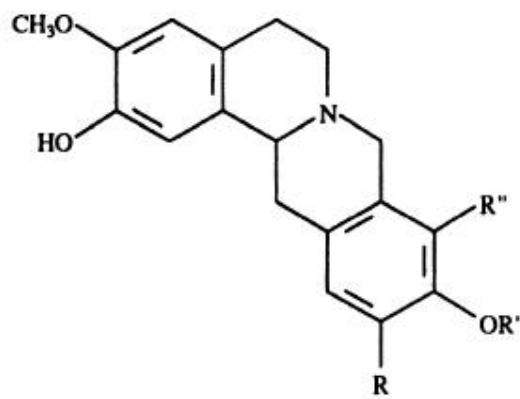
273 R = OCH₃ , R' = OH , R'' = H (42%)

274 R = H , R' = OCH₃ , R'' = OH (23%)
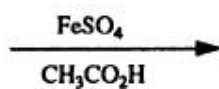
275 R = H , R' = CH₃ $\xrightarrow[CH_3CO_2H]{FeSO_4}$ **276** R = OH, R' = OCH₃ , R'' = H (55%)

(**277**) to the tetracyclic compound rhazinilam (**278**). (**240**) The mechanism of this transformation is thought to involve iminium ion formation and fragmentation in a manner analogous to the transformation of **233** to **235** (page 142), followed by dehydrogenation of the dihydropyrrole ring.

277 → FeSO₄ → 278 (30%)
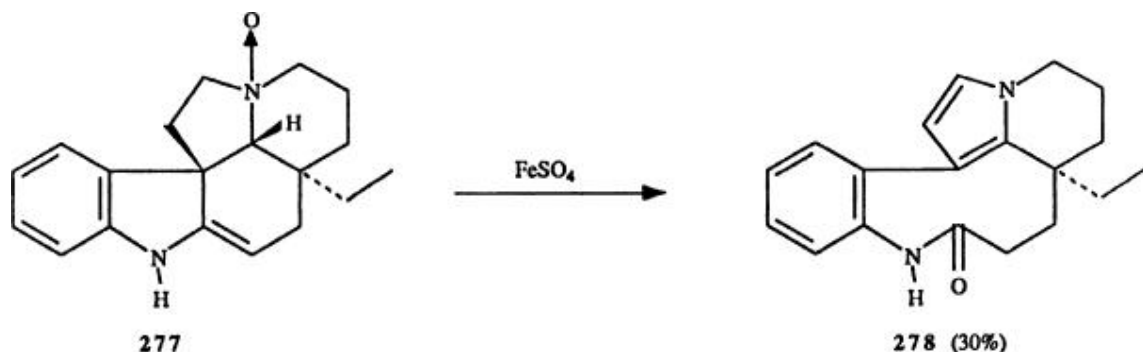
Intramolecular hydroxylation of nonactivated carbon centers, in a manner analogous to Hofmann–Löffler–Freytag chlorinations, is observed when *N*-oxides such as **279** are reacted with ferrous sulfate in 50% sulfuric acid. (**65**) Whereas formation of compound **280** is readily interpreted in terms of a six-membered transition state model (Eqs. **27–29**), the predominant formation of the secondary alcohol **281** from butyldimethylamine *N*-oxide requires that migration of the initially formed primary carbonium ion to the adjacent carbon center occur prior to hydroxylation. In dilute sulfuric acid solutions (0.5 N)

$n\text{-}C_4H_9N(CH_3)_2$ → FeSO₄ / 50% H₂SO₄ → $HOCH_2(CH_2)_3N(CH_3)_2$ + $CH_3CHOH(CH_2)_2N(CH_3)_2$

279   280 (4%)   281 (14%)

$(CH_3)_2\overset{+\cdot}{N}$ ⋯ H—CH₂   → $(CH_3)_2\overset{H+}{N}(CH_2)_3CH_2$ (27)

282

$282 + Fe(III)$ → $(CH_3)_2\overset{H+}{N}(CH_2)_3\overset{+}{C}H_2 + Fe(II)$ (28)

283

$$283 \xrightarrow[\text{H}_2\text{O}]{-2\text{H}^+} 280 \tag{29}$$
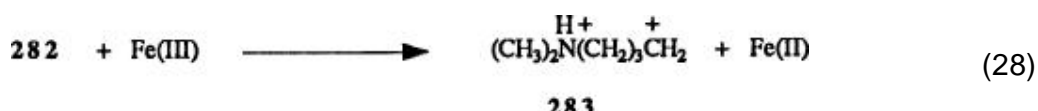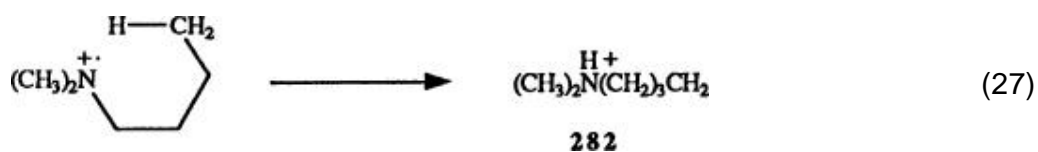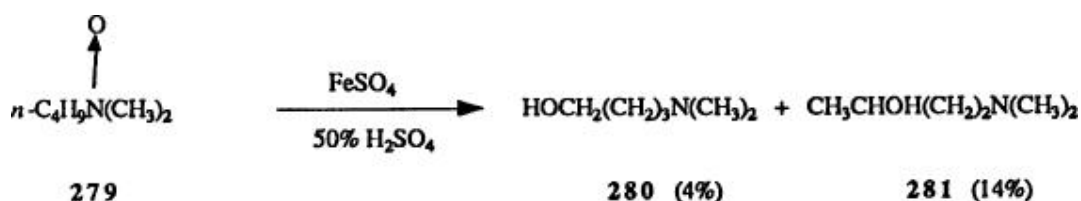
these same *N*-oxides undergo the Polonovski reaction.

Intermolecular trifluoroacetylation of cyclohexane, heptane, and decane has also been demonstrated using triethylamine *N*-oxide as the aminium radical cation source. (66) Only secondary trifluoroacetates are formed in these reactions, and the high selectivity observed for oxidation at the penultimate carbon center in the linear hydrocarbons correlates with the results obtained in free-radical chlorination with *N*-chloroammonium ions.

3.5.2.2. New Modifications: Silicon and Selenium Polonovski Reactions
Several new variations of the Polonovski reaction have appeared in the recent literature. The first of these employs *tert*-butyldimethylsilyl triflate as the activator and promotes the rearrangement of *N*-oxides to α -silyloxyamines **285** via the *O*-silylimmonium salts **284a**. (241-245) The intermediates **284a** are remarkably stable, however, and strong bases such as methyllithium or butyllithium are required to promote the transformation to **285**. At present it has not been determined whether this reaction occurs by an elimination–addition mechanism, as in the conventional Polonovski reaction (see Scheme 1), or by formation of an anion at the α -carbon center followed by migration of the silyloxy groups in a manner analogous to the Stevens rearrangement.

$$285 \text{ (or } 286) \xrightarrow{\text{Elec}^+} RR'(\text{Elec})\overset{+}{N}\text{----CHR''} \longrightarrow RR'N(\text{Elec}) + R'''F + R''CHO \quad (30)$$

287

$$\text{Elec} = H, CO_2C_6H_5, C_6H_5CO, \text{Alkyl}$$

$$285 \text{ (or } 286) \xrightarrow{\text{Nu}} RR'\overset{+}{N}\text{==CHR''} \longrightarrow RR'NCH(\text{Nu})R''$$

288

$$(31)$$

$$\text{Nu} = CN, C_6H_5, \text{Alkyl}, CH\text{==}CH_2$$
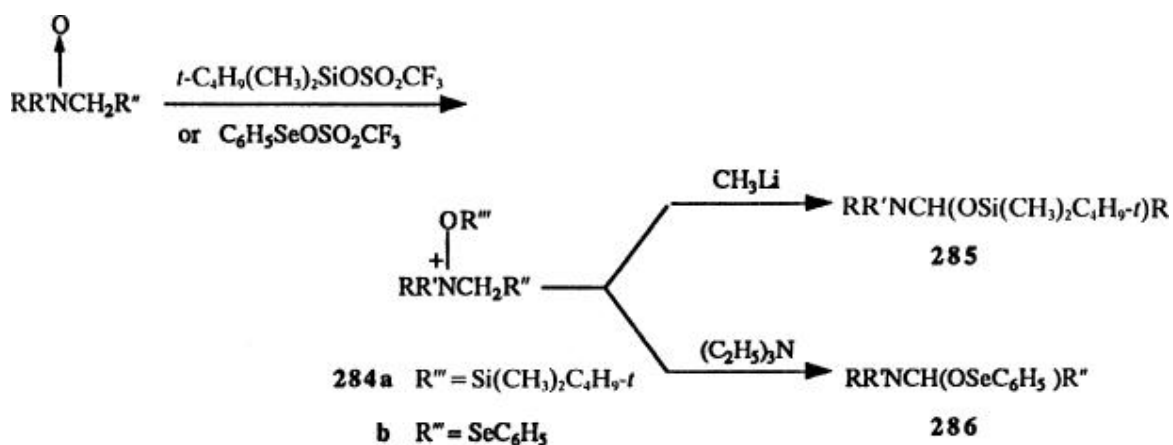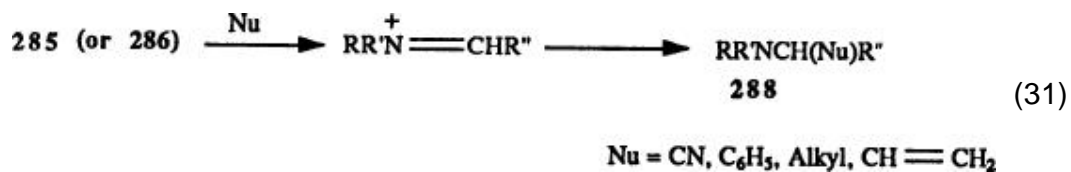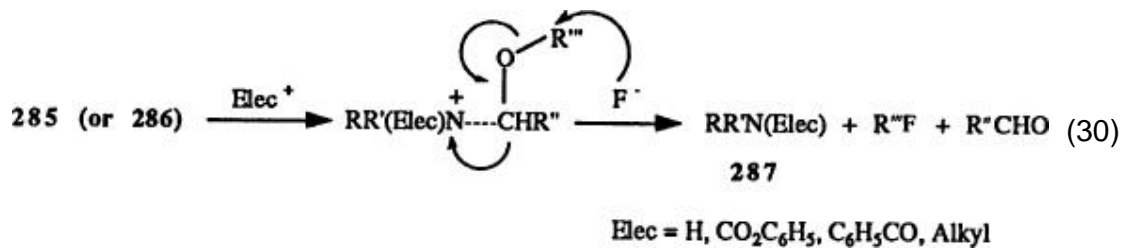
In a second variation benzeneselenyl triflate is employed as the activator and α-selenyloxyamines **286** are obtained. (246) The interesting feature of this reaction is that the O-selenylimonium salts **284b** are labile, and quantitative rearrangement to **286** is observed using weaker bases such as triethylamine or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

289

1. t-$C_4H_9(CH_3)_2SiOSO_2CF_3$
2. CH_3Li
3. $(CH_3)_3SiCN$

291 (71%)

290

1. $C_6H_5SeOSO_2CF_3$
2. $(C_2H_5)_3N$
3. C_6H_5COCl

292 (61-76%)

293

1. t-$C_4H_9(CH_3)_2SiOSO_2CF_3$
2. CH_3Li
3. C_6H_5COCl

294 (67%)

226

1. t-$C_4H_9(CH_3)_2SiOSO_2CF_3$
2. CH_3Li
3. C_6H_5COCl

295 (51%)
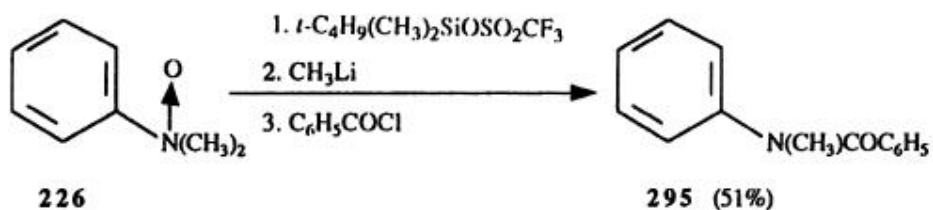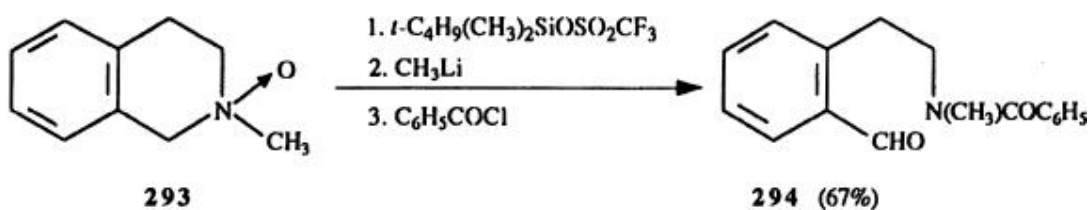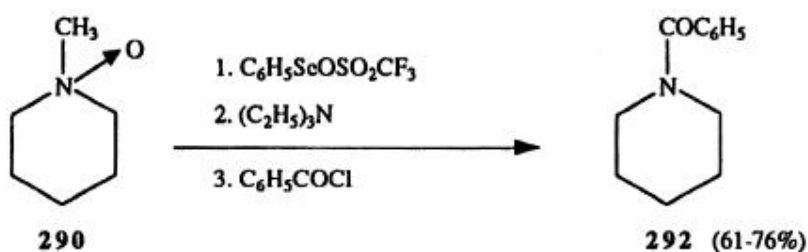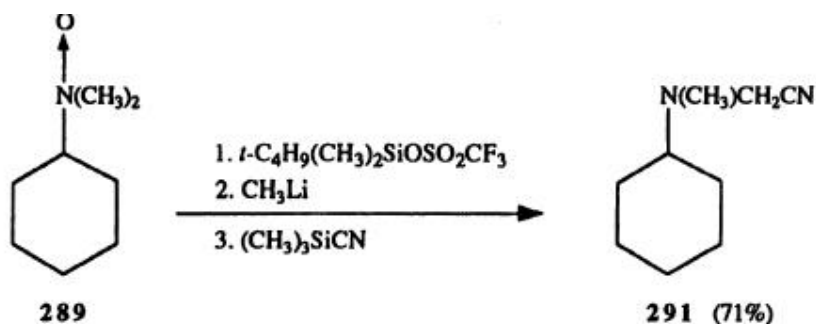
Electrophilic reagents react with intermediates **285** and **286** by reaction at nitrogen. This triggers a fragmentation process in which the amine product **287**, an aldehyde, and a silicon or selenium derivative are produced (Eq. 30). Electrophiles that can be used include benzoyl chloride, phenyl chloroformate, acetic acid, and alkyl halides. The latter reaction is particularly interesting since it enables the replacement of one alkyl group on nitrogen by another, although the yields are modest. The reaction of **285** and **286** with nucleophiles such as Grignard and organoaluminum reagents and trimethylsilyl cyanide presumably occurs via an intermediate iminium ion and results in introduction of the substituent at the α -carbon position of **288** (Eq. 31).

The results obtained with unsymmetrical *N*-oxides reveal that the regiochemistry of the above reactions with trialkylsilicon triflate and the phenylselenyl triflate is determined by both the accessibility and the relative acidity of the α hydrogens. For instance, the reaction of *N*-oxide **289** and in particular *N*-methylpiperidine *N*-oxide (**290**) under the above conditions leads to exclusive formation of compounds **291** and **292**. (241, 243, 244, 246)

The corresponding reaction of dimethylbenzylamine *N*-oxide gives a mixture of products as steric and relative acidity factors operate in opposition to one another. (241, 243, 244, 246) In contrast, the ring-opened compound **294** is the only product observed in the reaction of *N*-methyltetrahydroisoquinoline *N*-oxide (**293**) with *tert*-butyldimethyl silyl triflate, methyllithium, and benzoyl chloride. (241, 244) Another interesting aspect of this triflate modification of the Polonovski reaction is that dealkylation of dimethylaniline *N*-oxide (**226**) is efficient, giving **295** in 51% yield.

4. Experimental Procedures

4.1.1.1. N,N-Dimethylacetamide [N-Demethylation] (31)
To a solution of trimethylamine *N*-oxide (10 g, 0.133 mol) in 100 mL of chloroform (water- and ethanol-free) was added 0.5 mL of acetic anhydride. On addition of a further 4 mL of the anhydride the reaction mixture began to boil, and after a total of 11.5 mL of anhydride had been added (1 equivalent = 12.5 mL) no further heat was liberated. At the beginning of the reaction the odor of formaldehyde could be detected. An additional 13.5 mL of anhydride was then added and the resulting reaction mixture was refluxed for 3 hours. At the end of this period an ice-cold solution of 20% sodium hydroxide was added dropwise, provoking the precipitation of sodium acetate. The aqueous phase was then extracted three times with chloroform. The combined organic phases were combined and distilled. *N,N*-Dimethylacetamide distilled

at 180–190° (67% yield); n_D^{25} 1.4371 (authentic sample n_D^{25} 1.4370).

4.1.1.2. 3-Methyl-6-cyano-1,2,3,5,6,11C-7H-hexahydro[3,4-c]pyridocarbazole (112) [Iminium Ion Formation, Intramolecular Cyclization] (140)
The indolesubstituted tetrahydropyridine **111** (0.200 g, 0.75 mmol) was dissolved in 2 mL of dry methylene chloride and treated at 0° with trifluoroacetic anhydride (0.5 mL). After stirring for 15 minutes at 0° followed by 1 hour at room temperature, the reaction was stopped by the addition of 2 N hydrochloric acid (3 mL). The resulting mixture was then stirred at 70° for 20 minutes, cooled, neutralized, and extracted with ethyl acetate. The combined organic layers were washed, dried, and concentrated. The crude product mixture was separated by preparative TLC on silica gel. Compound **112** (0.092 g, 50%) was obtained as a mixture of two isomers (amorphous solid). IR (CHCl$_3$) 3460, 2240, 1665 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 2.60, 2.65 (2s, NCH$_3$), 4.86, 4.94 (2 m, 1*H*), 5.86, 5.98 (2 m, 1*H*); mass spectrum *m/z* (rel. intensity): 263 (100), 262 (98).

4.1.1.3. N-Acetyl-N-methyl-2,4,6-trimethylaniline [N-Demethylation] (42)
A solution of *N,N*-dimethyl-2,4,6-trimethylaniline *N*-oxide (325 mg, 1.8 mmol) in 2.5 mL of acetic anhydride was heated at 60° for 3 hours. The excess anhydride was then evaporated in vacuo, the residue was dissolved in 10 mL of methylene chloride, and stirred with 10 mL of 2 N sodium hydroxide. The methylene chloride layer was dried and concentrated, giving a colorless oil which was sublimed at 0.7 torr (bath temperature 89°). The product was obtained as colorless crystals (320 mg, 77%); mp 52–52.5°; IR (CCl$_4$) 3010, 2900, 2850, 1660, 1480, 1420, 1375, 1350, 1310, 1285, 1170, 1135, 1080, 1025, 970, 855 cm^{-1}; ^{1}H NMR (CCl$_4$) δ 1.60 (s, 3*H*), 2.13 (s, 6*H*), 2.25 (s, 3*H*), 3.00 (s, 3*H*), 6.83 (s, 3*H*).

4.1.1.4. N-Methyl-2-cyano-3-ethyl-3-piperideine (123b) [Iminium Ion Formation, Cyanide Trapping] (144)

1-Methyl-3-ethyl-3-piperideine *N*-oxide (14.1 g, 0.1 mol) was dissolved in 200 mL of methylene chloride and stirred under a nitrogen atmosphere at 0°. Trifluoroacetic anhydride (28.0 mL, 0.2 mol) was added via syringe over 15 minutes and the resulting mixture was stirred at 0° for 1 hour and at room temperature for 15 minutes. The mixture was then concentrated in vacuo, redissolved in 75 mL of methylene chloride and, under a rapid stream of nitrogen and with rapid agitation, treated with an aqueous solution of potassium cyanide (10 g in 50 mL of H_2O) preadjusted to pH 4.0 by the addition of both solid sodium acetate and solid citric acid. The resulting two-phase reaction mixture was stirred rapidly for 15 minutes, basified with aqueous 10% sodium carbonate and extracted with methylene chloride. The combined organic layers were washed with water, dried over sodium sulfate, and concentrated (bath temperature <35°), giving an orange liquid. The product was obtained as a pale yellow liquid (10.9 g, 72%) after filtration down a short column of alumina, eluting with methylene chloride: hexane (1:1); IR (film) 2220 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.05 (t, $J = 6$ Hz, 3*H*), 2.02 (m, 2*H*), 2.16 (m, 1*H*), 2.29 (m, 1*H*), 2.45 (s, 3*H*), 2.49 (dd, 1*H*), 2.67 (dd, 1*H*), 3.87 (s, 1*H*), 5.62 (m, 1*H*); ^{13}C NMR (CDCl$_3$) δ 11.76, 25.34, 26.65, 43.28, 47.31, 56.48, 116.07, 122.16, 133.26; mass spectrum *m/z* (rel intensity): 150(20), 135(42), 122(100).

4.1.1.5. 5 α -Cyanovincadifformine [Iminium Ion Formation, Cyanide Trapping] (154)

To a stirred cooled (0°) solution of vincadifformine *N*-oxide (250 mg, 0.7 mmol) (**234**-*N*-oxide) in 4 mL of dry methylene chloride was added trifluoroacetic anhydride (0.2 mL) (argon atmosphere). After reaction for 1 hour at 0° followed by 1 hour at room temperature, the mixture was evaporated to dryness, redissolved in 4 mL of methylene chloride, and treated with an aqueous solution of potassium cyanide. The aqueous phase was immediately adjusted to pH 4.0 by addition of either trifluoroacetic acid or solid potassium acetate. The two-phase mixture was vigorously stirred for 15 minutes, then basified by addition of solid sodium carbonate and extracted with chloroform. The product was obtained as colorless crystals (133 mg, 50%) after preparative TLC separation of the crude product mixture on silica gel plates (chloroform:methanol, 95:5); mp 212°; UV (C$_2$H$_5$OH) nm max 328, 302, 231; IR (CHCl$_3$) 2225, 1680, 1610 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.63 (t, $J = 7$ Hz, 3*H*), 3.78 (s, 3*H*), 3.9 (m, 1*H*); ^{13}C NMR (CDCl$_3$) δ 7.1, 24.8, 29.0, 32.6, 38.7, 47.3, 48.6, 51.2, 53.4, 54.9, 69.8, 93.4, 109.7, 118.0, 121.3, 123.1, 128.2, 135.5, 143.6, 166.8; mass spectrum *m/z* (rel. intensity): 363(100), 336(10), 214(98).

4.1.1.6. cis-(±)-1,2,3,3a,9,5,6,6a,7,8-Decahydropyrido[2,1,6-de]quinolizine (74) [Enamine Formation] (111)

Trifluoroacetic anhydride (4.5 mL, 32 mmol) was added over 10 minutes to a cold (–78°) stirred solution of 3a α ,6a α ,9a α -dodecahydropyrido[2,1,6-*de*]quinolizine *N*-oxide (3.4 g, 16 mmol) in 32 mL of dry methylene chloride, and the mixture was allowed to warm to room temperature. After 12 hours, 20 mL of 50% aqueous potassium hydroxide solution was added at 0°. The water layer was extracted with methylene chloride and the combined organic phase was dried over sodium sulfate plus potassium carbonate and concentrated in vacuo to give a dark brown oil. The product (1.9 g, 50%) was obtained as a colorless oil (discolors on exposure to air) by bulb to bulb distillation (50–52°, 0.15 mm Hg); mp (picrate) 127–128°; IR (film) 2930, 2840, 2800, 2775, 1645, 1445, 1320 cm^{-1}; ^{1}H NMR δ 2.28 (br t, J = 10 Hz, 1H), 2.54 (br t, J = 10 Hz, 1H), 4.42 (br d, J = 6 Hz, 1H); ^{13}C NMR δ 21.9, 23.3, 24.0, 30.2, 32.6, 33.1, 34.2, 58.4, 59.9, 98.2, 142.6; mass spectrum *m/z* (rel. intensity): 177(62), 176(100), 162(42), 149(18), 148(32), 135(20), 134(34), 120(15).

4.1.1.7. $\triangle$ ^{6}-Dehydrodeoxynupharidine (68) [Enamine Formation] (36)
A solution of nupharidine (1.0 g, 4.0 mmol) in 20 mL of anhydrous alcohol-free chloroform was cooled to 0° under nitrogen. When freshly distilled acetic anhydride (3 g, 29.5 mmol) was added, the solution warmed slightly. The resulting solution was kept at 0° for 2 hours and at 25° for 120 hours. A gentle stream of dry nitrogen was bubbled into the reaction mixture throughout. The solvent was then removed and methanolic potassium hydroxide (10%) was added to the residue to pH 10. The mixture was then taken up in ether and the resulting solution was washed three times with small portions of water. The ether phase was dried over anhydrous sodium sulfate and evaporated giving a brown oil (0.80 g), which was purified by column chromatography on alumina (Act II). Elution with hexane–ether (95:5) afforded 700 mg (82%) of product

which crystallized on stirring for several days at –10°; mp ~30°; $[\alpha]_D^{25} - 137.4°$

(C$_2$H$_5$OH); UV (CH$_3$OH) nm max 243; IR (CH$_2$Cl$_2$) 2532, 1678, 1597, 1504, 1453, 1437, 1374, 873 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.96 (d, 5.5 Hz, CH$_3$), 1.50 (d, J = 1.5 Hz, CH$_3$), 3.50 (q, J = 8 and 4 Hz, 1H, 5.66 (s, 1H), 6.44 (m, 1H), 7.41 (m, 2H); mass spectrum *m/z* (rel. intensity): 231 (100), 216 (46), 176 (31), 174 (19), 95 (64).

4.1.1.8. δ ^{20}-Dregamine (157) [Enamine Formation] (161)
Acetic anhydride (1.5 mL) was added to a stirred solution of dregamine *N*-oxide (0.300 g, 0.80 mmol) in 20 mL of methylene chloride at 0°. The resulting solution was stirred at room temperature for 15 hours and then evaporated under vacuum. Any residual anhydride was eliminated by repeated evaporation with benzene. The product was obtained pure (0.214 g, 75%) after preparative TLC separation of the crude product mixture on neutral silica-gel

plates (chloroform with a saturated ammonia atmosphere); $[\alpha]_D^{20} + 195°$

(CH_3OH); UV (C_2H_5OH) nm max 240, 318; IR 3450, 1725, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.1 (t, 3H), 2.2. (q, 2H), 2.9 (s, 6H), 5.7 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.3, 40.3, 50.3, 54.6, 113.5, 170.5, 189.4; mass spectrum, m/z: 352, 293, 180, 122.

4.1.1.9. N-Methyl-2-piperidein-4-one (171) [Enaminone Formation] (120)
A solution of *m*-chloroperbenzoic acid (11 eq.) in 20 mL of methylene chloride was added to a cooled (–40°) stirred solution of freshly distilled *N*-methylpiperidine-4-one (1.18 mL, 10 mmol) in 20 mL of dry methylene chloride. Stirring was continued at this temperature for 30 minutes followed by addition of acetic anhydride (1.04 mL, 11 mmol) and triethylamine (6.9 mL, 50 mmol). After stirring for a further 60 minutes at 0° the reaction was stopped by the addition of ice-cold aqueous sodium bicarbonate solution. The aqueous phase was extracted with methylene chloride. The combined extracts were dried and concentrated, and the residue was distilled under reduced pressure (110°, 1.0 mm Hg). The product was obtained as a yellowish oil (0.55 g, 50%). ^{1}H NMR ($CDCl_3$) δ 2.5 (t, J = 8 Hz, 2H), 3.1 (s, 3H), 3.5 (t, J = 8 Hz, 2H), 4.85 (d, J = 8 Hz, 1H), 7.1 (d, J = 8 Hz, 1H).

4.1.1.10. 1-(1-Cyanoethyl)-3-ethyl-1,2,5,6-tetrahydropyridine (64) [Carbon — Carbon Bond Fragmentation, Cyanide Trapping] (107, 109)
Excess 30% hydrogen peroxide (3.5 mL) was added to a solution of 1-(1-carbomethoxyethyl)-3-ethyl-1,2,5,6-tetrahydropyridine (4.05 g, 20.5 mmol) in 20 mL of 1:1 methylene chloride–ethanol, and the resulting solution was stirred at 62° for 28 hours. Excess peroxide was destroyed by the addition of 10% palladium on carbon (0.300 g) with continued stirring at 60° for 7 hours. The mixture was then filtered, concentrated, redissolved in methylene chloride, dried over sodium sulfate, and finally concentrated under vacuum. The *N*-oxide obtained as a semisolid yellow oil (3.50 g, 86%) was immediately used in the following step. Trifluoroacetic anhydride (4.60 mL, 35 mmol) was added via syringe over 15 minutes to a cooled (–10°) solution of the *N*-oxide (3.50 g, 17.4 mmol) in 40 mL of dry methylene chloride (argon atmosphere). The resulting mixture was stirred at 0° for 1 hour and at room temperature for 15 minutes.

A solution of potassium cyanide (1.70 g, 1.5 equiv) in 10 mL of water was then added to the reaction and the aqueous layer adjusted to pH 5 by the addition of solid sodium acetate. The resulting reaction mixture was stirred at room temperature for 30 minutes, basified to pH 10 by the addition of aqueous sodium carbonate solution, and extracted several times with methylene chloride. The combined extracts were washed with water, dried over sodium sulfate, and concentrated to give a pale brown oil (2.10 g). The product was obtained as a nearly colorless oil (1.35 g, 48%) after passage of the crude mixture down a short column of alumina (methylene chloride:hexane, 1:1). IR 2240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.02 (t, J = 7.4 Hz, 3H), 1.48 (d, J = 7.2 Hz, 3H),

1.99 (q, *J* = 7.4 Hz, 2*H*), 2.20 (br s, 2*H*), 2.45–2.86 (m, 2*H*), 2.97 (br s, 2*H*), 3.77 (q, *J* = 7.2 Hz, 1*H*), 5.45 (br s, 1*H*); ^{13}C NMR (CDCl$_3$) δ 11.56, 16.62, 25.32, 27.14, 46.23, 51.16, 51.81, 117.00, 117.13, 136.22; mass spectrum *m/z* (rel. intensity): 164(55), 149(56), 135(100).

4.1.1.11. 17-Oxa-18-oxo-D-homo-5 α ,13 α-androst-15-ene (**192**) [Carbon ─ Carbon Bond Fragmentation] (*173*)

Trifluoroacetic anhydride (1.0 mL) was added to a cooled (0°) solution of 16 β -dimethylamino-15 β ,18-oxido-5 α ,13 α -androstane *N*-oxide (**190**) (902 mg, 2.71 mmol) in chloroform and the resulting mixture was stirred at room temperature for 1 hour. The reaction was then poured into an ice-cold aqueous solution of sodium carbonate and extracted with chloroform. The combined organic phase was washed with 5% hydrochloric acid, water, then dried and concentrated. The residue (783 mg) was purified by column chromatography on silica gel. The product (438 mg, 50%) was eluted with hexane:benzene (1:1). This unstable compound was characterized by its mass spectrum *m/z* 288 and by reduction to the corresponding alcohol; mp 128° (acetone–hexane); [α]$_D$ – 112° (*c* 0.16, CHCl$_3$).

4.1.1.12. Mitomycin Derivative **178** [Pyrrole Ring Formation] (*172*)

A solution of the mitosane *N*-oxide (**177**) (5.1 mg, 0.011 mmol) in 300 µL of chloroform at room temperature was treated with acetic anhydride. Stirring was continued for 10 minutes, after which the volatiles were removed in vacuo. Application of the residue to a preparative TLC plate followed by elution with 20% ethyl acetate in hexanes gave 4.8 mg (98%) of pyrrole **178** as a faintly yellow oil; ^{1}H NMR δ 7.46–7.23 (m, 11*H*), 6.37–6.34 (m, 1*H*), 5.11, 5.05 (ABq, *J* = 11.3 Hz, 2*H*), 4.53 (s, 2*H*), 4.29–4.14 (m, 2*H*), 3.86 (s, 3*H*), 3.84 (s, 3*H*), 3.46–3.37 (m, 1*H*), 2.30 (s, 3*H*); IR (CCl$_4$): 2935, 1625, 1555, 1485, 1282, 1118 cm^{-1}; MS *m/z* 455 (M$^+$, 39), 364(32), 335(23), 334(100), 243(15).

4.1.1.13. △ ^{15,20}-Dehydroxyvinblastine (**212**) [Carbon ─Carbon Bond Fragmentation, Coupling] (*178*)

Trifluoroacetic anhydride (0.115 mL, 0.8 mmol) was added to a stirred solution of cathananthine *N*-oxide (100 mg, 0.3 mmol) and vindoline (135 mg, 0.3 mmol) in 0.83 mL of dry methylene chloride maintained under a nitrogen atmosphere at –78°. After 30 minutes excess solvent and trifluoroacetic anhydride were removed by distillation in vacuo at 20°. The residue was dissolved in 5.7 mL of methanol and excess sodium borohydride was added at 0°. After 15 minutes the reaction mixture was poured into 100 mL of water and extracted with chloroform. The pure product (114 mg, 50%) was obtained after preparative TLC separation of the crude residue on silicagel plates (ethyl acetate:methanol, 96:4) (two minor components were also isolated in this way); mp 208–210° dec (CH$_3$OH) $[\alpha]_D^{22} + 19°$(*c* 0.70, CH$_3$OH); IR 1740, 1615 cm^{-1}; UV (CH$_3$OH) nm (ε) 263 (17,500), 290 (14,300), 297 (13,400); CD 258

(14.0), 305 (6.5); ^{1}H NMR δ 9.77 (1H), 7.87 (br s, 1H), 6.52 and 6.03 (s, 2 × 1 H), 5.76 (dd, $J_{14,15}$ = 9.4 and $J_{3,14}$ ~ 3.8 Hz, 1H), 5.4 (1H), 5.37 (s, 1H), 5.22 (br d, 1H, J = 9.4 Hz), 3.74 (s, 3H), 3.70 and 3.55 (s, 3H), 2.65 (s, 3H), 2.07 (s, 3H), 0.96 (t, 3H, $J_{18¢,19¢}$ = 7.5 Hz, 1H), 0.81 (t, 3H, $J_{18,19}$ = 7 Hz); mass spectrum m/z: 792.4085 (calc. 792.4098, $C_{46}H_{56}N_4O_8$, M$^+$) 761, 733, 633, 611, 469, 336, 282.1340 (calcd. 282.1341, $C_{14}H_{20}NO_5$), 136, 135.1043 (calcd. 135.1048, $C_9H_{13}N$), 122, 121, 107.

4.1.1.14. Protoberberine Alkaloids Coreximine (*272*) and Scoulerine (*273*) [Iron–Polonovski Reaction] (*238*)

A mixture of (±)-reticuline N-oxide (**271**) (69 mg, 0.2 mmol) and FeSO$_4$·7H$_2$O (112 mg, 0.4 mmol) in methanol (10 mL) was stirred for 40 hours at 10–15° under a nitrogen atmosphere. After evaporation of the solvent, the residue was partitioned between chloroform and a saturated aqueous solution of sodium hydrogen carbonate. The aqueous layer was further extracted with chloroform. The combined chloroform layers were washed with brine, dried (Na$_2$SO$_4$), and evaporated to give a syrup which was purified by preparative TLC on silica gel, using chloroform–methanol (9:1, v/v) as eluant. The less-polar fraction gave (±)-scoulerine (**273**) (15.2 mg, 23%), which on recrystallization from methanol afforded crystals, mp 183–185°; the IR (CHCl$_3$) and ^{1}H NMR (CDCl$_3$) spectra were identical to those of an authentic sample.

The more polar fraction gave (±)-coreximine (**272**) (27.7 mg, 42%), which on recrystallization from methanol afforded prisms, mp 238–239°; the IR (KBr) and ^{1}H NMR (CDCl$_3$) spectra were superimposable on those of an authentic sample. The most polar fraction gave a mixture (15 mg) of reticuline and N-norreticuline.

4.1.1.15. 1-(4-Methoxybenzyl)-1,2,3,4,5,6,7,8-octahydroisoquinoline [Iron–Polonovski Reaction] (*235*)

To a cooled (ice/salt) stirred solution of 1-(4-methoxybenzyl)-2-methyl-1,2,3,4,5,6,7,8-octahydroisoquinoline (2.71 g, 10 mmol) in 10 mL of dichloromethane was added in small portions over a period of 10 minutes m-chloroperbenzoic acid (2.0 g, 85% purity, 10 mmol). The mixture was stirred for 20 minutes and then treated with iron(II) chloride (0.7 mL of 1 M solution in water). Stirring and cooling were continued for 1 hour and then stirring continued for 2 hours at room temperature. Ethylenediamine (600 mg), sodium hydroxide (10 mL of 2 N solution), and petroleum ether (20 mL) were added and, after vigorous shaking, the layers were separated. The aqueous layer was extracted with 1:3 ether/petroleum ether (2 × 60 mL), and the combined extracts were dried with potassium carbonate, filtered, and concentrated in vacuo. The product was characterized as its cyclobutanecarboxamide by treatment with cyclobutanecarboxylic acid chloride (900 mg, 8 mmol) and triethylamine (1.0 g). The mixture was washed successively with water, dilute hydrochloric acid, and dilute sodium hydroxide.

Drying and evaporation of the solvent gave 2-cyclobutanoyl-1-(4-methoxybenzyl)-1,2,3,4,5,6,7,8-octahydroisoquinoline as an oil, yield: 2.2 g (65%); bp 190–200°/0.3 torr. Anal. Calcd for $C_{22}H_{29}NO_2$: C 77.84; H 8.61; N 4.13. Found: C 77.58; H 8.69; N 4.38.

4.1.1.16. (–)-Nornuciferine (254) [Sulfur Dioxide Polonovski Reaction] (234)

A solution of (–)-nuciferine (0.100 g) in methanol (10 mL) and 30% hydrogen peroxide (2 mL) was stirred at room temperature overnight, after which time TLC showed the complete disappearance of the starting material. A suspension of 5% Pd on charcoal (0.020 g) was added and the mixture was stirred for 2 hours in order to decompose excess hydrogen peroxide. The filtered solution was saturated with sodium chloride and extracted with chloroform. Evaporation of the dried (Na_2SO_4) extract gave an oil, which was further dried by repeated addition of 2:5 methanol–benzene and evaporation in vacuo to give a foam of *N*-oxide **252** (0.100 g). To this foam was added liquid sulfur dioxide (10 mL), followed by *N,N*-dimethylacetamide (1 mL). After 48 hours at about –70°, excess liquid SO_2 was removed, concentrated hydrochloric acid (1 mL) was added, and the mixture was heated (steam bath) until SO_2 was no longer evolved. Basification with aqueous ammonia, followed by chloroform extraction, yielded a crude product (0.043 g) which was purified by chromatography on silica. Elution with chloroform gave a few milligrams of recovered starting material, after which chloroform–methanol (99:1) eluted the major product, which was converted to the hydrochloride. After several crystallizations from methanol–ethyl acetate there was obtained 0.039 g (34%) of pure (–)-nornuciferine hydrochloride, mp 268–270° dec, [α]$_D$ (C_2H_5OH) – 122°.

5. Tabular Survey

The data summarized in the tables were derived by searching *Chemical Abstracts* and by cross referencing each publication. A computer search from 1968 to June 1988 was performed on the CAS Registry File. The earlier literature was searched by hand.

The tabular survey is divided into seven tables, five of which group examples of the use of different activating reagents in the Polonovski reaction. The two other tables deal specifically with application of the acid anhydride promoted Polonovski reaction to macrolides and to the synthesis of coupled indole alkaloids. Within each table the reactions are ordered according to increasing number of carbon atoms of the substrate. Yields are given in parentheses, with a dash indicating that no yield was reported. Some yields have been calculated by the author from the literature data.

The following abbreviations are used throughout the Tables:

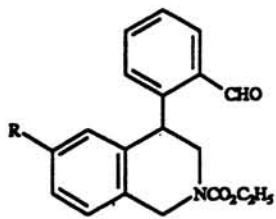|	
Ac	acetyl
TBDMSOTf	*tert*-butyldimethylsilyl triflate
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DMF	*N,N*-dimethylformamide
DPEA	diisopropylethylamine
MCPBA	*m*-chloroperbenzoic acid
THF	tetrahydrofuran
TMAA	tetramethylammonium acetate
TMSCl	trimethylsilyl chloride

Table I. Polonovski Reaction Employing Acylating Reagents

View PDF

Table II. Synthesis of Coupled Indole Alkaloids

[View PDF](#)

Table III. Polonovski Reaction Applied to 16-Macrolides

[View PDF](#)

Table IV. Polonovski Reactions Not Requiring an Acylating Agent

[View PDF](#)

Table V. Iron Salt Initiated Polonovski Reaction

[View PDF](#)

Table VI. Sulfur Dioxide Polonovski Reaction

[View PDF](#)

Table VII. Silicon and Selenium Polonovski Reaction

[View PDF](#)

TABLE I.   Polonovski Reaction Employing Acylating Reagents
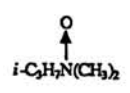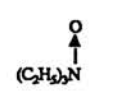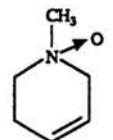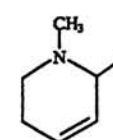
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₃ (CH₃)₂N→O	(CH₃CO)₂O, CH₃CO₂H, 20-40°	(CH₃)₂NCOCH₃ (70)	33
	(CH₃CO)₂O, CHCl₃ , 20-40°	" (82)	33
	CH₃COCl, CHCl₃ , 20-40°	" (42)	33
	C₆H₅COCl, CHCl₃ - C₂H₅N, 20-40°	" (62)	33
	(CF₃CO)₂O, CH₂Cl₂ , 0°	$CH_2=\overset{+}{N}(CH_3)_2$ (100)	99,100
	CH₃COCl (1 eq), CHCl₃ , <15°	(CH₃)₂NCH₂O₂CCH₃ (80)	40
	C₆H₅COCl or CH₃COCl, CH₂Cl₂ , NaHCO₃	H₂CO (60-80)	247
	C₆H₅COCl, H₂O, HCO₃⁻	" (35)	247
	1. CH₃COSC₆H₅ CH₂Cl₂ 2. H₂O-C₂H₅OH, heat	" (15-20)	247
C₅ i-C₃H₇N(CH₃)₂→O	(CH₃CO)₂O, <30°	i-C₃H₇N(CH₃)COCH₃ + (CH₃)₂NCOCH₃ (50) (50)	31
	(CF₃CO)₂O, <30°	(CH₃)₂NCOCF₃ (85)	31
C₆ (C₂H₅)₃N→O	(CH₃CO)₂O, CHCl₃ , 0°	(C₂H₅)₂NCOCH₃ (50-70)	31
(1-methyl-1,2,5,6-tetrahydropyridine N-oxide)	1. (CF₃CO)₂O CH₂Cl₂ , 0° 2. KCN	(1-methyl-2-cyano-1,2,5,6-tetrahydropyridine) (58)	144

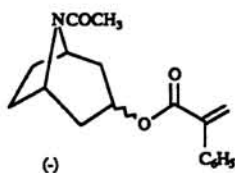TABLE I.   POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
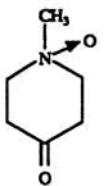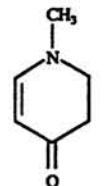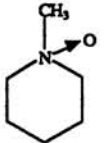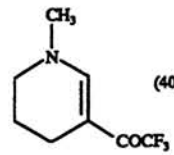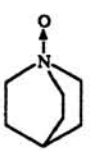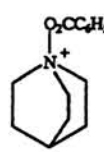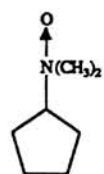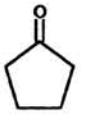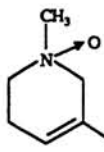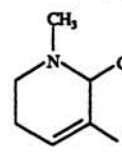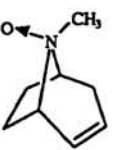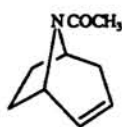
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C$_6$ cont.	(CH$_3$CO)$_2$O, CH$_3$Cl , (C$_2$H$_5$)$_3$N, $-$ 40 to 0°	(50)	120
	(CF$_3$CO)$_2$O, CH$_2$Cl$_2$, 20°	(40)	217
CH$_2$=CH(CH$_2$)$_2$N(CH$_3$)$_2$	(CH$_3$CO)$_2$O, (C$_2$H$_5$)$_2$O, 20°	CH$_2$=CH(CH$_2$)$_2$N(CH$_3$)COCH$_3$ + (CH$_3$)$_2$NCOCH$_3$ I II I : II = 4.5 : 1	248,249
C$_7$	C$_6$H$_5$COCl	(90)	29
	(CH$_3$CO)$_2$O, <30°	+ (CH$_3$)$_2$NCOCH$_3$ (68) (30)	31
	1. (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, 0° 2. KCN	(61-89)	144,151
CH$_2$=CH(CH$_2$)$_3$N(CH$_3$)$_2$	(CH$_3$CO)$_2$O, (C$_2$H$_5$)$_2$O, 20°	CH$_2$=CH(CH$_2$)$_3$N(CH$_3$)COCH$_3$ + (CH$_3$)$_2$NCOCH$_3$ I II I : II = 4.5 : 1	248,249
C$_8$	(CH$_3$CO)$_2$O	(-)	2

166

167

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)

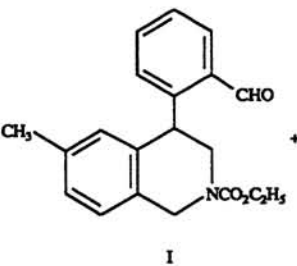| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₈ cont.

	$(CH_3CO)_2O$	(60)	2
	$R = CH_3, n\text{-}C_4H_9$ ... $= R'SO_2Cl$	(-)	250
	"	" (-)	250
	"	(-)	250
	$(CH_3CO)_2O$	(-)	2
$p\text{-}ClC_6H_4N(CH_3)_2$	1. $(CH_3CO)_2O$, -30 to 0° 2. OH⁻	(60) + $p\text{-}ClC_6H_4N(CH_3)_2$ (3) + $p\text{-}ClC_6H_4N(CH_3)COCH_3$ (32)	33
$o\text{-}ClC_6H_4N(CH_3)_2$	1. $(CH_3CO)_2O$, -30 to 0° 2. OH⁻	$o\text{-}ClC_6H_4N(CH_3)COCH_3$ (46) + $o\text{-}ClC_6H_4N(CH_3)_2$ (12)	33
	$(CH_3CO)_2O$, 0°	(50-60)	149

168

169

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)			REFS.

C₈ cont.
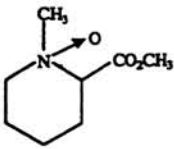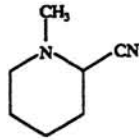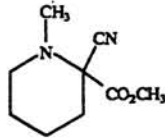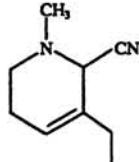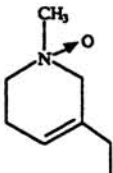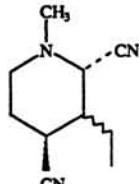
	1. (CH₃CO)₂O, -30 to 0° 2. OH⁻	$C_6H_5N(CH_3)COCH_3$ + o-$HOC_6H_4N(CH_3)_2$ + $C_6H_5N(CH_3)_2$ I II III (27-30) (32) (8)			33
	(CH₃CO)₂O, TMAA (0.4 eq), -30 to 0°	(50-53) (10) (13)			33
	1. (CH₃CO)₂O, H₂O, 0 to 10° 2. OH⁻	(-) (84) (3)			33
	1. (CH₃CO)₂O, CHCl₃ 2. OH⁻	(50) (18-24) (8)			33
	1. (CH₃CO)₂O, DMF 2. OH⁻	(84) (4) (7)			33
	1. (CH₃CO)₂O, THF 2. OH⁻	(90) (1) (2)			33

| | 1. H₂O₂
 2. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
 3. KCN | (53) | | | 107 |
| | 1. MCPBA
 2. (CF₃CO)₂O, CH₂Cl₂, -15 to 0°
 3. KCN | (50) | | | 107 |

| | 1. (CF₃CO)₂O, CH₂Cl₂
 2. KCN | (72) | | | 144 |
| | 1. (CF₃CO)₂O, CH₂Cl₂
 2. (C₂H₅)₂AlCN, KCN | (37) | | | 149 |

TABLE I.   Polonovski Reaction Employing Acylating Reagents (*Continued*)

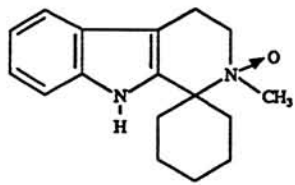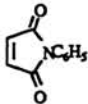| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₈ cont.			
	1. (CF₃CO)₂O, CH₂Cl₂, 0° 2. KCN	(46-70)	144
	(CH₃CO)₂O, <30°	+ H₂CO (98) (30)	31
	(CF₃CO)₂O	+ H₂CO (45-50) (30)	31
	1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20° 2. KCN	 I R= H , R'= CN I : II = 1 : 1 (80) II R= CN, R'= H	251
$CH_2=CH(CH_2)_4N(CH_3)_2 \to O$	(CH₃CO)₂O, (C₂H₅)₂O, 20°	$CH_2=CH(CH_2)_4N(CH_3)COCH_3$ + $(CH_3)_2NCOCH_3$ I II I : II = (4.5 : 1)	248,249
C₉			
$p\text{-}ClC_6H_4CH_2N(CH_3)_2 \to O$	(CH₃CO)₂O, 100°, 1 h	$p\text{-}ClC_6H_4CH_2N(CH_3)COCH_3$ + $(CH_3)_2NCOCH_3$ (12) (78) + $p\text{-}ClC_6H_4CHO$ (74)	30
$p\text{-}O_2NC_6H_4CH_2N(CH_3)_2 \to O$	"	$p\text{-}ClC_6H_4CH_2N(CH_3)COCH_3$ + $(CH_3)_2NCOCH_3$ (7) (45) + $p\text{-}O_2NC_6H_4CHO$ (90)	30,138
$C_6H_5CH_2N(CH_3)_2 \to O$	"	$C_6H_5CH_2N(CH_3)COCH_3$ + $(CH_3)_2NCOCH_3$ (23) (71) + C_6H_5CHO (68)	30,138

TABLE I. Polonovski Reaction Employing Acylating Reagents (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₉ cont.			

o-CH₃C₆H₄N(CH₃)₂

	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
	1. (CH₃CO)₂O, 2. OH⁻	o-CH₃C₆H₄N(CH₃)COCH₃ + o-CH₃C₆H₄N(CH₃)₂ (52) (7-10)	33

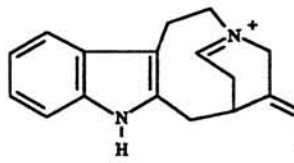p-CH₃C₆H₄N(CH₃)₂

	CONDITIONS	I	II	III	REFS.
	1. (CH₃CO)₂O, -30 to 0° 2. OH⁻	(15)	(72)	(4)	33
	1. (CH₃CO)₂O, 0°, H₂O 2. OH⁻	(-)	(71)	(4)	
	1. (CH₃CO)₂O, CH₃CO₂H, -50° 2. OH⁻	(-)	(80)	(4)	
	1. (CH₃CO)₂O, CHCl₃, 0° 2. OH⁻	(17-23)	(45)	(4)	
	1. (CH₃CO)₂O, DMF, 0° 2. OH⁻	(34)	(18)	(12)	
	1. (CH₃CO)₂O, THF, 0° 2. OH⁻	(53-72)	(19)	(6-12)	

Product structure (I):
CH₃ — aromatic ring with N(CH₃)COCH₃ and OH substituents
+ p-CH₃C₆H₄N(CH₃)COCH₃ (II) + p-CH₃C₆H₄N(CH₃)₂ (III)

p-CH₃OC₆H₄N(CH₃)₂

	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
	1. (CH₃CO)₂O, -30 to 0° 2. OH⁻	CH₃O—ring—N(CH₃)₂, OH (60) + p-CH₃OC₆H₄N(CH₃)COCH₃ (10) + p-CH₃OC₆H₄N(CH₃)₂ (13)	33

m-CH₃OC₆H₄N(CH₃)₂

	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
	1. (CH₃CO)₂O, 2. OH⁻	OH—ring—N(CH₃)₂, OCH₃ (60) + m-CH₃OC₆H₄N(CH₃)COCH₃ (19-24) + m-CH₃OC₆H₄N(CH₃)₂ (7)	33

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
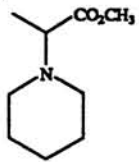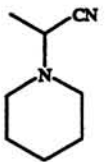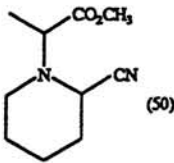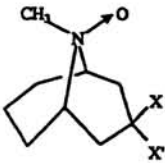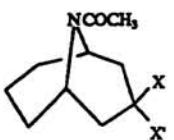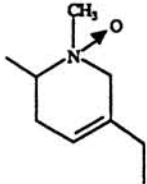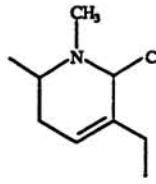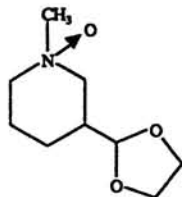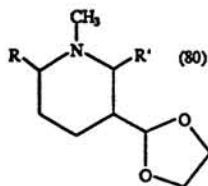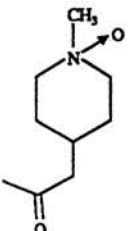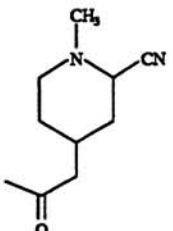
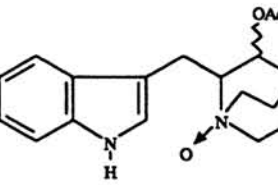| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₉ cont.			
	1. H₂O₂ 2. (CF₃CO)₂O, CH₂Cl₂, 0 to 20° 3. KCN	(55)	107,252
	1. MCPBA 2. (CF₃CO)₂O, CH₂Cl₂, -15 to 0° 3. KCN	(50)	107,252
n-C₇H₁₅N(CH₃)₂	(CH₃CO)₂O, CHCl₃, <30°	*n*-C₇H₁₅N(CH₃)COCH₃ + (CH₃)₂NCOCH₃ (75) (15) + *n*-C₆H₁₃CHO (10)	31
	(CF₃CO)₂O, CHCl₃, <30°	*n*-C₇H₁₅N(CH₃)COCF₃ + (CH₃)₂NCOCF₃ (57) (19) + *n*-C₆H₁₃CHO (24)	31
	(CH₃CO)₂O		2
X= H, X'= OH X= X'= O		X= H, X'= OAc (-) X= X'= O (-)	
	1. (CF₃CO)₂O, CH₂Cl₂, 0° 2. OH⁻	(65-80)	144
	1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20° 2. KCN	(80) I R= CN, R'= H II R= H, R'= CN I : II = 3 : 1 (80)	251,253
	1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20° 2. KCN	(74)	143

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
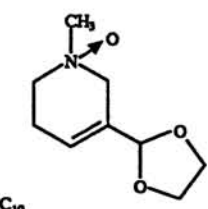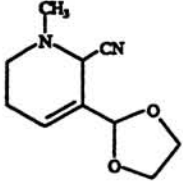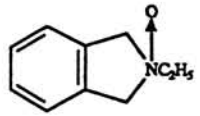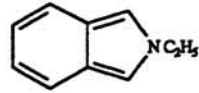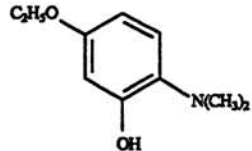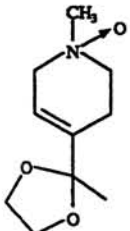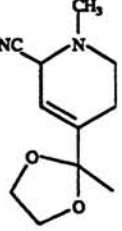
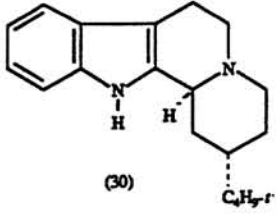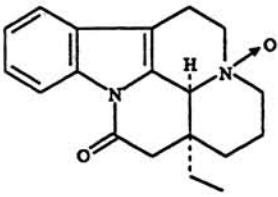| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₉ cont.			
	1. (CF₃CO)₂O, CH₂Cl₂, 0° 2. KCN	(52)	254
C₁₀			
m-CF₃C₆H₄CH₂N(CH₃)₂	(CH₃CO)₂O, 100°, 1 h	m-CF₃C₆H₄CH₂N(CH₃)COCH₃ + (CH₃)₂NCOCH₃ (12) (76)	30
p-CH₃C₆H₄CH₂N(CH₃)₂	"	p-CH₃C₆H₄CH₂N(CH₃)COCH₃ + (CH₃)₂NCOCH₃ (13) (67)	30
p-CH₃OC₆H₄CH₂N(CH₃)₂	"	p-CH₃OC₆H₄CH₂N(CH₃)COCH₃ + (CH₃)₂NCOCH₃ (17) (73)	30,138
	(CF₃CO)₂O, 20°	Polymer	138
	(CH₃CO)₂O, (C₂H₅)₃N, 0°	(75)	171
p-C₂H₅OC₆H₄N(CH₃)₂	1. (CH₃CO)₂O, -30 to 0° 2. OH⁻	(60)	33
C₆H₅N(C₂H₅)₂	1. (CH₃CO)₂O, -30 to 0° 2. OH⁻	C₆H₅N(C₂H₅)COCH₃ + o-HOC₆H₄N(C₂H₅)₂ (35) (4)	33
	1. (CF₃CO)₂O, CH₂Cl₂, 0° 2. KCN	(45-90)	145,146

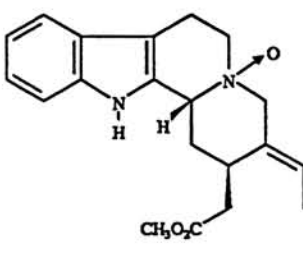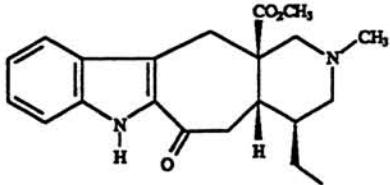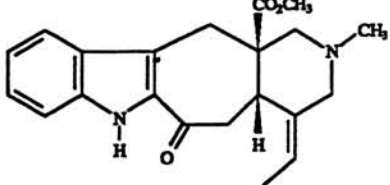TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
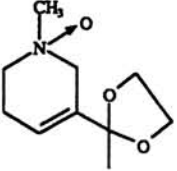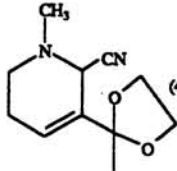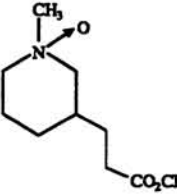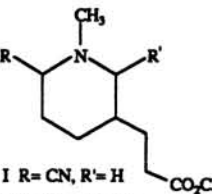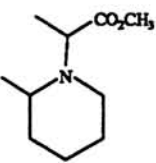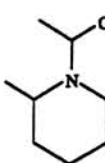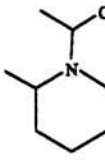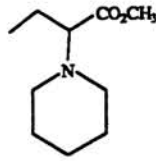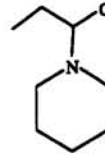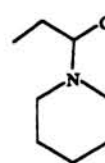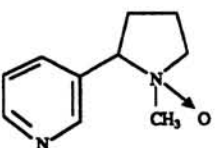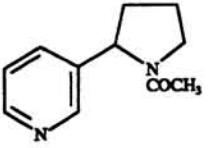
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C$_{10}$ cont.

1. (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, 0°
2. KCN

(45-65)

254

1. (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, 0 to 20°
2. KCN

I R= CN, R'= H
II R= H , R'= CN
I : II= 1 : 1 (80)

251

1. H$_2$O$_2$
2. (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, 0 to 20°
3. KCN

(31)

107

1. MCPBA
2 (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, -15 to 0°
3. KCN

(43)

107

1. H$_2$O$_2$
2. (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, 0 to 20°
3. KCN

(48)

107

1. MCPBA
2 (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, -15 to 0°
3. KCN

(42)

107

(CH$_3$CO)$_2$O, 20 to 100°

(-)

2

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)

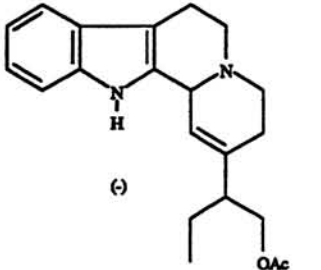| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₁₁ (structure)	(CH₃CO)₂O, 0°, 12 h	(structure) (50-60)	170
(structure)	1. H₂O₂ 2. (CF₃CO)₂O, CH₂Cl₂, 0 to 20° 3. KCN	(structure) (48)	107
	1. MCPBA 2. (CF₃CO)₂O, CH₂Cl₂, -15 to 0° 3. KCN	(structure) (61)	107
(structure)	(CH₃CO)₂O, CHCl₃, heat	(structure) (71)	42
C₁₂ (structure)	1. (CF₃CO)₂O, CH₂Cl₂, -78 to 20° 2. OH⁻	(structure) (56)	111
(structure)	(CH₃CO)₂O, 0°	(structure) (50-60)	170
(structure)	1. (CF₃CO)₂O, CH₂Cl₂, 0° 2. KCN	(structure) (70)	255
(structure)	(CH₃CO)₂O, (C₂H₅)₃N, 0°	(structure) (75)	171

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₁₂ cont.			
	1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20° 2. KCN	 I R= H , R'= CN II R= CN , R'= H I : II = 1 : 3 (80)	251,256
	(CF₃CO)₂O, CH₂Cl₂, -50 to 0°	(90)	167
	(CH₃CO)₂O, <30°	 R= CH₃ (64) (36) R= CF₃ (30) (70)	31
	(CF₃CO)₂O		
	(CH₃CO)₂O, <30°	 R= CH₃ (64) (17) R= CF₃ (40) (40)	31
	(CF₃CO)₂O		
m,p-(CH₃O)₂C₆H₃(CH₂)₂N(CH₃)₂	(CF₃CO)₂O, 20°, 1 h	 (33)	138
C₁₃			
(C₆H₅)₂NCH₃	C₆H₅COCl, C₅H₅N	(C₆H₅)₂NCOC₆H₅ + *o*-HOC₆H₄N(CH₃)C₆H₅ (4) (26) + (C₆H₅)₂NCH₃ (26-34)	33

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
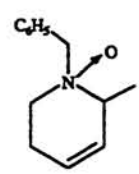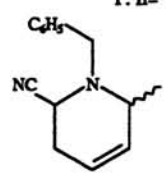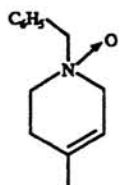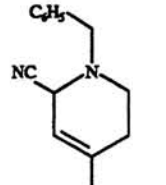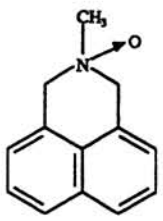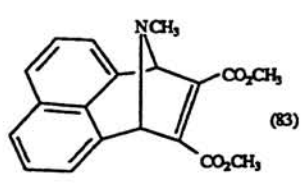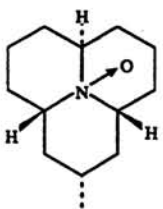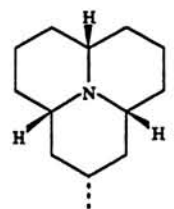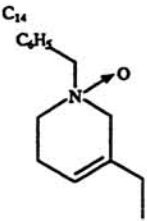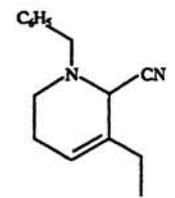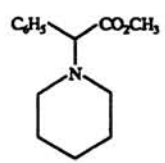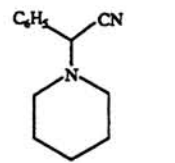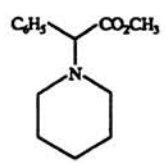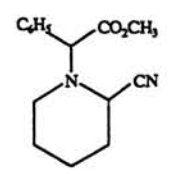
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₁₃ cont.

	(CH₃CO)₂O, (C₂H₅)₂O, 20°	CH₂=CH(CH₂)₃N(CH₃)₂ + (CH₃)₂NCOCH₃	248,249
		I II	
		I : II = 4.5 : 1	

| | 1. (CF₃CO)₂O, CH₂Cl₂, 0°
 2. KCN | (57) | 255 |

| | 1. (CF₃CO)₂O, CH₂Cl₂, 0°
 2. KCN | (60) | 255 |

| | (CH₃CO)₂O, (C₂H₅)₃N, -10°
 CH₃O₂CC≡CCO₂CH₃ | (83) | 23 |

| | 1. ClCO₂CH₃, CH₂Cl₂, 0 to 20°
 2. H₂-Pt | (60) | 37 |

C₁₄

| | 1. (CF₃CO)₂O, CH₂Cl₂, 0°
 2. KCN | (69) | 144,255 |

| | 1. H₂O₂
 2. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
 3. KCN | (31) | 107 |

| | 1. MCPBA
 2. (CF₃CO)₂O, CH₂Cl₂, -15 to 0°
 3. KCN | (43) | 107 |

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
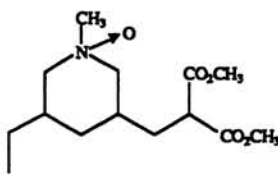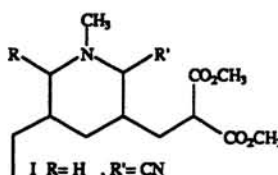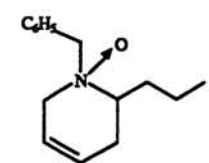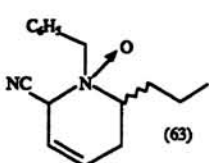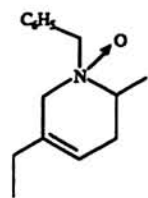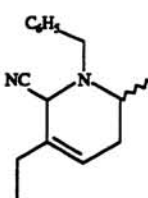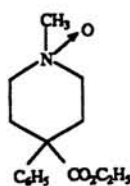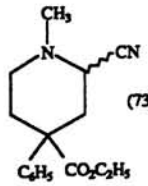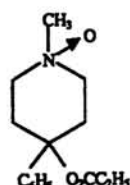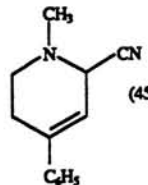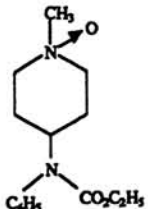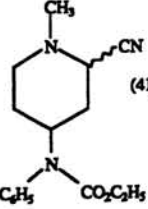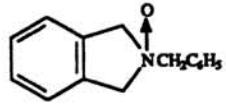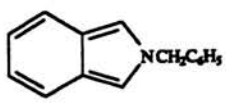
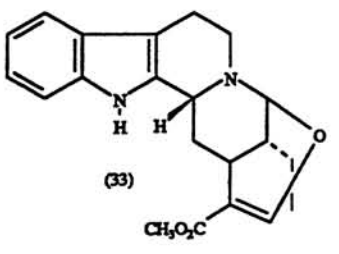| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₁₄ cont.

1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
2. KCN

I R= H , R'= CN
II R= CN , R'= H

I : II= 1 : 1 (80)

251,256

C₁₅

1. (CF₃CO)₂O, CH₂Cl₂, 0°
2. KCN

(63)

148,255

1. (CF₃CO)₂O, CH₂Cl₂, 0°
2. KCN

(63)

255

1. (CF₃CO)₂O, 0 to 50°
2. KCN

(73)

257

1. (CF₃CO)₂O, 0 to 50°
2. KCN

(45)

257

1. (CF₃CO)₂O, 0 to 50°
2. KCN

(41)

257

(CH₃CO)₂O, (C₂H₅)₃N, 0°

(75)

171

TABLE I.   POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
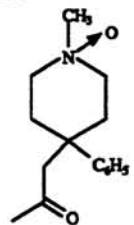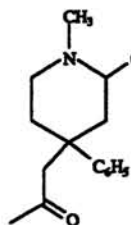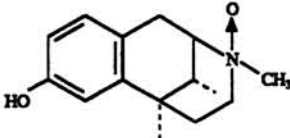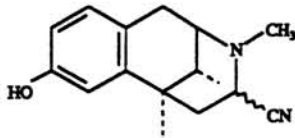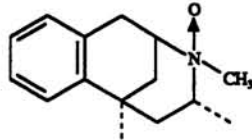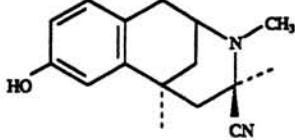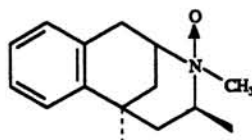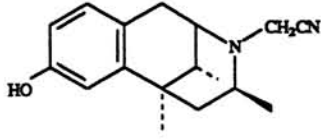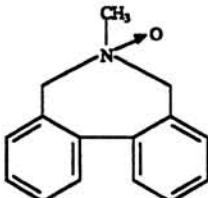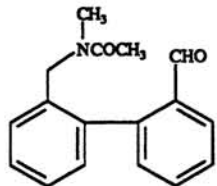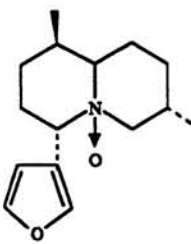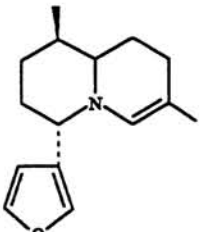
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₁₅ cont.			
	1. (CF₃CO)₂O, CH₂Cl₂ , 0 to 20° 2. KCN	(87)	143
	1. (CF₃CO)₂O, 0 to 50° 2. KCN	(67)	153,257
	1. (CF₃CO)₂O, 0 to 50° 2. KCN	(60)	110
	1. (CF₃CO)₂O, 0 to 50° 2. KCN	(86)	110
	(CH₃CO)₂O	(-)	23
	(CH₃CO)₂O, CHCl₃ , 0 - 20°, 120 h	(82)	36

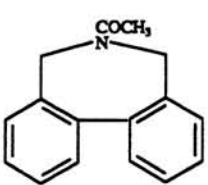TABLE I.   POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
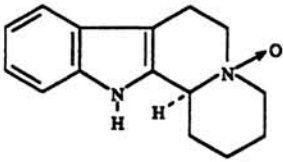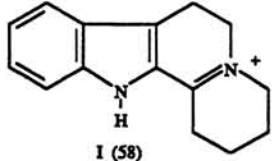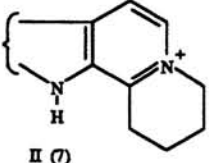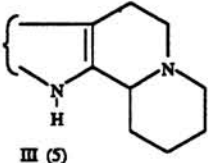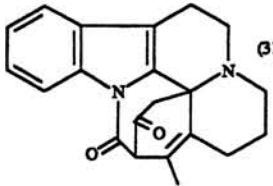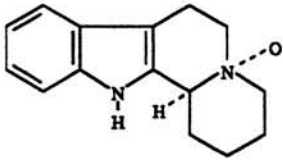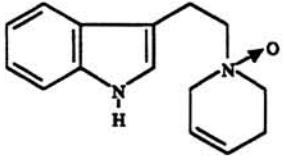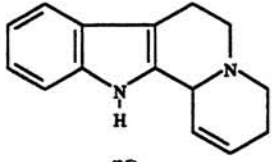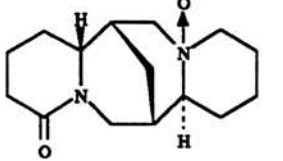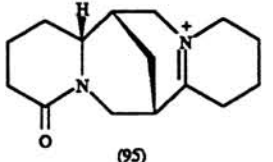
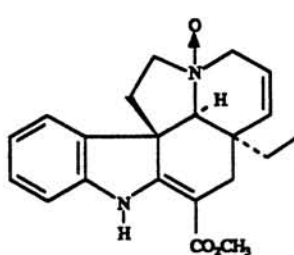| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₁₅ cont.

| | (CH₃CO)₂O, CH₃CO₂H, heat | I (58) | 119 |

II (7)   III (5)

	(CF₃CO)₂O, CF₃CO₂H, heat	I (67) + II (4) + III (0.2)	119
	CF₃CO₂H, CH₂Cl₂, 20 min	I (50)	119
	(CH₃CO)₂O, CH₂Cl₂	(31)	119

	(CH₃CO)₂O, CH₃CO₂H, heat	I (31) + II (16) + III (16)	119
	(CF₃CO)₂O, CF₃CO₂H, heat	I (70) + II (7) + III (0.1)	119
	(CF₃CO)₂O, CH₂Cl₂, 20°	I (50)	119

| | 1. (CF₃CO)₂O, CF₃CO₂H, 0 to 20° 2. HCl, 70° | (35) | 140,258 |

| | (CH₃CO)₂O, 50°, 5 h | (95) | 112 |

192

193

TABLE I.   POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
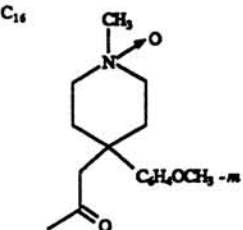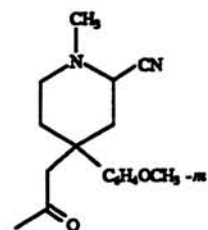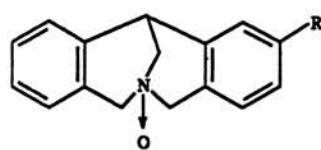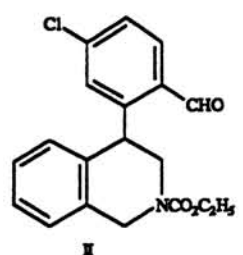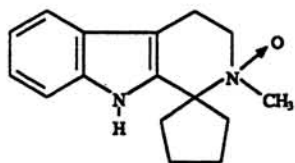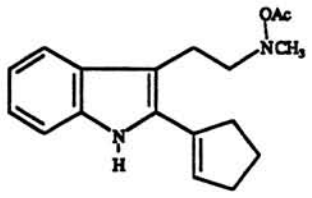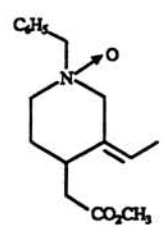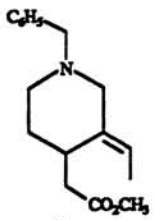
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C_{16}	1. $(CF_3CO)_2O$, CH_2Cl_2, 0 to 20° 2. KCN	(56)	143
R=H	1. $(CF_3CO)_2O$ 2. $ClCO_2C_2H_5$	I R=H (95)	39,106
R= Cl	1. $(CF_3CO)_2O$ 2. $ClCO_2C_2H_5$	I· R= Cl + II I : II = 1 : 1.7 (95)	39,106
	$(CF_3SO_2)_2O$	I : II = 1 : 1.2 (80)	39,106
	$(CH_3CO)_2O$, CH_2Cl_2, 0°	(83)	208
C_{17}	1. $(CF_3CO)_2O$ 2. $NaBH_4$	(-)	108

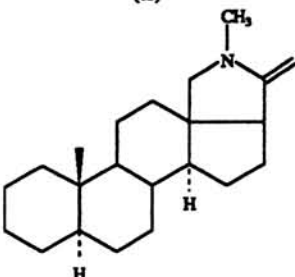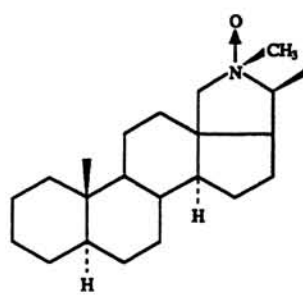TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
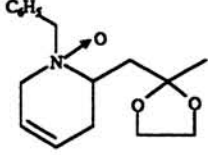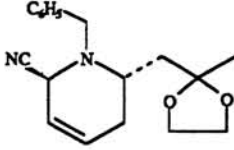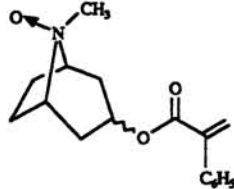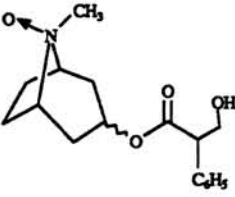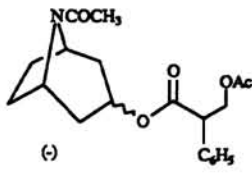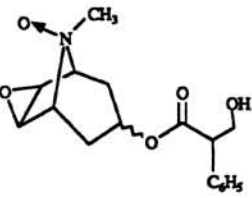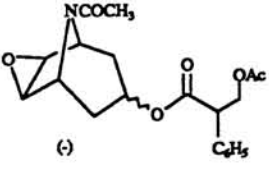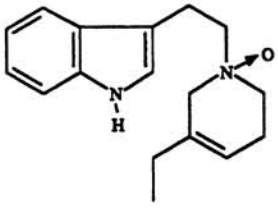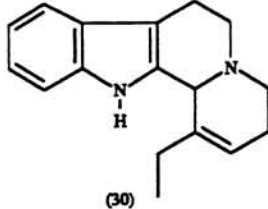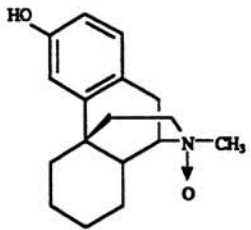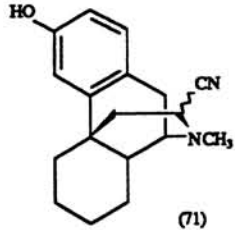
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₁₇ cont.

	1. (CF₃CO)₂O, CH₂Cl₂, 0° 2. KCN	(71)	147
	(CH₃CO)₂O	(-)	2
	(CH₃CO)₂O	(-)	2
	(CH₃CO)₂O	(-)	2
	1. (CF₃CO)₂O, CF₃CO₂H, 0 to 20° 2. HCl, 70°	(30)	140,258
	1. (CF₃CO)₂O, 0 to 50° 2. KCN	(71)	153,257

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
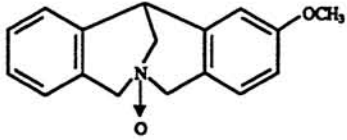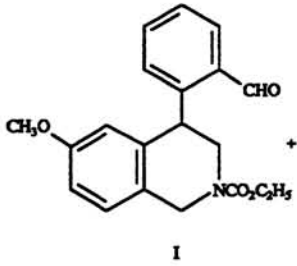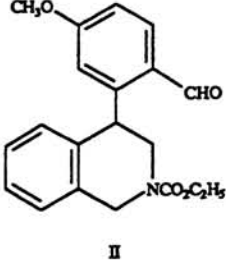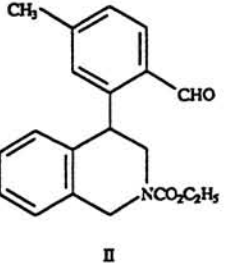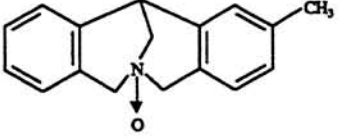
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₁₇ cont.

39,106

I   II

	1. (CH₃CO)₂O, CH₂Cl₂, 20° 2. ClCO₂C₂H₅	I : II = 2 : 1 (75)	
	1. (CH₃CO)₂O, (C₂H₅)₃N, 20° 2. ClCO₂C₂H₅	I : II = 3 : 1 (71)	
	1. CH₃COCl, CH₂Cl₂, 20° 2. ClCO₂C₂H₅	I : II = 1 : 1 (92)	
	1. (CF₃CO)₂O, CH₂Cl₂ 0° 2. ClCO₂C₂H₅	I : II = 1 : 1 (95)	
	1. (CF₃SO₂)₂O, CH₂Cl₂, 0° 2. ClCO₂C₂H₅	I : II = 1 : 5 (89)	
	1. p-CH₃C₆H₄SO₂Cl, CH₂Cl₂, 20° 2. ClCO₂C₂H₅	I : II = 1 : 1.3 (63)	
	1. CF₃SO₂Cl, CH₂Cl, 20° 2. ClCO₂C₂H₅	I : II = 1 : 1.8 (25)	

39,106

I   II

| | 1. (CF₃CO)₂O, CH₂Cl₂ 0°
2. ClCO₂C₂H₅ | I : II = 1.8 : 1 (85) | |
| | 1. (CF₃SO₂)₂O, CH₂Cl₂, 0°
2. ClCO₂C₂H₅ | I : II = 1 : 1 (76) | |

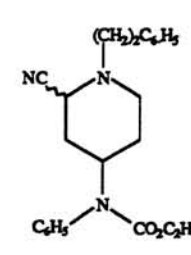TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
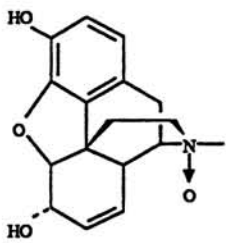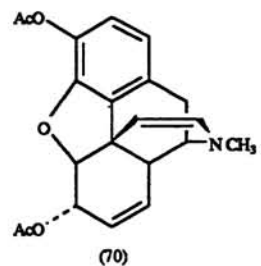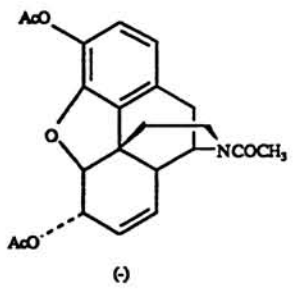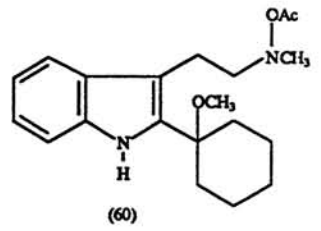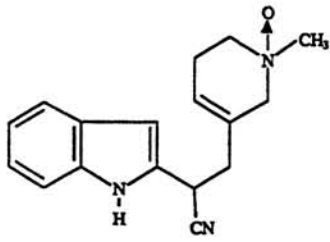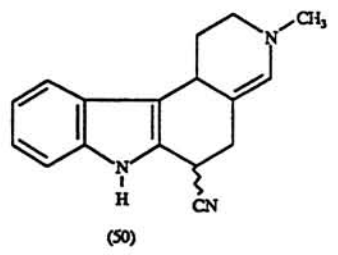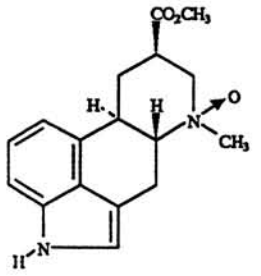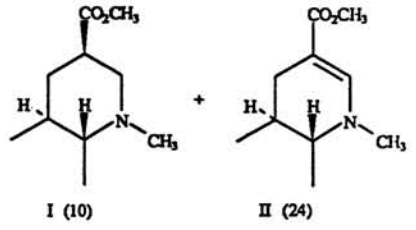
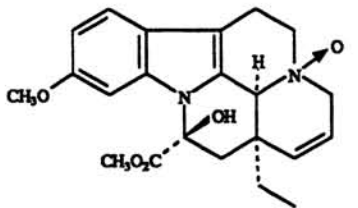| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C17 cont.

CH3COCl, 65°, 3 h

(70)

35

(CH3CO)2O

(-)

259

1. (CF3CO)2O , CH2Cl2, 0°
2. CH3OH

(60)

208

(CF3CO)2O, CH2Cl2, 0 to 20°

(50)

140

(CH3CO)2O, CHCl3

I (10)   II (24)

120

(CH3CO)2O, CH2Cl2, (C2H5)3N, -40 to 0°

I (<3)   II (45-50)

TABLE I.   POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
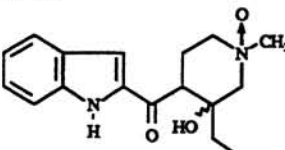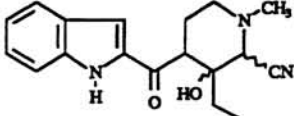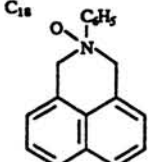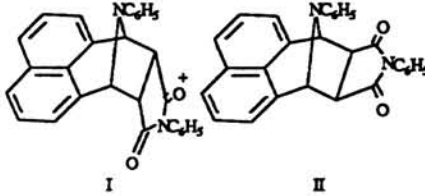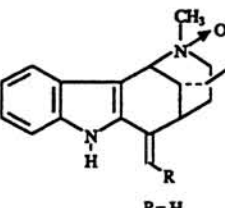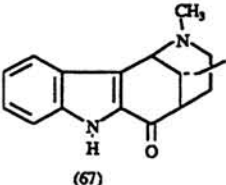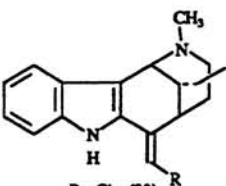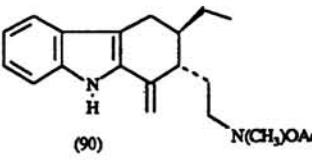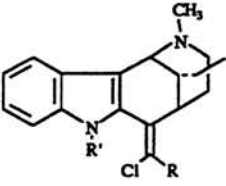
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C_{17} cont.

$(CF_3CO)_2O$, CH_2Cl_2

(41)

260

C_{18}

$(CH_3CO)_2O$, $(C_2H_5)_3N$, -10°

(with N-phenylmaleimide structure)

I + II (52)

125

R = H

1. $(CF_3CO)_2O$, dioxane, 0°
2. NaHCO$_3$

(67)

261

R = H

CH$_3$COX
X = Cl
X = Br
X = I

R = Cl   (80)
R = Br   (40)
R = I   (25)

261

R = H

1. CH$_3$COCl, CH$_2$Cl$_2$, -60°
2. NaBH$_4$

N(CH$_3$)OAc

(90)

261

R = Cl

CH$_3$COCl

I (R = Cl, R' = H) , II (R = H, R' = Cl)
I : II = (40) : (40)

261

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
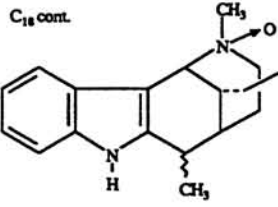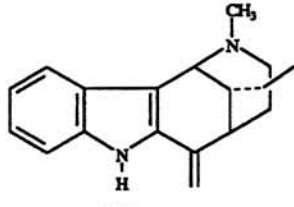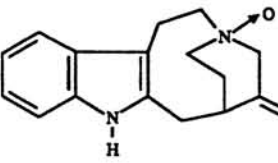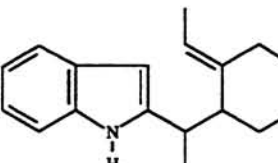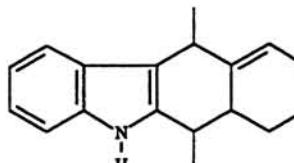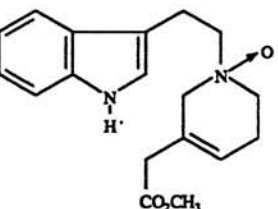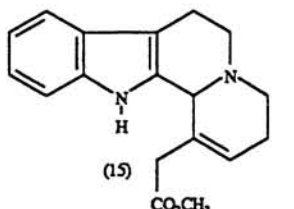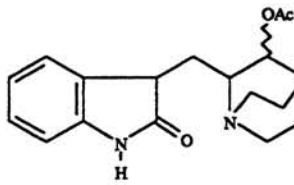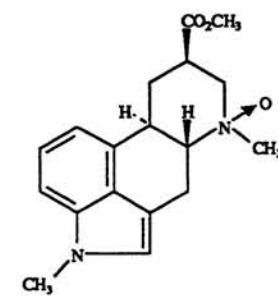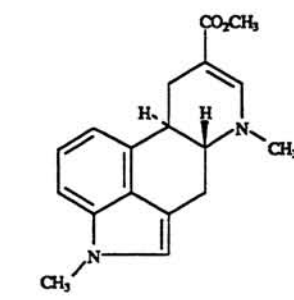
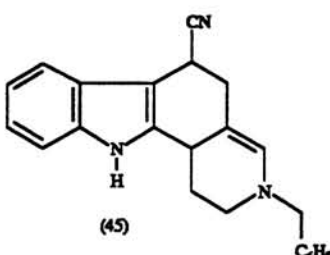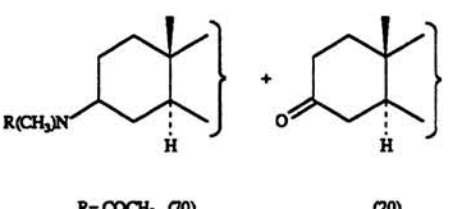| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₁₈ cont.	(CF₃CO)₂O, CH₂Cl₂	(85)	261
	(CF₃CO)₂O, CH₂Cl₂, -78 to 20°	(-)	139
	(CF₃CO)₂O, CH₂Cl₂, 0°	(92)	141
	1. (CF₃CO)₂O, CH₂Cl₂ 2. CH₃OH, heat	(15)	258,140
	(CF₃CO)₂O, CH₂Cl₂	(40)	210
	(CH₃CO)₂O, CH₂Cl₂, (C₂H₅)₃N -40 to 0°	(47)	120

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
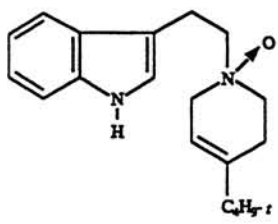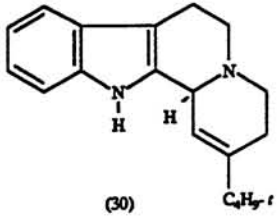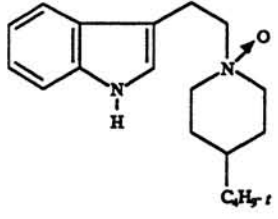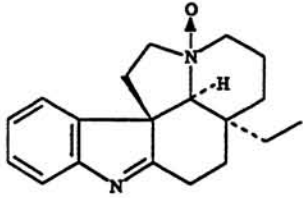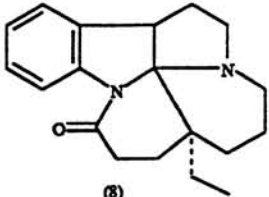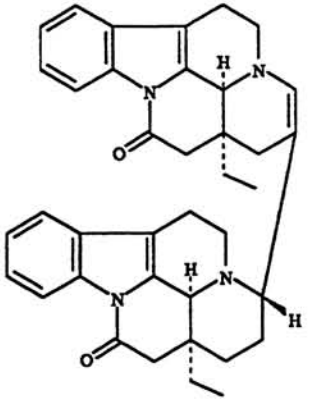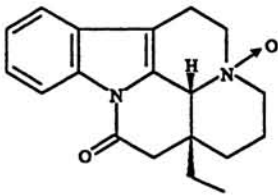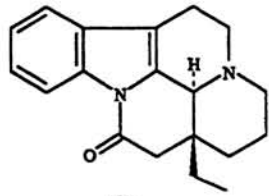
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₁₉			

	1. $(CF_3CO)_2O$, CH_2Cl_2, 20° 2. HCl, heat		258,140
		(30)	
	1. $(CF_3CO)_2O$, CH_2Cl_2, 20° 2. HCl, heat		258,140
		(30)	
	1. $(CF_3CO)_2O$, CH_2Cl_2, 0° 2. HCl, 60°		213
		(8)	
	$(CH_3CO)_2O$, 20°, 24 h		160
		(52)	
	1. $(CF_3CO)_2O$, CH_2Cl_2, 0 to 20° 2. NaCNBH₃		126
		(50)	

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
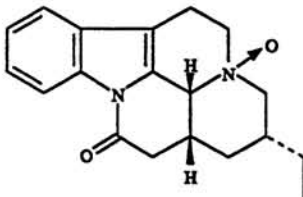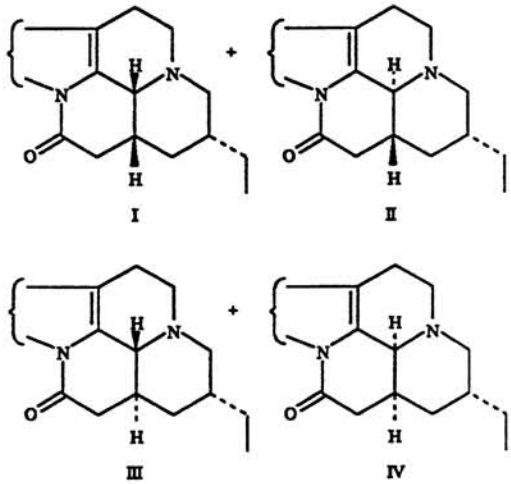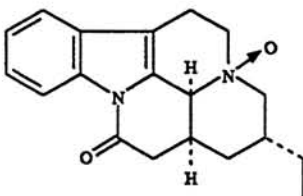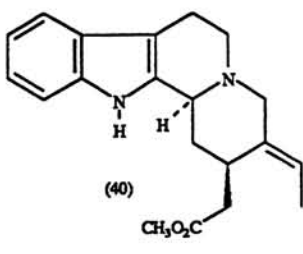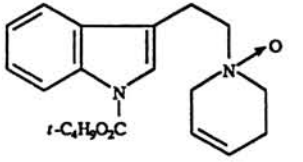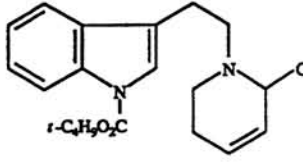
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₁₉ cont.

1. (CF₃CO)₂O, 50°, 2 h
2. NaBH₄, CH₃OH

I + II

III + IV

I : II : III : IV = 25 : 45 : 20 : 4

262

1. (CF₃CO)₂O, 50°, 2 h
2. NaBH₄, CH₃OH

I : II : III : IV = 25 : 45 : 20 : 4

262

C₂₀

1. (CF₃CO)₂O, CH₂Cl₂, -78 to 0°
2. NaBH₄

(40)

137

1. (CF₃CO)₂O, CH₂Cl₂, -15°
2. KCN

(43)

149

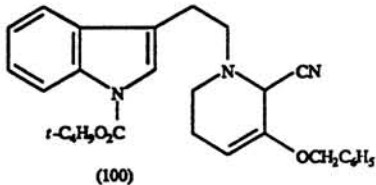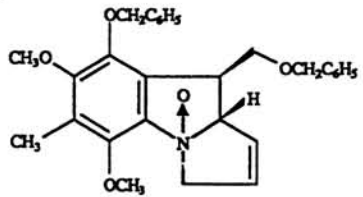TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
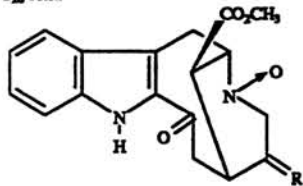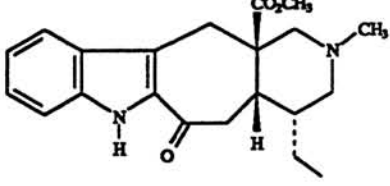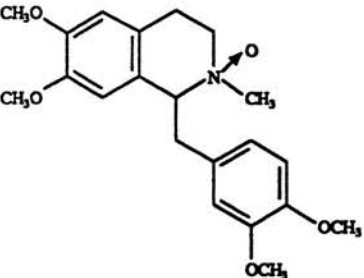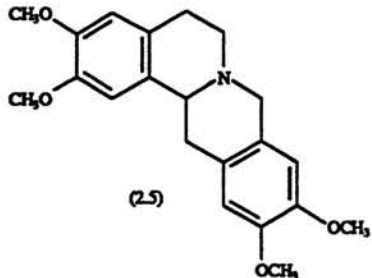
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₂₀ cont. R = H, (R)- C₂H₅	1. (CF₃CO)₂O, 0 to 20° 2. NaCNBH₃	 (90)	176
	CF₃CO₂COCH₃, CH₂Cl₂, 20°	" (87)	161
	(CH₃CO)₂O, 20° 15 h	 (80)	161
	CH₃COCl, NaOH, CH₂Cl₂	" (88)	161
R = H, (S)- C₂H₅	1. (CF₃CO)₂O, 0 to 20° 2. NaCNBH₃	 (50)	176
R = CHCH₃	1. (CF₃CO)₂O, 0 to 20° 2. NaCNBH₃	 (5)	176
C₂₁	(CF₃CO)₂O, 20°, 1 h	 (2.5)	138

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
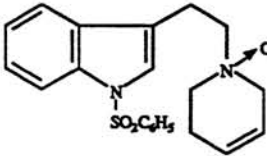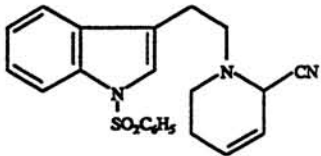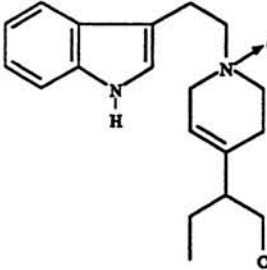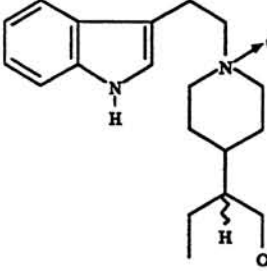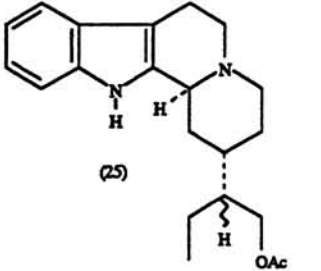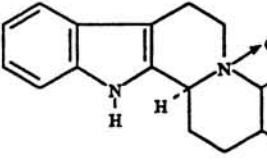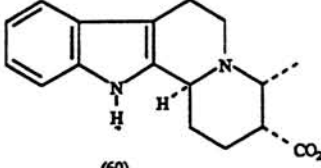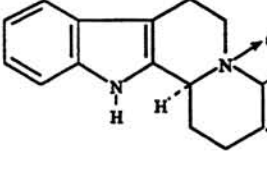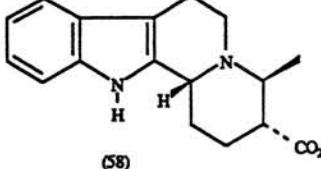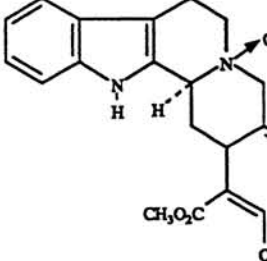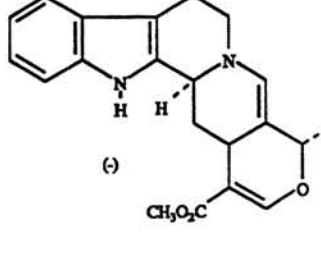
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₂₁ cont.

1. (CF₃CO)₂O, CH₂Cl₂, 0°
2. KCN

(52) — 150

1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
2. HCl, heat

(-) — 258,140

1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
2. HCl, heat

(25) — 136

1. (CF₃CO)₂O, CH₂Cl₂, 0°
2. NaBH₄

(60) — 263

1. (CF₃CO)₂O, CH₂Cl₂, 0°
2. NaBH₄

(58) — 263

(CF₃CO)₂O, CH₂Cl₂

(-) — 158

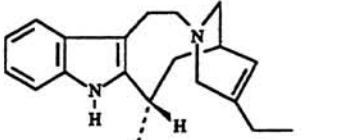TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
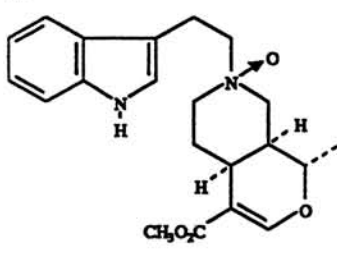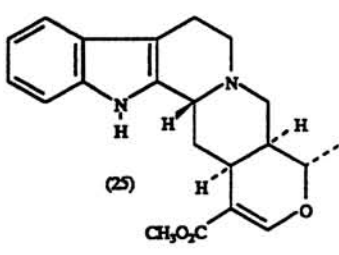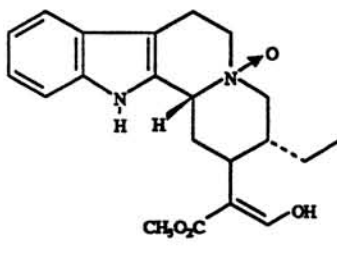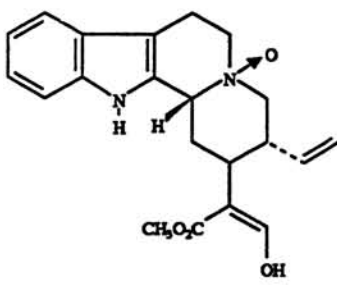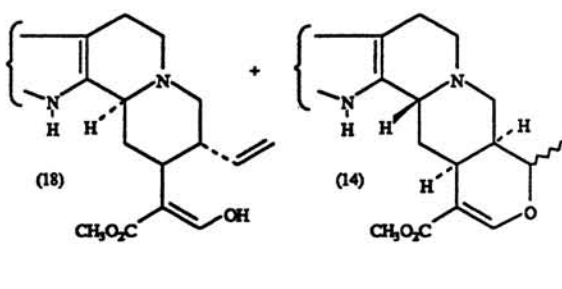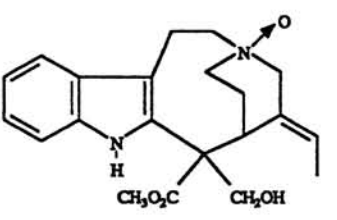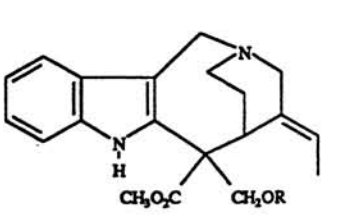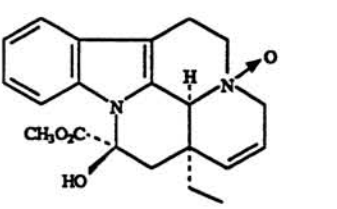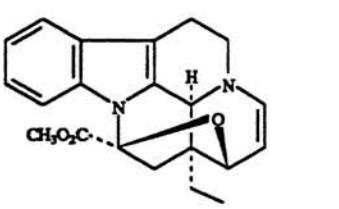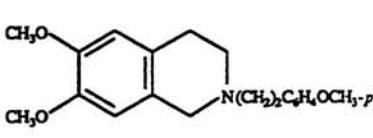
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₂₁ cont.

(CF₃CO)₂O, CF₃CO₂H - CH₂Cl₂, 20°

(25)

132,133

(CF₃CO)₂O, CH₂Cl₂, 0°

(33)

128

1. (CF₃CO)₂O, CH₂Cl₂, -78°
2. NaCNBH₃

(18)   +   (14)

264

1. (CF₃CO)₂O, CH₂Cl₂, -5°
2. OH⁻

R = H   (25)
R = COCH₃ (12)

175

(CF₃CO)₂O, CH₂Cl₂, 0° to 20°

(20)

265

(*m*,*p*-CH₃OC₆H₄(CH₂)₂)₂NCH₃

(CF₃CO)₂O, CH₂Cl₂, 0°

(7)

138
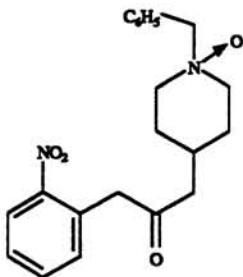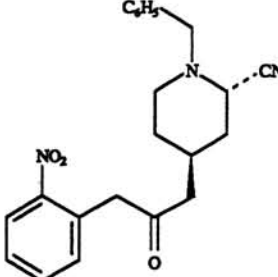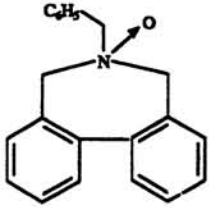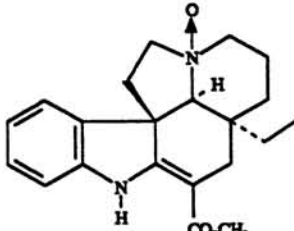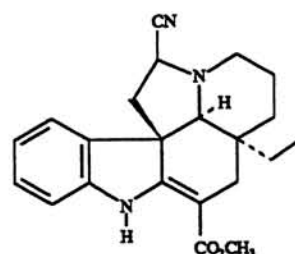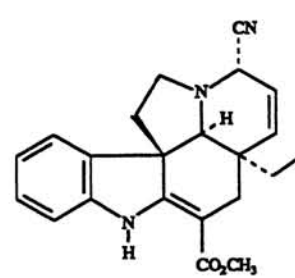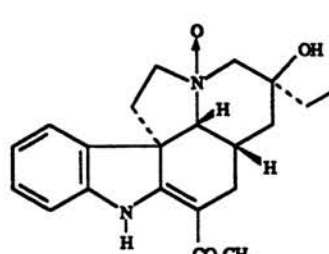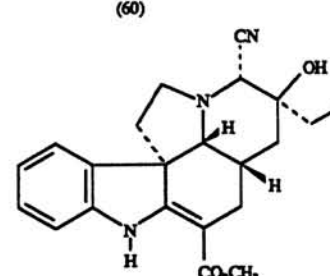
214

215

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₂₁ cont.

1. (CF₃CO)₂O, CH₂Cl₂, 0°
2. KCN

266

(70)

(CH₃CO)₂O

23

(-)

1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
2. KCN

154

(50)

1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
2. KCN

154

(60)

1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
2. KCN

154
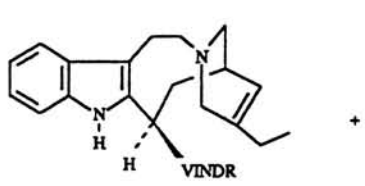
TABLE I.   POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
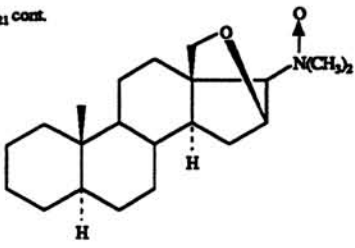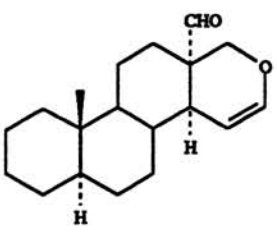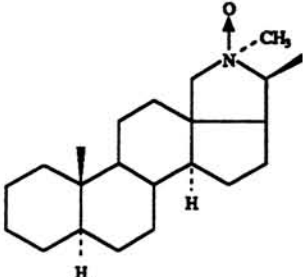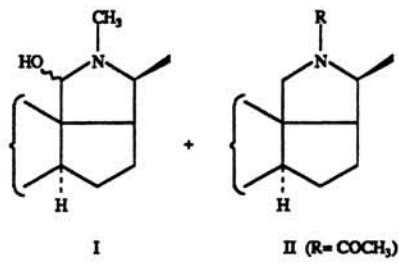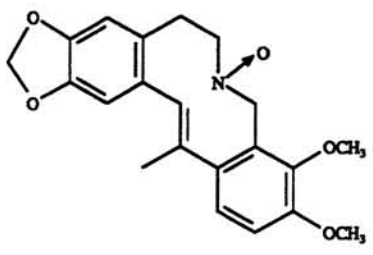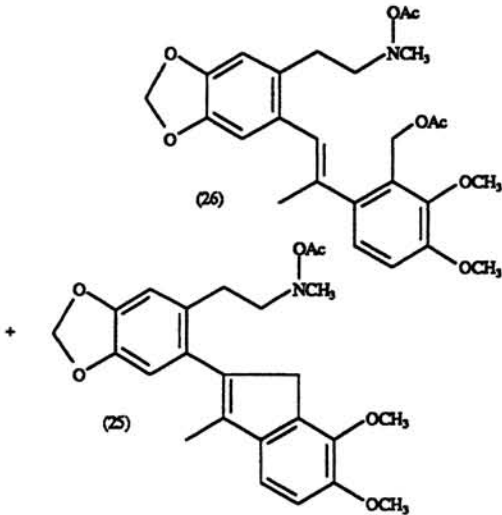
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₂₁ cont.	(CF₃CO)₂O, CH₂Cl₂, 0 to 20°	 (65)	173,99
	(CH₃CO)₂O or (CF₃CO)₂O	 (-)	130
	(CH₃CO)₂O	 I : II = 1 : 4	130
	(CF₃CO)₂O	I + II (R=H) I : II = 1 : 4	130
	(CH₃CO)₂O		209

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
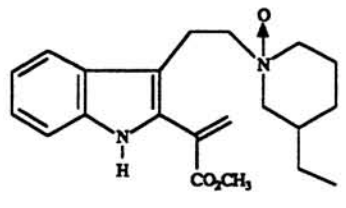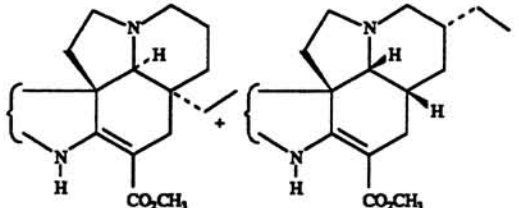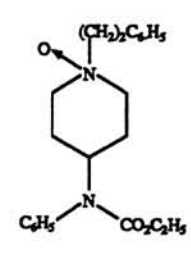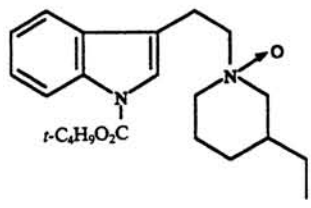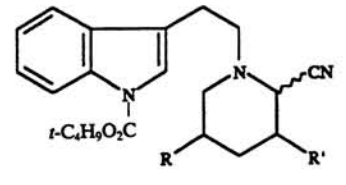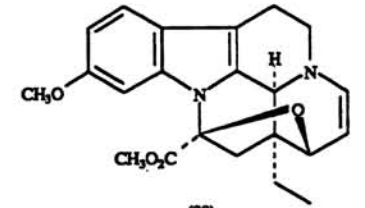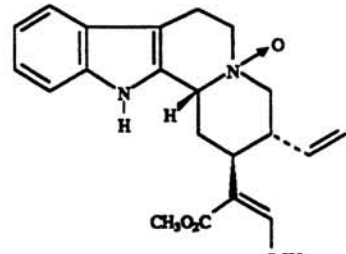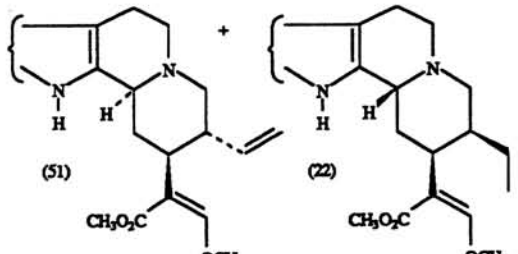
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₂₁ cont.

	(CH₃CO)₂O, C₅H₅N, 20°	(12) (-)	159

C₂₂

	1. (CF₃CO)₂O, 0 to 50° 2. KCN	(45)	257

	1. (CF₃CO)₂O, CH₂Cl₂, 0° 2. KCN	I R=H, R'=C₂H₅ + II R=C₂H₅, R'=H I : II = 3 : 2 (70)	251

	(CF₃CO)₂O, CH₂Cl₂, 0 to 20°	(20)	140

	1. (CF₃CO)₂O, CH₂Cl₂, 0° 2. NaCNBH₃	(51) (22)	264

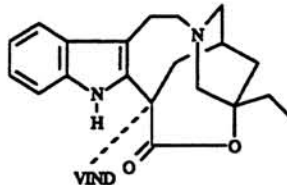TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
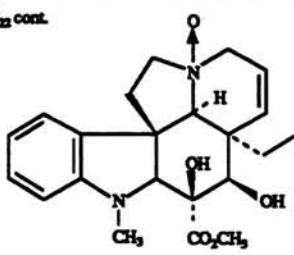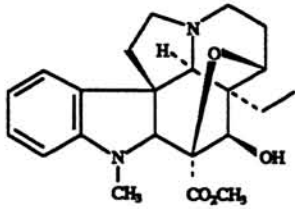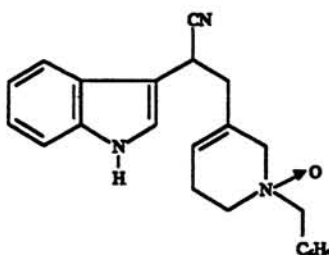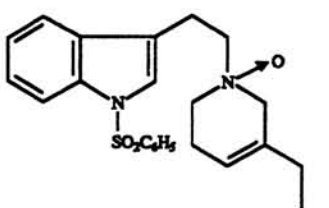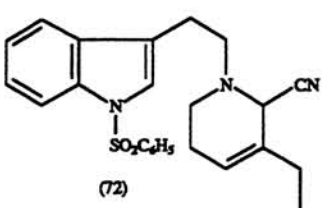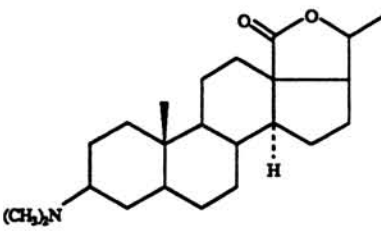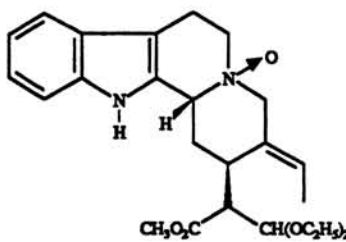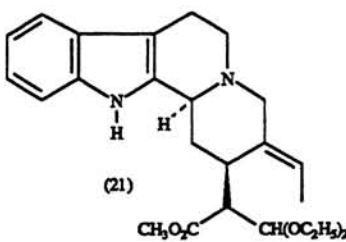
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₂₂ cont.

1. (CF₃CO)₂O, CH₂Cl₂, 0°
2. NaBH₄

(50)

155

(CF₃CO)₂O, CH₂Cl₂, 0° to 20°

(45)

140

1. (CF₃CO)₂O, CH₂Cl₂, 0°
2. KCN

(72)

150

(CH₃CO)₂O, CHCl₃, 40°, 3 h

R= COCH₃ (70)   (20)

12

1. (CF₃CO)₂O, CHCl₃
20°, 0.5 h
2. NaHCO₃

R= H (40)   (55-60)

12

C₂₃

1. (CF₃CO)₂O, CH₂Cl₂, -78 to 0°
2. NaBH₄

(21)

137

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
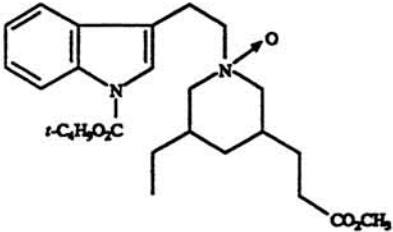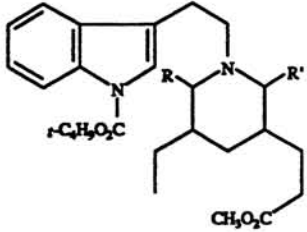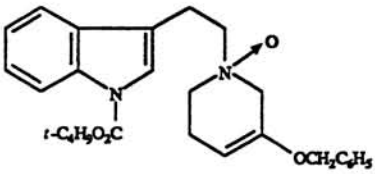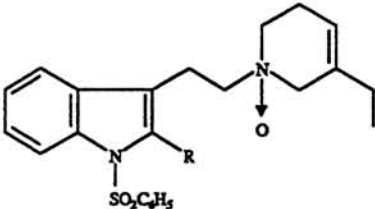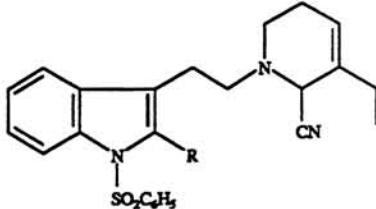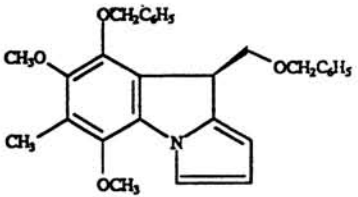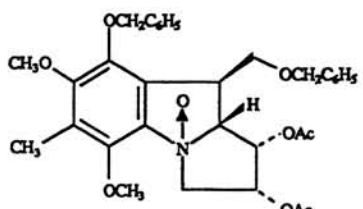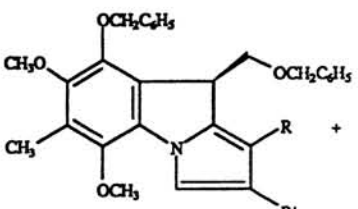
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₂₆

1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
2. KCN

I R= CN, R'= H   II R= H R'= CN

I : II = 1 : 1 (75)

267

C₂₇

1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
2. KCN

(100)

142

1. (CF₃CO)₂O, CH₂Cl₂, 0 to 20°
2. KCN

268

I   R= C(OH)(CO₂CH₃)CH₃

II R= C(CO₂CH₃)=CH₂

I (>90)

II (74)

C₂₉

(CH₃CO)₂O

(73)

172

C₃₃

(CH₃CO)₂O, CH₃OH - CDCl₃

R= OAc, R'= H (9)

R= H , R'= OAc (2)

172

TABLE I. POLONOVSKI REACTION EMPLOYING ACYLATING REAGENTS (*Continued*)
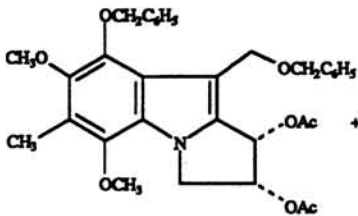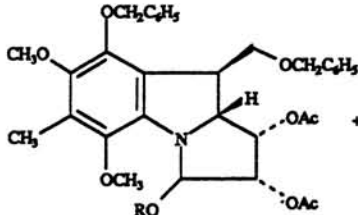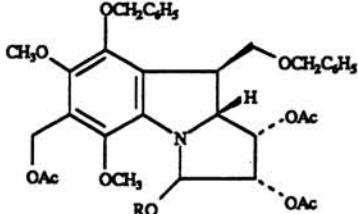
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C$_{33}$ cont.			

(25)

R = CH$_3$ (20)

R = H   (6)

(18)

TABLE II. Synthesis of Coupled Indole Alkaloids

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₁₉
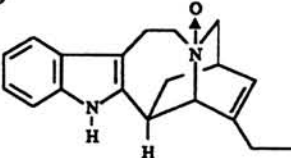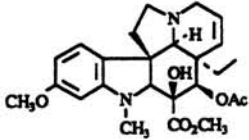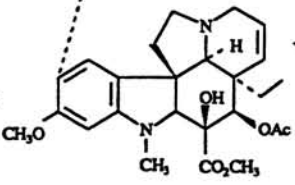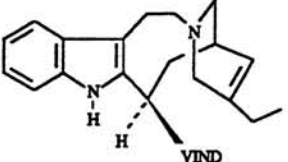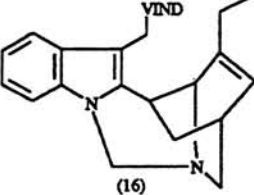
1. (CF₃CO)₂O, CH₂Cl₂, -50°,

VINDOLINE

2. NaBH₄

269,270

VIND =

(8)

(-)

(16)

TABLE II. SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
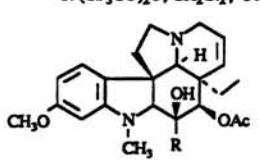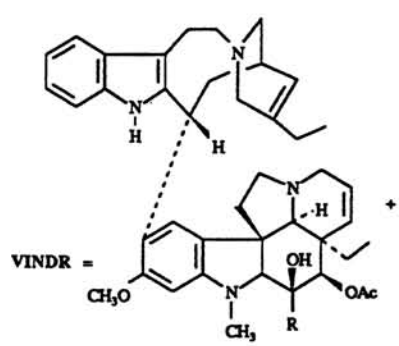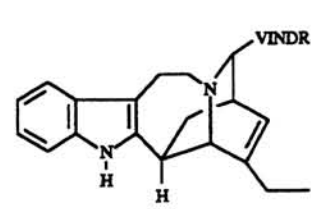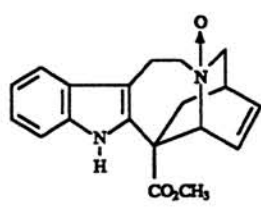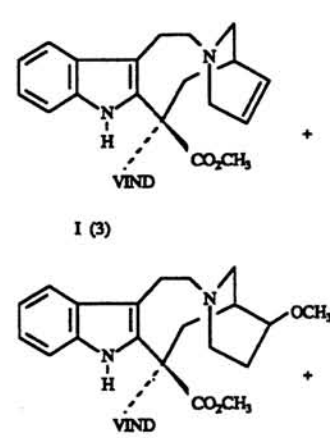
C₁₉ cont.

1. (CF₃CO)₂O, CH₂Cl₂, -30 to -10°

a R= CO₂CH₃ (VINDOLINE)
b R= CONHCH₃

2. NaBH₄

VINDR =

Ia (27), Ib (22)

IIa (11), IIb (8)

IIIa (32)

181,271

1. (CF₃CO)₂O, CH₂Cl₂, -78°,
   VINDOLINE,
2. NaBH₄

I (3)

II (4)

272

TABLE II. SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)
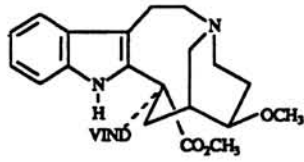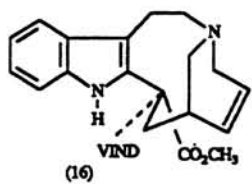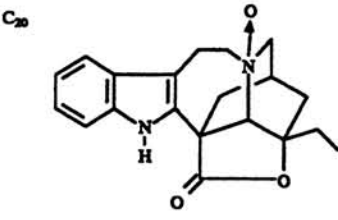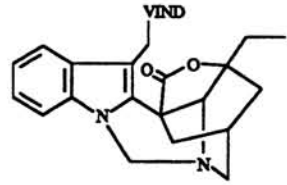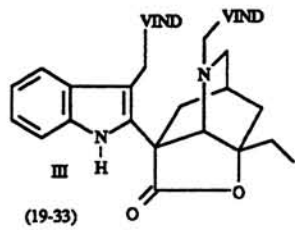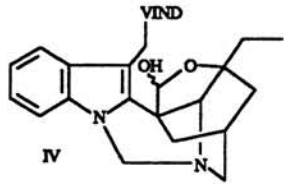
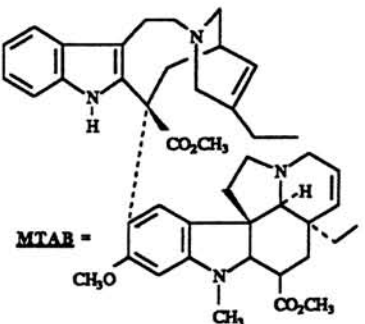| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
		III (5)	
	1. (CF₃CO)₂O, CH₂Cl₂, -20° VINDOLINE 2. NaBH₄	II + (16) (16) 	272
C₂₀ 	1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄	I (-)	196
		II (-)	
	1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄	II + III (15) (19-33) 	197
	1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄	II + IV (62) (10) 	200, 201

TABLE II.   SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)
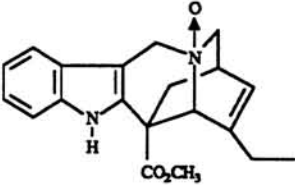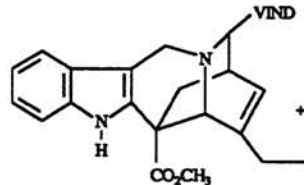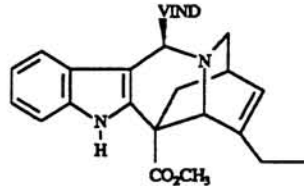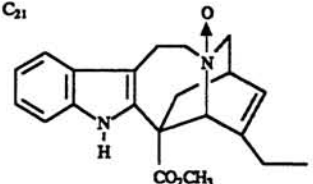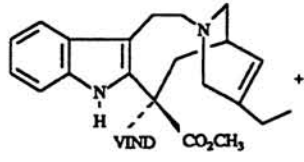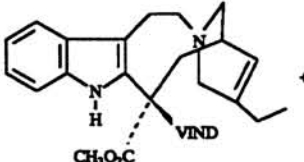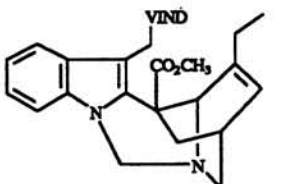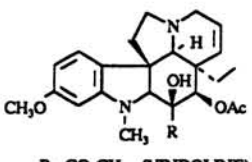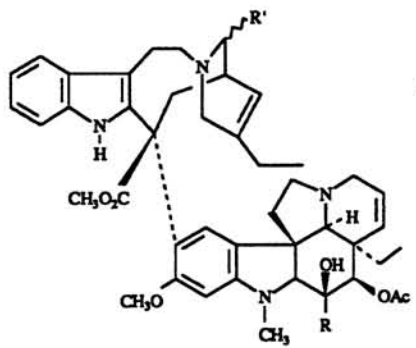
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

1. (CF₃CO)₂O, CH₂Cl₂ , 0,
   VINDOLINE
2. NaBH₄

(28)

(33)

270

C₂₁

1. (CF₃CO)₂O, CH₂Cl₂ , -50°
   VINDOLINE
2. NaBH₄

(50)

(10)

(4-10)

177-180,
203

1. (CF₃CO)₂O, CH₂Cl₂, -50°,

R= CO₂CH₃ (VINDOLINE)
R= CONHCH₃

2. NaBH₄

I   R= CO₂CH₃,   R'= H   (50)
II   R= CO₂CH₃,   R'= OH   (8)
III R= CONHCH₃,   R'= H   (25-50)
IV   R= CONHCH₃,   R'= OH   (2-7)

181,271

TABLE II.   SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)
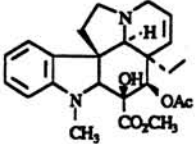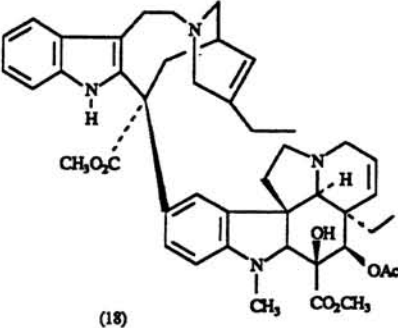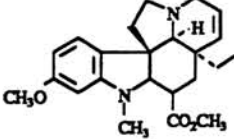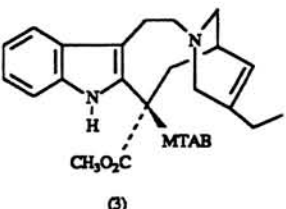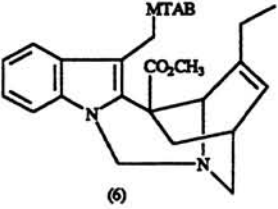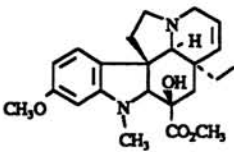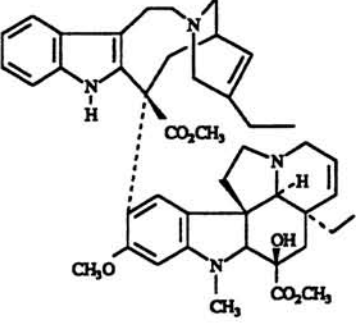
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C_{21} cont.

1. $(CF_3CO)_2O$, CH_2Cl_2, -50°,

2. $NaBH_4$

(18)

178

1. $(CF_3CO)_2O$, CH_2Cl_2, -50°,

2. $NaBH_4$

$\underline{MTAB}$ =

(19)

178

+

(3)

+

(6)

1. $(CF_3CO)_2O$, CH_2Cl_2, -50°

2. $NaBH_4$

(32)

273

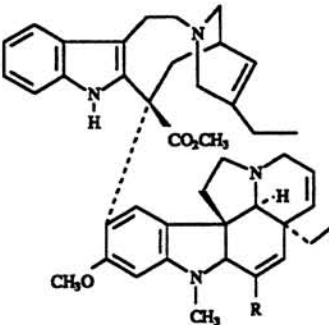TABLE II. Synthesis of Coupled Indole Alkaloids (*Continued*)
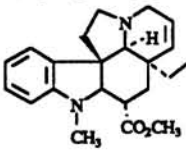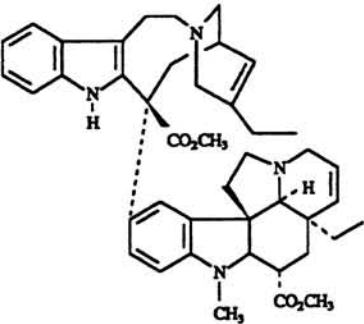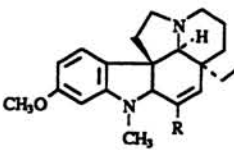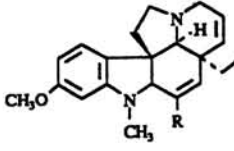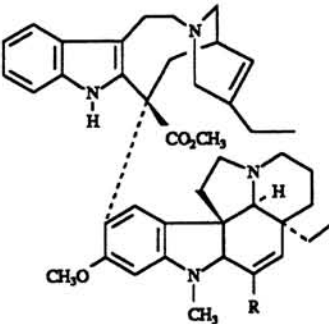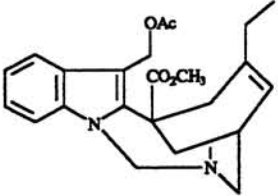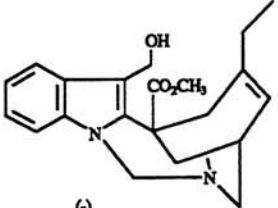
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS

C₂₁ cont.

1. (CF₃CO)₂O, CH₂Cl₂, -50°,

2. NaBH₄

(12)

178

1. (CF₃CO)₂O, CH₂Cl₂,

I R= CO₂CH₃ (VINDOLINE)
II R= CONHCH₃

2. NaBH₄

I (45) II (36)

273

1. (CF₃CO)₂O, CH₂Cl₂,

I R= CO₂CH₃ (VINDOLINE)
II R= CONHCH₃

2. NaBH₄

I (30) II (22)

273

(CH₃CO)₂O, CH₂Cl₂

(40)

203

CH₃COCl, NaOH

(-)

203

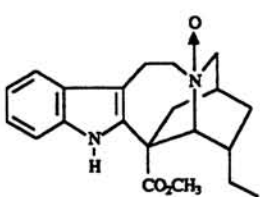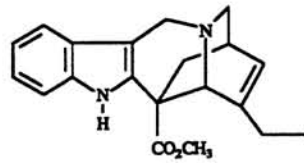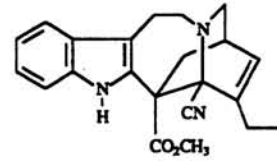TABLE II. SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)
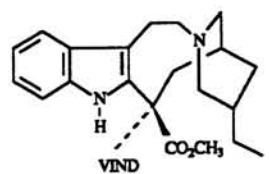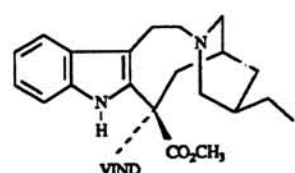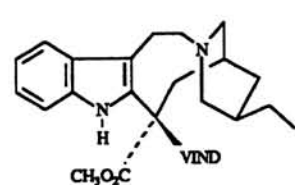
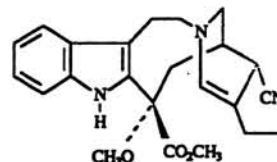| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₂₁ cont.

1. $(CH_3CO)_2O$, CH_2Cl_2
2. HCl-H₂O, heat

(66)

270

1. $(CF_3CO)_2O$, CH_2Cl_2
2. KCN, CH₃OH

(17) +

274

(13) +

(51)

1. $(CF_3CO)_2O$, CH_2Cl_2, -10°
   VINDOLINE
2. NaBH₄

I (5)

180,181,
+ 271

II (13) +
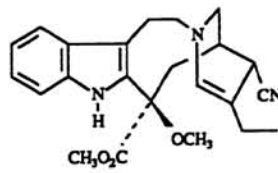

III

TABLE II. SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)
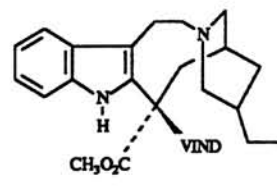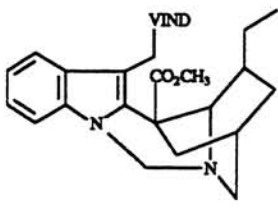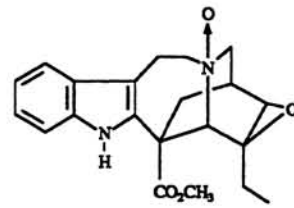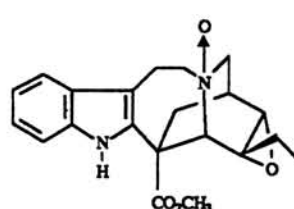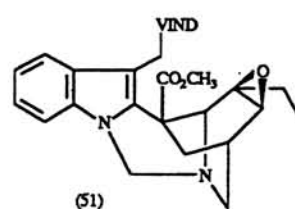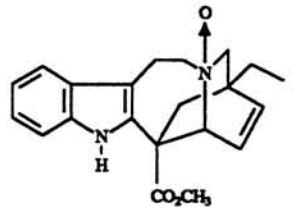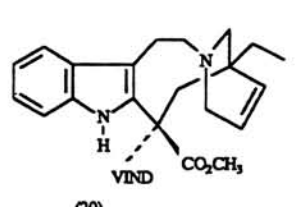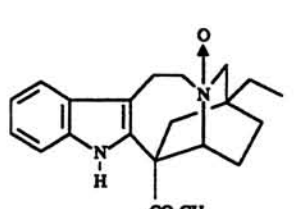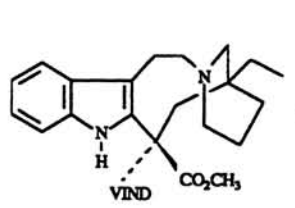
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₂₁ cont.			

IV   III + IV (14)

| | 1. (CF₃CO)₂O, CH₂Cl₂, -30° VINDOLINE 2. NaBH₄ | I + II (-) | 180,181, 270 |

| | 1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄ | I (10) + III (19) + IV (4) + | 178,203 |

V (9)

| | 1. (CF₃CO)₂O, CH₂Cl₂, -50° VINDOLINE 2. NaBH₄ | (6-20)   LEUROSINE | 195,199, 201 |

| | 1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄ | (51) | 200,201 |

| | 1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄ | (20) | 178 |

| | 1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄ | (11) | 178 |

TABLE II. SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C$_{21}$ cont.

(17)
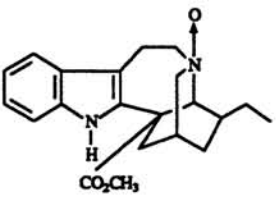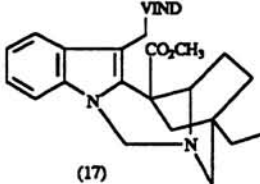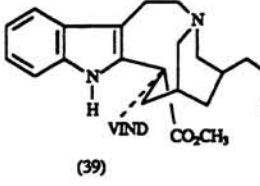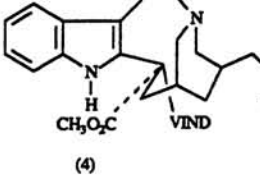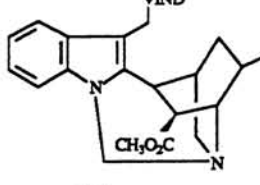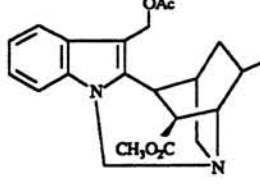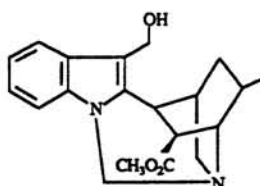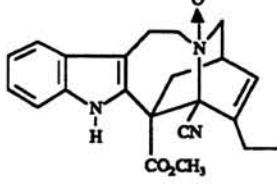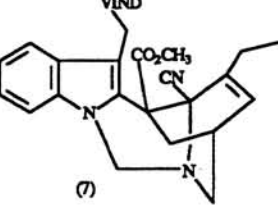
1. (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, VINDOLINE
2. NaBH$_4$

(39)

(10)

(4)

178,203

(17)

(CH$_3$CO)$_2$O, CH$_2$Cl$_2$

(40)

203

CH$_3$COCl, NaOH

(-)

203

C$_{22}$

1. (CF$_3$CO)$_2$O, CH$_2$Cl$_2$, -70 to 0°
VINDOLINE
2. NaBH$_4$

(7)

274

TABLE II.   SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)
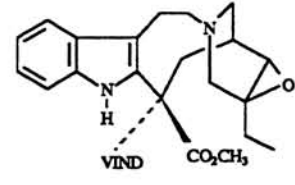
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
	1. (CF₃CO)₂O, CH₂Cl₂, -10° VINDOLINE 2. NaBH₄	(6)	274
	1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄	(10) + (5)	275
	1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄	(10) + (-)	198
	1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄	(6) + (42)	198

C₂₃

TABLE II. SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)
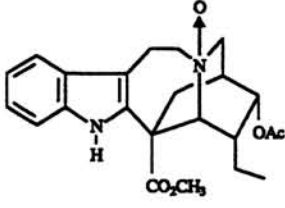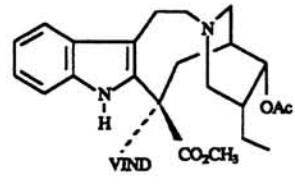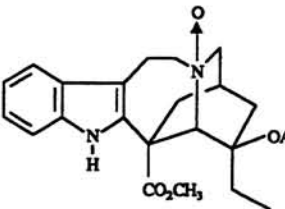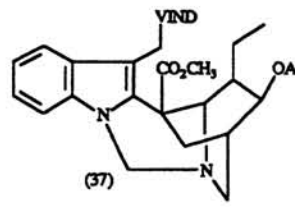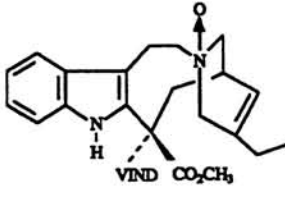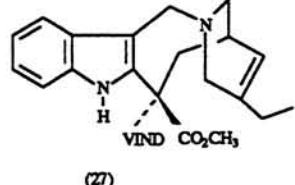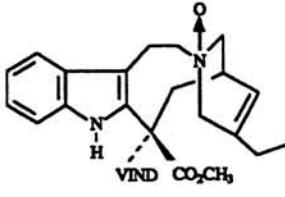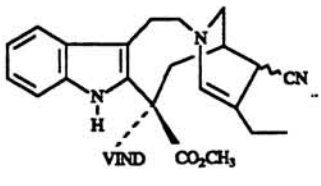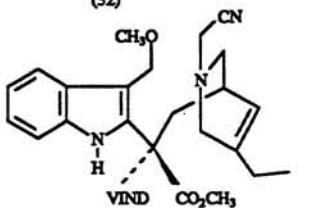
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
	1. (CF₃CO)₂O, CH₂Cl₂, VINDOLINE 2. NaBH₄	 (4) (37)	198
	1. (CCl₃CO)₂O, VINDOLINE 2. NaBH₄	 (-)	187,202
	1. (CF₃CO)₂O, CH₂Cl₂, 2. THF-H₂O	 (27)	206,207
	1. (CF₃CO)₂O, CH₂Cl₂ 2. KCN, CH₃OH	 (32) (54)	207

C₄₆

TABLE II. SYNTHESIS OF COUPLED INDOLE ALKALOIDS (*Continued*)

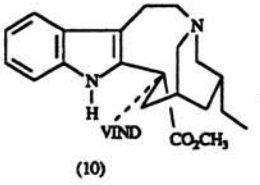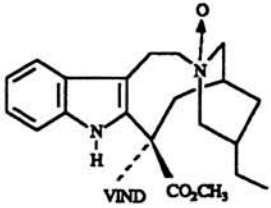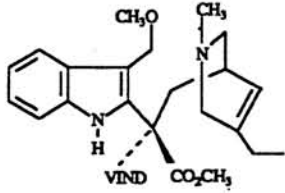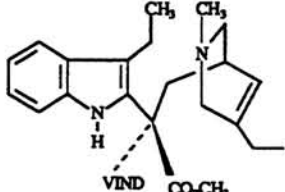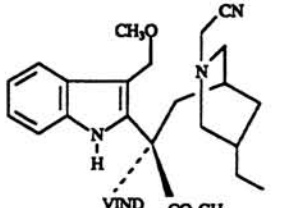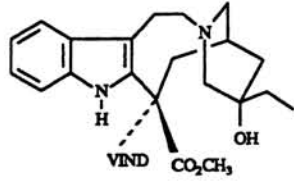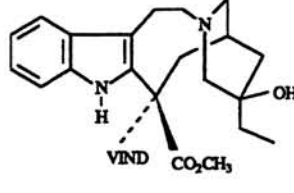| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₄₆ cont.			
	1. (CF₃CO)₂O, CH₂Cl₂ 2. NaBH₄, CH₃OH	 (30)	207
	1. (CF₃CO)₂O, CH₂Cl₂ 2. NaB(CN)H₃, CH₃OH	 (35)	207
	1. (CF₃CO)₂O, CH₂Cl₂ 2. KCN, CH₃OH	 (50)	207
	1. (CH₃CO)₂O, CH₂Cl₂ 2. Tl(OAc)₃ 3. NaBH₄	 (30) VINBLASTINE	204,205, 270
	1. (CH₃CO)₂O, CH₂Cl₂ 2. OsO₄ 3. NaBH₄	 (25) LEUROSIDINE	204,205, 270

TABLE III.   POLONOVSKI REACTION APPLIED TO 16-MACROLIDES
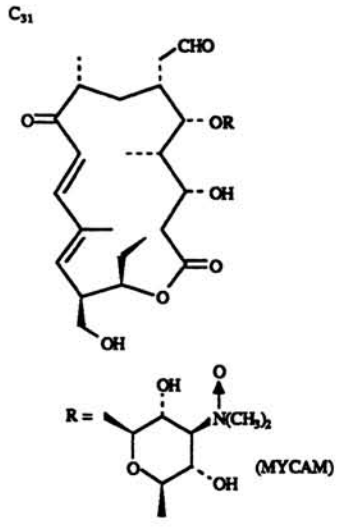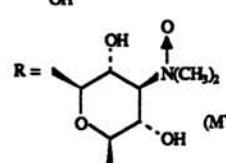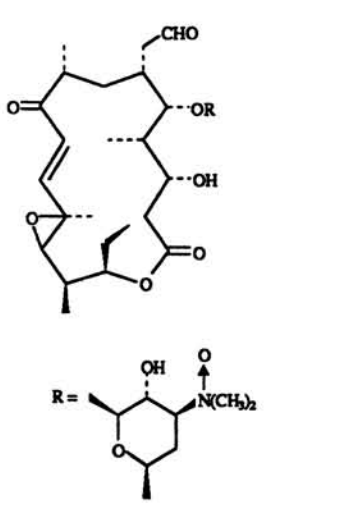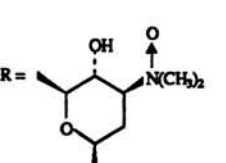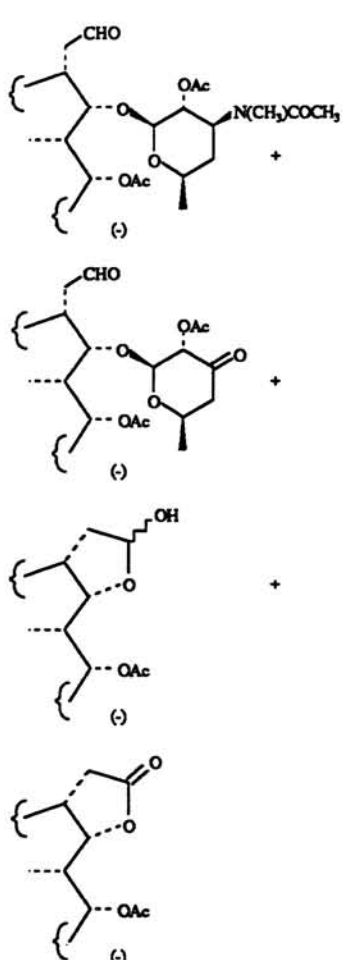
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₃₁	(CH₃CO)₂O, CHCl₃ , heat, 1.5 h	I (10)	165
(MYCAM)	1. (CF₃CO)₂O, CHCl₃ 2. NaOAc, THF-H₂O, heat	I (35-40)	276,277
	1. (CF₃CO)₂O, THF, DPEA	I (39)	277
	1. (ClCH₂CO)₂O, CHCl₃ 2. 0.1 N HCl-C₅H₅N	I (30)	277
	(CH₃CO)₂O, C₅H₅N, 25°, 15 h	(-) + (-) + (-) + (-)	278

TABLE III. POLONOVSKI REACTION APPLIED TO 16-MACROLIDES (*Continued*)
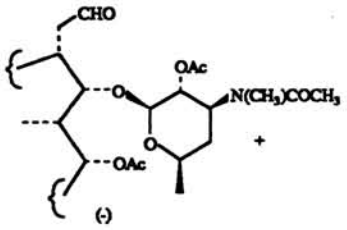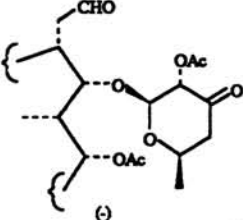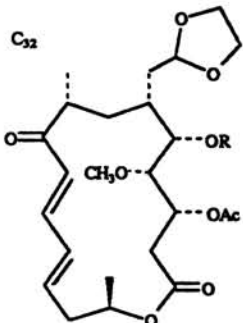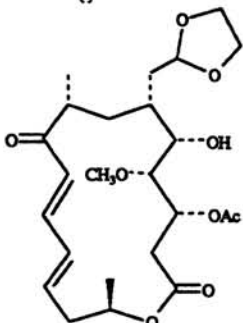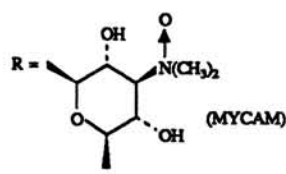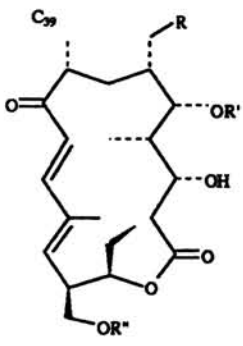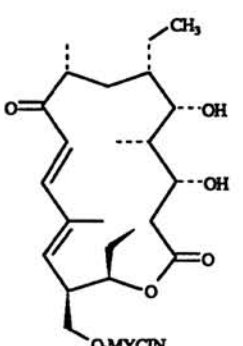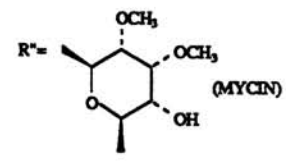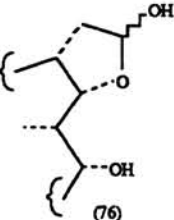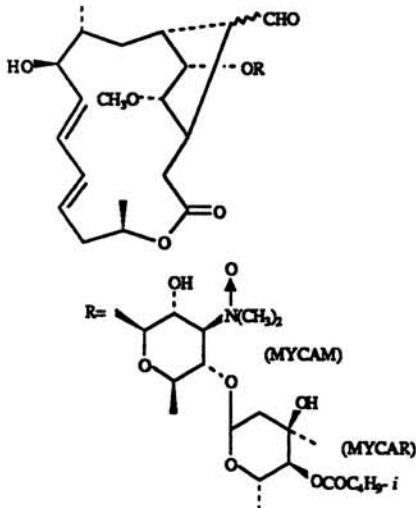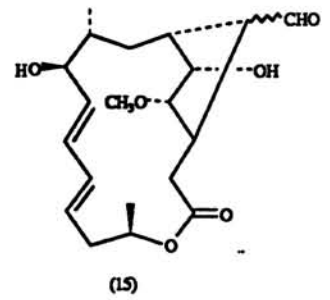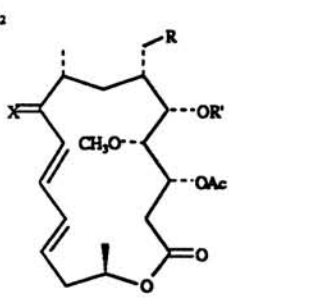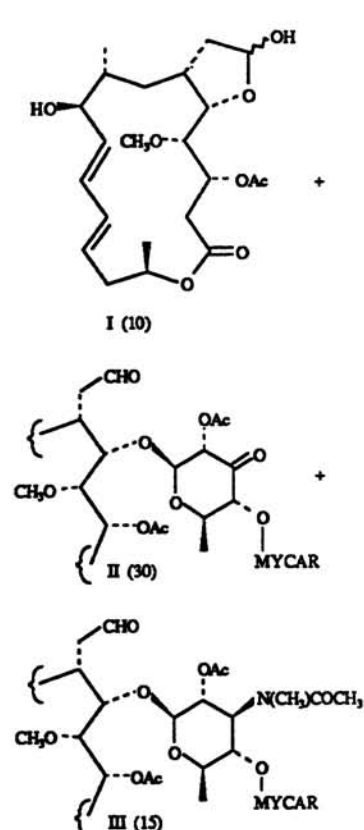
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C$_{31}$ cont.

$(CH_3CO)_2O$, $CHCl_3$, 25°, 8 h

278

(-)

(-)

C$_{32}$

$(CH_3CO)_2O$, $CHCl_3$, heat 1 h

279

(57)

R = (MYCAM)

C$_{39}$

$(CH_3CO)_2O$, C_5H_5N, 25°, 15 h

165

O-MYCIN

(80)

R = CH$_3$, R' = MYCAM

R'' = (MYCIN)

R = CHO, R' = MYCAM
R'' = MYCIN

1. $(CF_3CO)_2O$, C_5H_5N
2. K_2CO_3, CH_3OH, 0°

166

(76)

TABLE III.   POLONOVSKI REACTION APPLIED TO 16-MACROLIDES (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₄₀

(CH₃CO)₂O, CHCl₃ , heat, 1.5 h

(15)

280,281

R= (MYCAM) (MYCAR) OCOC₄H₉-*i*

C₄₂

R= CHO, R'= MYCAM - MYCAR
X= H, -OH

(CH₃CO)₂O, CHCl₃ , heat, 1.5 h

163

I (10)

II (30)

III (15)

TABLE III.   POLONOVSKI REACTION APPLIED TO 16-MACROLIDES (*Continued*)
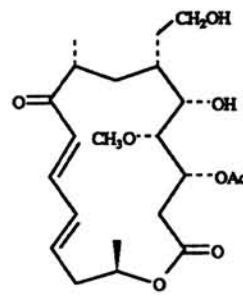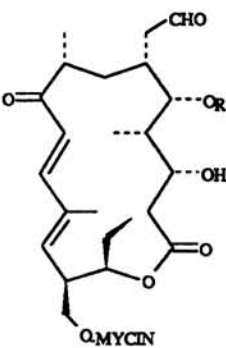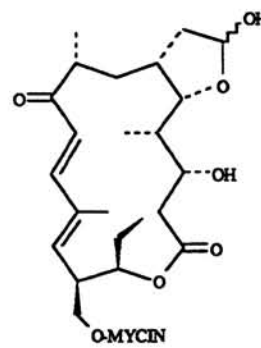
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₄₂ cont.			
	1. (CH₃CO)₂O, C₅H₅N 2. H⁺	II + IV II : IV= 1 :1	164
R= CH₂OH, R'= MYCAM-MYCAR X= O	(CH₃CO)₂O, CHCl₃, heat, 1.5 h	 (9)	162,280
C₅₀ R= MYCAM-MYCAR	(CH₃CO)₂O, CHCl₃, heat, 1.5 h	 (10)	165
	1. (CF₃CO)₂O, C₅H₅N 2. K₂CO₃, CH₃OH, 0°	(65)	166

TABLE IV. POLONOVSKI REACTIONS NOT REQUIRING AN ACYLATING AGENT

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C_7			
(1-methyl-5-methoxy-tetrahydropyridin-3-one)	MCPBA	(95)	216
C_9			
(1-methyl-5-isopropoxy-tetrahydropyridin-3-one)	MCPBA	(95)	216
(2-dimethylamino-benzoic acid, $N(CH_3)_2$, CO_2H)	$HCO_2H - H_2O_2$	(2-methylamino-benzoic acid, $NHCH_3$, CO_2H) (91)	212
C_{10}			
(dimethyl 1-methylpiperidine-2,3-dicarboxylate, CO_2CH_3, CO_2CH_3)	MCPBA	(50)	217
C_{11}			
(2-(pyrrolidin-1-yl)-NHCHO)	$HCO_2H - H_2O_2$	(90)	212
(morpholine-NHCHO)	$HCO_2H - H_2O_2$	(90)	212
C_{12}			
(2-(pyrrolidin-1-yl)-NHCOCH$_3$)	$HCO_2H - H_2O_2$	(90)	212

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C$_{12}$ cont.

$HCO_2H - H_2O_2$ (90)   212

$HCO_2H - H_2O_2$ (90)   212

$HCO_2H - H_2O_2$ (23)   212

C$_{13}$

$HCO_2H - H_2O_2$ (90)   212

$HCO_2H - H_2O_2$ (90)   212

MCPBA   (50)   217

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C$_{14}$

MCPBA

  (95)

215

HCO$_2$H - H$_2$O$_2$

  (90)

212

C$_{15}$

HCO$_2$H - H$_2$O$_2$

  (70)

212

C$_{16}$

MCPBA

  (79)

217

C$_{17}$

HCO$_2$H - H$_2$O$_2$

  (90)

212

C$_{18}$

HCO$_2$H - H$_2$O$_2$

  (90)

212

TABLE IV. POLONOVSKI REACTIONS NOT REQUIRING AN ACYLATING AGENT (*Continued*)
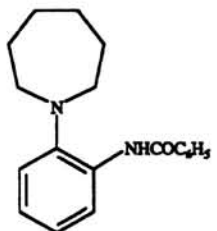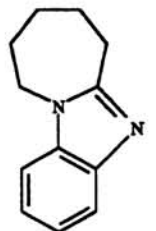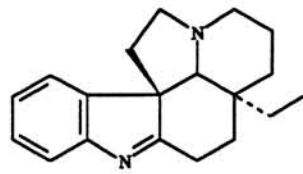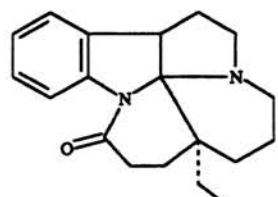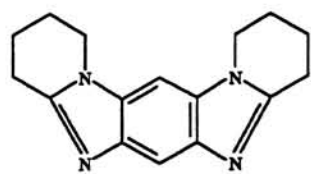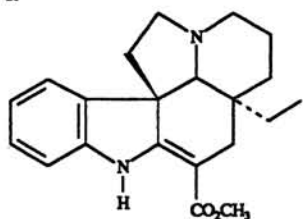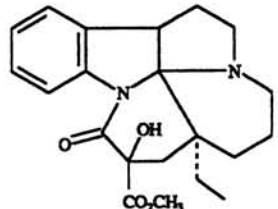
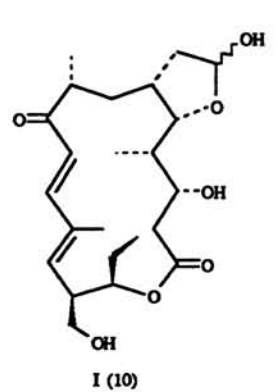| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C19			
	HCO$_2$H - H$_2$O$_2$	(90)	212
C14			
	MCPBA	(-)	213
C20			
	HCO$_2$H - H$_2$O$_2$	(74)	212
C21			
	MCPBA	(-)	214

TABLE V. IRON SALT INITIATED POLONOVSKI REACTION

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₃ $(CH_3)_3N \uparrow O$	FeSO₄, 0.49 N H₂SO₄, heat, 9 h (pH 1-2)	H_2CO + $(CH_3)_2NH$ + $(CH_3)_3N$ (65) (60) (35)	63
C₃ $i\text{-}C_3H_7N(CH_3)_2 \uparrow O$	FeSO₄, 0.49 N H₂SO₄, heat, 17 h	H_2CO (50)	63
C₆ $(C_2H_5)_3N \uparrow O$	FeSO₄, 0.49 N H₂SO₄, heat, 5 h	CH_3CHO (25)	63
	FeSO₄, CF₃CO₂H, C₆H₁₂, 65°, 12 h	$C_4H_{11}O_2CCF_3$ (25)	66
$n\text{-}C_4H_9N(CH_3)_2 \uparrow O$	FeSO₄, 0.49 N H₂SO₄, heat, 9 h	H_2CO + $n\text{-}C_4H_9NHCH_3$ + $n\text{-}C_4H_9N(CH_3)_2$ (37) (-) (-)	63
	FeSO₄, Tartaric acid, 80°, 40 min (pH 6.3)	$n\text{-}C_3H_7CHO$ + H_2CO I II I + II = (30)	
	FeSO₄, 50% H₂SO₄, heat	$HOCH_2(CH_2)_3N(CH_3)_2$ + $CH_3CHOH(CH_2)_2N(CH_3)_2$ (4) (14)	65
$t\text{-}C_4H_9N(CH_3)_2 \uparrow O$	FeSO₄, 0.49 N H₂SO₄, heat, 17 h	H_2CO (42)	63
C₇ $n\text{-}C_5H_{11}N(CH_3)_2 \uparrow O$	FeSO₄, 50% H₂SO₄, heat	$CH_3CHOH(CH_2)_3N(CH_3)_2$ (72)	65
C₈ $C_6H_5N(CH_3)_2 \uparrow O$	FeSO₄, 0.49 N H₂SO₄, heat, 2 h	H_2CO + $C_6H_5N(CH_3)_2$ (8) (-)	63
C₉ $(n\text{-}C_4H_9)_2NCH_3 \uparrow O$	FeSO₄, 0.49 N H₂SO₄, heat, 5 h	$n\text{-}C_3H_7CHO$ + H_2CO I II I : II = 1 : 2 (25)	63
$C_6H_5CH_2N(CH_3)_2 \uparrow O$	FeSO₄, 0.49 N H₂SO₄, heat, 5 h	C_6H_5CHO + $C_6H_5CH_2NHCH_3$ + $C_6H_5CH_2N(CH_3)_2$ (85) (-) (-)	63

TABLE V.   IRON SALT IINITIATED POLONOVSKI REACTION (*Continued*)
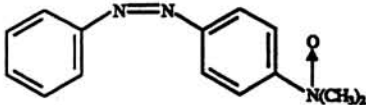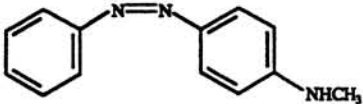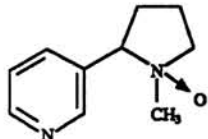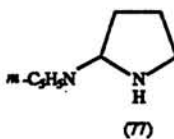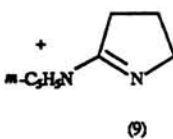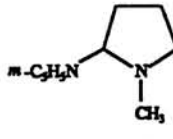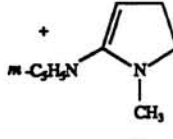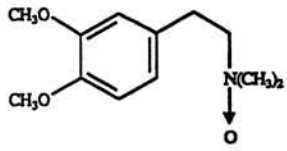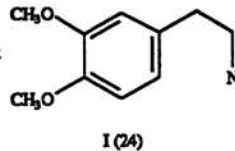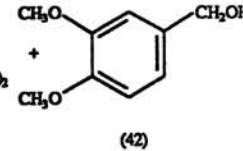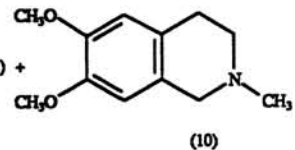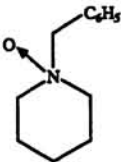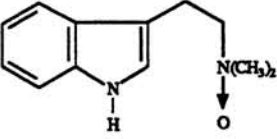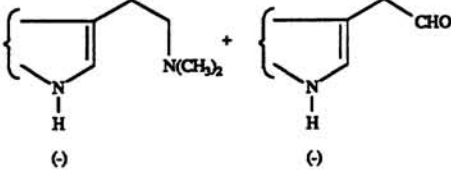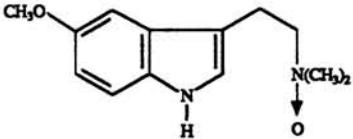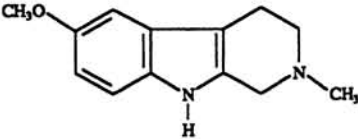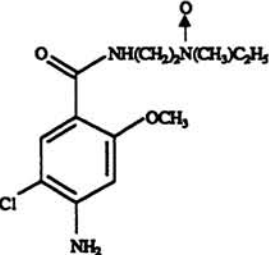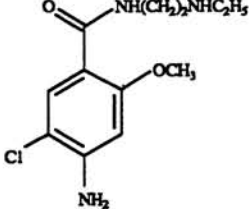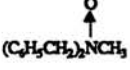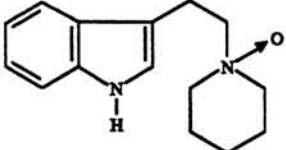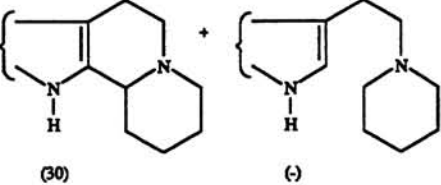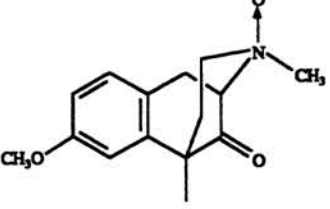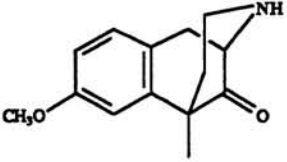
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₇			
	FeSO₄, Tartaric acid, 80°, 40 min (pH 6.3)	C₆H₅CHO + H₂CO (-)　　(-)	63
C₁₀			

| | FeSO₄, 0.49 N H₂SO₄, heat, 5 h | H₂CO (15) | 63 |

| | FeSO₄ | | 282 |

| C₆H₅(CH₂)₂N(CH₃)₂ | FeSO₄ | (C₆H₅CH₂)₂ + C₆H₅(CH₂)₂NHCH₃ + C₆H₅CH₂OH
(14)　　　(9)　　　(3) | 64 |

| | Fe(NO₃)₃, Tartaric acid | H₂CO + | 72 |

(72)

C₁₂			
(nC₄H₉)₃N	FeSO₄, 0.05 M H₂SO₄, heat	(n-C₄H₉)₂NH + (n-C₄H₉)₃N I (29)　　II (64)	65
	FeSO₄, 50% H₂SO₄, heat	I (30) + II (5) + (n-C₄H₉)₂N(CH₂)₃CH₂OH (6) + (n-C₄H₉)₂N(CH₂)₂CH(OH)CH₃ (39)	65

| | FeSO₄, 0.05 M H₂SO₄, heat | | 64 |

I (24)　　　(42)

| | FeSO₄, 0.05 M H₂SO₄ - C₅H₅N, (pH 5.8), heat | I (43) + II (31) + | 64 |

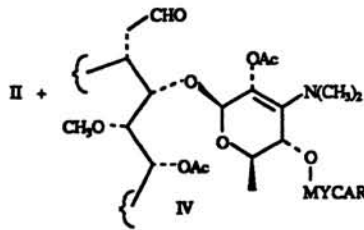(10)

TABLE V. IRON SALT INITIATED POLONOVSKI REACTION (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C$_{12}$ cont

| | FeCl$_2$ (cat) , H$_2$O, -10 to 20°, 3 h | C$_6$H$_5$CHO (67) | 235 |

| | FeSO$_4$, CH$_3$CO$_2$H - H$_2$O, 60° | (-) + (-) | 283 |

+ H$_2$CO (-)

C$_{13}$

| | FeSO$_4$, CH$_3$CO$_2$H - H$_2$O, 60° | (12) | 283 |

| | FeCl$_2$ (cat) , H$_2$O, -10 to 20°, 3 h | (63) | 235 |

C$_{15}$

(C$_6$H$_5$CH$_2$)$_2$NCH$_3$

| | FeSO$_4$, CH$_3$CO$_2$H - H$_2$O, 60° | C$_6$H$_5$CHO (27) | 63 |

| | FeSO$_4$, CH$_3$OH - CH$_3$CO$_2$H, heat | (30) + (-) | 284 |

| | FeCl$_2$ (cat) , H$_2$O, -10 to 20°, 3 h | (68) | 235 |

TABLE V. IRON SALT IINITIATED POLONOVSKI REACTION (*Continued*)
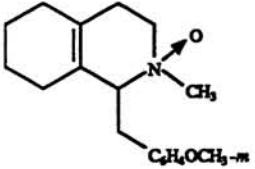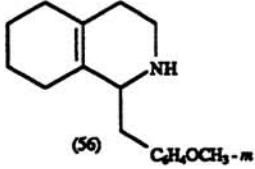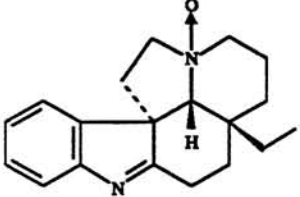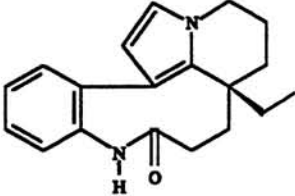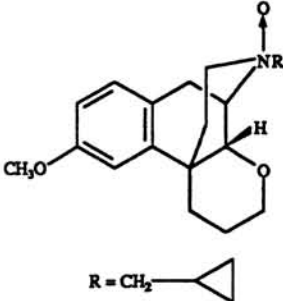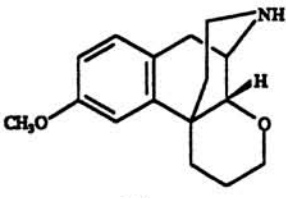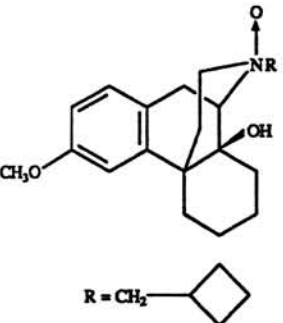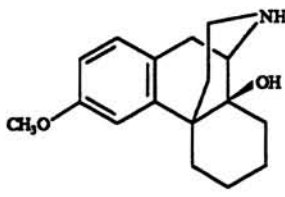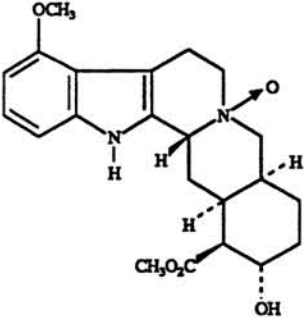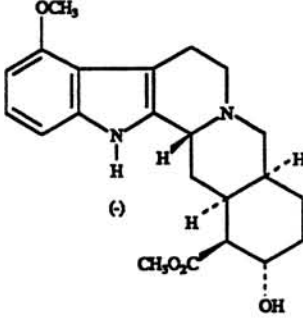
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₁₈

FeCl₂ (cat) , H₂O,
-10 to 20°, 3 h

(56)

235

FeSO₄ , H₂O

(30)

240

R = CH₂—◁

FeCl₂ (cat) , H₂O,
-10 to 20°, 3 h

(80)

235

C₂₂

R = CH₂—◻

FeCl₂ (cat) , H₂O
-10 to 20°, 3 h

(89)

235

FeSO₄ , heat

(-)

228

TABLE VI. Sulfur Dioxide Polonovski Reaction

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C₃

(CH₃)₃N (with O)
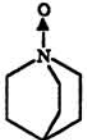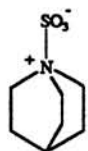
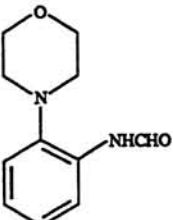| | SO_2 , C_6H_6 | $(CH_3)_3\overset{+}{N}$—$\overset{-}{O}SO_2$ (90) | 95 |
| | SO_2 liq. | $(CH_3)_2NCH_2OSO_2H$ (90) | 98 |
| | SO_2 , H_2O | $(CH_3)_2NH + H_2CO$ (50) | 95 |

C₆

$(C_2H_5)_3N$ (with O)

| | SO_2 , C_6H_6 | $(C_2H_5)_3\overset{+}{N}O$—$\overset{-}{S}O_3$ (90) | 95 |

C₇

| | SO_2 , C_2H_5OH, or C_6H_6 , $CHCl_3$, H_2O | (89) | 97 |

C₈

$C_6H_5N(CH_3)_2$ (with O)

| | SO_2 , H_2O , 0° | $C_6H_5N(CH_3)_2$ + $o\text{-}HO_3SC_6H_4N(CH_3)_2$
(20)   (56)
+ $p\text{-}HO_3SC_6H_4N(CH_3)_2$
(18) | 96 |

C₉

$C_6H_5CH_2N(CH_3)_2$ (with O)

| | SO_2 , H_2O , 20° | $C_6H_5CH_2N(CH_3)_2$ + C_6H_5CHO
I (18)   II (14)
+ $C_6H_5CH_2NHCH_3$
III (56) | 138 |
| | SO_2 , H_2O , 0° | I (35) + II (52) + III (8) | 96 |

$p\text{-}O_2NC_6H_4CH_2N(CH_3)_2$ (with O)

| | SO_2 , H_2O , 20° | $p\text{-}O_2NC_6H_4CH_2N(CH_3)_2$ + $p\text{-}O_2NC_6H_4CHO$
(20)   (6)
+ $p\text{-}O_2NC_6H_4CH_2NHCH_3$
(44) | 138 |

C₁₀

$p\text{-}CH_3OC_6H_4CH_2N(CH_3)_2$ (with O)

| | SO_2 , H_2O , 20° | $p\text{-}CH_3OC_6H_4CH_2N(CH_3)_2$ + $p\text{-}CH_3OC_6H_4CHO$
(19)   (13)
+ $p\text{-}CH_3OC_6H_4CH_2NHCH_3$
(50) | 138 |

TABLE VI. SULFUR DIOXIDE POLONOVSKI REACTION (*Continued*)
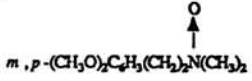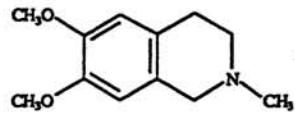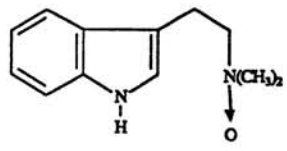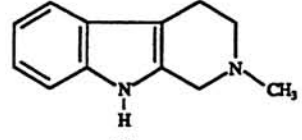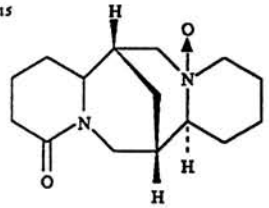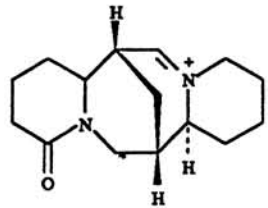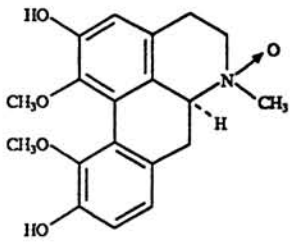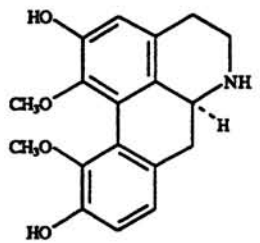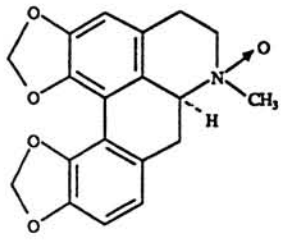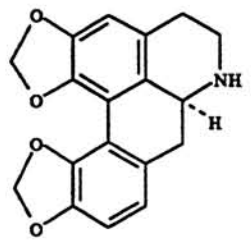
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₁₀ cont.			
	SO₂ , H₂O , 0°	C₆H₅N(C₂H₅)₂ + *o*-HO₃SC₆H₄N(C₂H₅)₂	96
		I (30) II (45)	
		+ *p*-HO₃SC₆H₄N(C₂H₅)₂	
		III (15)	
	SO₂ , H₂O , 70°	I (51) + II (34) + III (10)	96
C₁₂			
	SO₂ , H₂O , 20°	*m*,*p*-(CH₃O)₂C₆H₃(CH₂)₂NHCH₃	138,236
		I (46)	
		+ *m*,*p*-(CH₃O)₂C₆H₃(CH₂)₂N(CH₃)₂	
		II (18)	
	SO₂, HCO₂H , 20°	+ II (29)	138,236
		(61)	
	SO₂, HCO₂H , 20°		138
		(58)	
C₁₅			
	SO₂		114
C₁₉		(-)	
	1. SO₂ liq.		234
	2. HCl - H₂O	(18)	
	1. SO₂ liq.		234
	2. HCl - H₂O	(28)	

TABLE VI. SULFUR DIOXIDE POLONOVSKI REACTION (*Continued*)
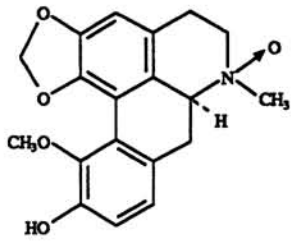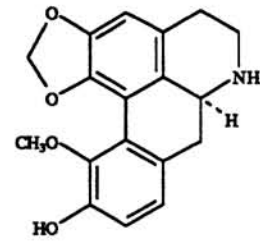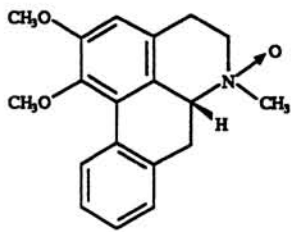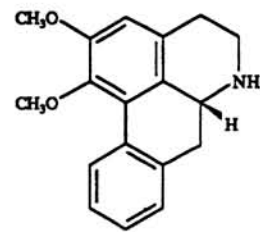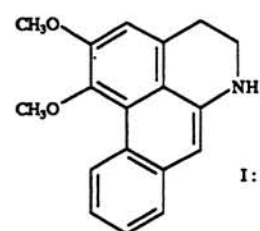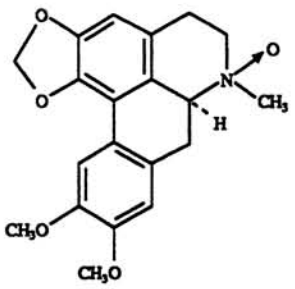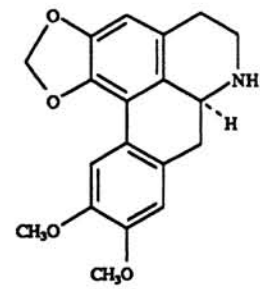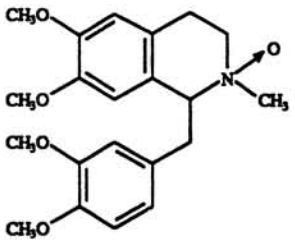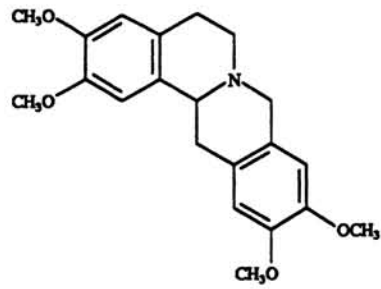
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C₁₉ cont.			
	1. SO₂ liq. 2. HCl - H₂O	(22)	234
	1. SO₂ liq. 2. HCl - H₂O	I (34)	234
	1. SO₂, CH₃OH - C₆H₆ 2. OH⁻	+ I I : II = 2 : 5 II	234
C₂₀	1. SO₂ liq. 2. HCl - H₂O	(32)	234
C₂₁	SO₂, HCO₂H	(15)	138

TABLE VI. SULFUR DIOXIDE POLONOVSKI REACTION (*Continued*)
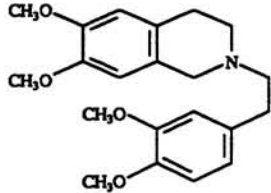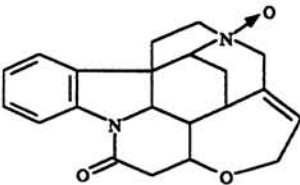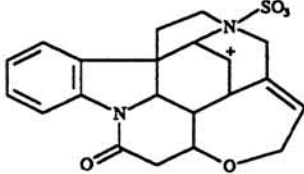
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.

C$_{21}$ cont.

$\left[m,p\text{-}(CH_3O)_2C_6H_3(CH_2)_2\right]_2NCH_3$ SO$_2$, HCO$_2$H

(40)

+ $\left[m,p\text{-}(CH_3O)_2C_6H_3(CH_2)_2\right]_2NCH_3$

(30)

138

SO$_2$ - H$_2$O

96

TABLE VII. SILICON AND SELENIUM POLONOVSKI REACTION
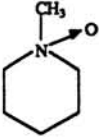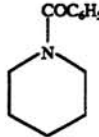
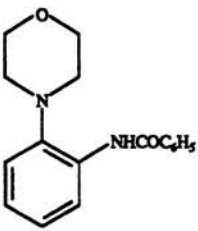| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)		REFS.
C₆				

C_6

(C₂H₅)₃N (with O)

	1. TBDMSOTf, CH₂Cl₂, 0°	(C₂H₅)₂NCOC₆H₅	(57)	241,244
	2. CH₃Li, THF, 0°			
	3. C₆H₅COCl			
	1. TMSCl, CH₂Cl₂, 0°	(C₂H₅)₂NCO₂C₆H₅	(57)	241,244
	2. C₄H₉Li, THF, 0°			
	3. ClCO₂C₆H₅			
	1. TBDMSOTf, CH₂Cl₂, 0°	(C₂H₅)₂NR		245
	2. CH₃Li, THF, 0°	R = C₆H₅CH₂	(65)	
	3. RX, (C₄H₉)₄NF, 110°, 10 h	= C₈H₁₇	(51)	
	RX = C₆H₅CH₂Cl	= C₂H₅O₂CCH₂	(31)	
	= C₈H₁₇Br			
	= C₂H₅O₂CCH₂Br			

(N-methyl piperidine N-oxide structure)

	1. TBDMSOTf, CH₂Cl₂, 0°	(N-benzoyl piperidine structure, COC₆H₅)	(76)	241,244
	2. CH₃Li, THF, 0°			
	3. C₆H₅COCl			

TABLE VII.   Silicon and Selenium Polonovski Reaction (*Continued*)

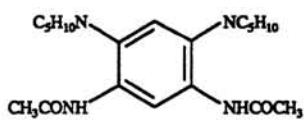| REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C$_6$ cont.	1. C$_6$H$_5$SeOSO$_2$CF$_3$, CH$_2$Cl$_2$, 0° 2. (C$_2$H$_5$)$_3$N or DBU, -78 to 40° 3. C$_6$H$_5$COCl	" (61)	246
	1. TMSCl, CH$_2$Cl$_2$, 0° 2. C$_4$H$_9$Li, THF, 0° 3. ClCO$_2$C$_6$H$_5$	(65)	241,244
	1. C$_6$H$_5$SeOSO$_2$CF$_3$, CH$_2$Cl$_2$, 0° 2. (C$_2$H$_5$)$_3$N or DBU, -78 to 40° 3. ClCO$_2$C$_6$H$_5$	" (41)	246
	1. TBDMSOTf, CH$_2$Cl$_2$, 0° 2. CH$_3$Li, THF, 0° 3. CH$_3$CO$_2$H, C$_5$H$_{11}$ONO	(33)	244
	1. TBDMSOTf, CH$_2$Cl$_2$, 0° 2. CH$_3$Li, THF, 0° 3. (CH$_3$)$_3$SiCl, TiCl$_4$, CH$_2$Cl$_2$, -78 to 20°	(61)	243

	1. TBDMSOTf, CH$_2$Cl$_2$, 0°
	2. CH$_3$Li, THF, 0°
	3. RX, (C$_4$H$_9$)$_4$NF, 110°, 10 h
	    RX = C$_6$H$_5$CH$_2$Cl
	    = C$_5$H$_{11}$Br
	    = C$_8$H$_{17}$Br
	    = C$_2$H$_5$O$_2$CCH$_2$Br
	    = C$_6$H$_5$COCH$_2$Br
		R = C$_6$H$_5$CH$_2$ (58)
		   = C$_5$H$_{11}$ (45)
		   = C$_8$H$_{17}$ (47)
		   = C$_2$H$_5$O$_2$CCH$_2$ (38)
		   = C$_6$H$_5$COCH$_2$ (33)
			245

	1. C$_6$H$_5$SeOSO$_2$CF$_3$, CH$_2$Cl$_2$, 0° 2. (C$_2$H$_5$)$_3$N or DBU, -78 to 40° 3. C$_6$H$_5$CH$_2$Cl	" (46) R = C$_6$H$_5$CH$_2$	246

	1. TBDMSOTf, CH$_2$Cl$_2$, 0°
	2. CH$_3$Li, THF, 0°
	3. RMgBr, C$_6$H$_5$CH$_3$, 20°
	    R = C$_6$H$_5$
	    = CH$_2$=CH
	    = C$_6$H$_5$CH$_2$
	    = C$_2$H$_5$
		R = C$_6$H$_5$ (74)
		   = CH$_2$=CH (51)
		   = C$_6$H$_5$CH$_2$ (52)
		   = C$_2$H$_5$ (47)
			242

TABLE VII. SILICON AND SELENIUM POLONOVSKI REACTION (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
	1. TBDMSOTf, CH$_2$Cl$_2$, 0°	*	242
	2. CH$_3$Li, THF, 0°		
	3. R$_3$Al		
	$\quad$ R = C$_4$H$_9$-i	R = C$_4$H$_9$-i (45)	
	$\quad$ = C$_2$H$_5$	= C$_2$H$_5$ (69)	
	1. C$_6$H$_5$SeOSO$_2$CF$_3$, CH$_2$Cl$_2$, 0°	* (32)	246
	2. (C$_2$H$_5$)$_3$N or DBU, -78 to 40°	R = C$_2$H$_5$	
	3. (C$_2$H$_5$)$_3$Al		

C$_8$

	1. C$_6$H$_5$SeOSO$_2$CF$_3$, CH$_2$Cl$_2$, 0°	+ (CH$_3$)$_2$NCOC$_6$H$_5$	246
	2. (C$_2$H$_5$)$_3$N or DBU, -78° to 40°		
	3. C$_6$H$_5$COCl	I ((64) II (11)	
	1. (CH$_3$)$_3$SiCl, CH$_2$Cl$_2$, 0°	I (23)	244
	2. C$_4$H$_9$Li, THF, 0°		
	3. C$_6$H$_5$COCl		
	1. TBDMSOTf, CH$_2$Cl$_2$, 0°	(71)	243
	2. CH$_3$Li, THF, 0°		
	3. (CH$_3$)$_3$SiCN, TiCl$_4$, CH$_2$Cl$_2$,		
	$\quad$ -78 to 20°		

C$_6$H$_5$N(CH$_3$)$_2$ ↑O	1. TBDMSOTf, CH$_2$Cl$_2$, 0°	C$_6$H$_5$N(CH$_3$)COC$_6$H$_5$ (51)	241,244
	2. CH$_3$Li, THF, 0°		
	3. C$_6$H$_5$COCl		
	1. (CH$_3$)$_3$SiCl, CH$_2$Cl$_2$, 0°	C$_6$H$_5$N(CH$_3$)CO$_2$C$_6$H$_5$ (40)	244
	2. C$_4$H$_9$Li, THF, 0°		
	3. ClCO$_2$C$_6$H$_5$		

C$_9$

C$_6$H$_5$CH$_2$N(CH$_3$)$_2$ ↑O	1. TBDMSOTf. CH$_2$Cl$_2$, 0°	(CH$_3$)$_2$NCOC$_6$H$_5$ (52)	241,244
	2. CH$_3$Li, THF, 0°	I	
	3. C$_6$H$_5$COCl	+ C$_6$H$_5$CH$_2$N(CH$_3$)COC$_6$H$_5$ (29)	
		II	
	1. C$_6$H$_5$SeOSO$_2$CF$_3$, CH$_2$Cl$_2$, 0°	I + II	246
	2. (C$_2$H$_5$)$_3$N or DBU, -78 to 40°	(65) (8)	
	3. C$_6$H$_5$COCl		

TABLE VII. SILICON AND SELENIUM POLONOVSKI REACTION (*Continued*)
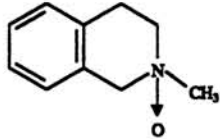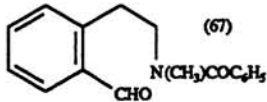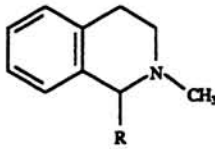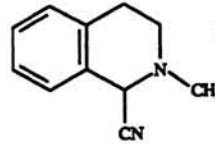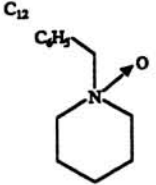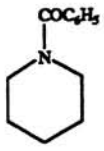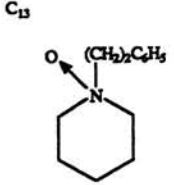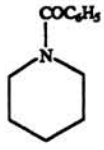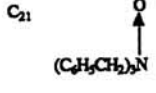
REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)	REFS.
C$_{10}$ cont.	1. TBDMSOTf, CH$_2$Cl$_2$, 0° 2. CH$_3$Li, THF, 0° 3. (CH$_3$)$_3$SiCN, TiCl$_4$, CH$_2$Cl$_2$, -78 to 20°	C$_6$H$_5$CH(CN)N(CH$_3$)$_2$ (22) + C$_6$H$_5$CH$_2$N(CH$_3$)CH$_2$CN (40)	243
	1. TBDMSOTf, CH$_2$Cl$_2$, 0° 2. CH$_3$Li, THF, 0° 3. C$_6$H$_5$COCl	(67)	241,244

	1. TBDMSOTf, CH$_2$Cl$_2$, 0°
	2. CH$_3$Li, THF, 0°
	3. RMgBr, C$_6$H$_5$CH$_3$, 20°
	   R = C$_6$H$_5$
	     = CH=CH$_2$
	     = C$_2$H$_5$
		R = C$_6$H$_5$ (56)
		 = CH=CH$_2$ (54)
		 = C$_2$H$_5$ (41)
			242

	1. TBDMSOTf, CH$_2$Cl$_2$, 0° 2. CH$_3$Li, THF, 0° 3. (CH$_3$)$_3$SiCN, TiCl$_4$, CH$_2$Cl$_2$, -78 to 20°	(63)	243
C$_{12}$	1. TBDMSOTf, CH$_2$Cl$_2$, 0° 2. CH$_3$Li, THF, 0° 3. C$_6$H$_5$COCl	(45)	244
C$_{13}$	1. C$_6$H$_5$SeOSO$_2$CF$_3$, CH$_2$Cl$_2$, 0° 2. (C$_2$H$_5$)$_3$N or DBU, -78° to 40° 3. C$_6$H$_5$COCl	(66)	246
C$_{21}$ (C$_6$H$_5$CH$_2$)$_3$N	1. TBDMSOTf, CH$_2$Cl$_2$, 0° 2. CH$_3$Li, THF, 0° 3. C$_6$H$_5$COCl	(C$_6$H$_5$CH$_2$)$_2$NCOC$_6$H$_5$ (88)	241,244
	1. TBDMSOTf, CH$_2$Cl$_2$, 0° 2. CH$_3$Li, THF, 0° 3. CH$_3$CO$_2$H	(C$_6$H$_5$CH$_2$)$_2$NH (67)	241,244

TABLE VII.   SILICON AND SELENIUM POLONOVSKI REACTION (*Continued*)

REACTANT	CONDITIONS	PRODUCT(S) and YIELDS (%)		REFS.
	1. TBDMSOTf, CH_2Cl_2, $0°$ 2. CH_3Li, THF, $0°$ 3. CH_3CO_2H, $C_5H_{11}ONO$	$(C_6H_5CH_2)_2NNO$	(85)	241,244
	1. $C_6H_5SeOSO_2CF_3$, CH_2Cl_2, $0°$ 2. $(C_2H_5)_3N$ or DBU, -78 to 40° 3. C_6H_5COCl	$(C_6H_5CH_2)_2NCOC_6H_5$ $+ \ C_6H_5CH_2NHCOC_6H_5$	(49) (39)	246
	1. TBDMSOTf, CH_2Cl_2, $0°$ 2. CH_3Li, THF, $0°$ 3. $(C_2H_5)_3Al$	$(C_6H_5CH_2)_2NCH(C_2H_5)C_6H_5$ (75)		242
	1. TBDMSOTf, CH_2Cl_2, $0°$ 2. CH_3Li, THF, $0°$ 3. $(CH_3)_3SiCN$, $TiCl_4$, CH_2Cl_2, -78 to 20°	$(C_6H_5CH_2)_2NCH(CN)C_6H_5$ (78)		243

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