The Chemistry of Enones
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CHAPTER 18

Reduction of α,β-unsaturated carbonyl compounds

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I. INTRODUCTION

The two main reduction modes of α,β-unsaturated aldehydes and ketones involve formal hydride attack at either the C-1 or C-3 of the enone system, leading to allylic alcohol or saturated carbonyl compound, respectively. It has been suggested that the relative importance of these paths depends on the relative 'hardness' or 'softness' of the substrate, defined in terms of coefficients of the lowest unoccupied molecular orbital (LUMO) (*vide infra*). While the 1, 2 addition is considered to be a more charge-controlled process, 1, 4 addition is a frontier-orbital controlled process.

In addition to these two reduction modes, which involve formal addition of a single hydrogen molecule to the substrate, it is also possible to add two hydrogen molecules, yielding the corresponding saturated alcohol. Alternatively, formal addition of two molecules of hydrogen may completely deoxygenate the substrate, giving the unsaturated hydrocarbon. Finally, total reduction with three hydrogen molecules would provide the saturated hydrocarbon.

The synthetic application of a given reduction method should be considered primarily in terms of its regioselectivity, stereochemical control and chemoselectivity. Regioselectivity refers mainly to selection between the 1, 4- and 1, 2-reduction modes. Stereochemical control refers to the relative and absolute configuration of the newly formed sp^3 centers at positions 1, 2 or 3 of the enone system. Chemoselectivity refers to the opportunity of selectively reducing the desired functionality in a complex molecule containing other easily reducible functional groups. Other important factors, particularly for reactions to be carried out in large scale, are the availability and cost of the given reducing system as well as convenience and simplicity of the procedures.

Available methods for reduction of carbonyl functionalities and, in particular, α,β-unsaturated ones may be divided conveniently into four classes, based on historic considerations. The earliest procedures, extensively used prior to the discovery of catalytic hydrogenation and metal hydride reductions, employed dissolving metals. In the broader sense, more recent developments, such as reduction with low-valent transition-metal compounds and electrochemical processes, may also be included in this category as they all proceed, in the mechanistic sense, via sequential addition of electrons and protons to the substrate molecule.

Catalytic hydrogenation may be regarded as the second generation of reducing systems. Indeed, both heterogeneous and homogeneous catalytic hydrogenation replaced many of the earlier dissolving metal techniques, although the latter are still used due to selectivity characteristics or convenience.

The discovery of metal hydrides and complex metal hydrides, particularly those of boron and aluminum in the early 1940s, have revolutionized the reduction of organic functional groups. These reagents may be regarded as the third generation of reducing systems. Extensive studies over the past fifty years have led to a broad variety of hydridic reagents whose reducing power and selectivity are controlled by appropriate modification of the ligands in the metal coordination sphere[1]. Hydridic reagents today include other main-group metal hydrides, such as silicon and tin derivatives, as well as a variety of transition-metal hydrides that are employed in stoichiometric quantities, such as the iron, copper, chromium and cobalt compounds.

The advent of organo-transition-metal chemistry within the past thirty years has generated a plethora of novel synthetic methods that provide new opportunities for selective reduction. Composite reducing systems comprised of a transition-metal catalyst and a relatively nonreactive hydride donor represent the fourth generation of reductants. The generally high selectivities provided by such systems arise from two main facts: (a) specific interaction between the transition-metal catalyst and the substrate functionality, and (b) selective, facile hydride transfer from the hydride-donor to the transition metal, and hence to the substrate. Many of the transfer-hydrogenation methods may be included within this fourth category as well. Therefore, although in many respects several transfer-hydrogenation techniques resemble regular catalytic hydrogenations, they are discussed in Section VI that deals with composite reducing systems.

II. ELECTRON-TRANSFER REDUCTIONS

A. Dissolving-metal Reductions

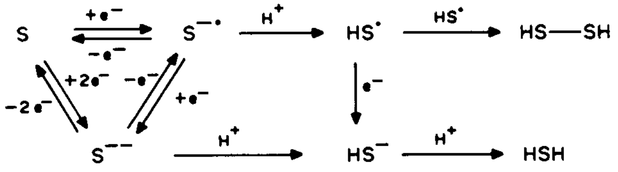
A variety of organic functional groups are reduced by active metal either in the presence of a proton donor or followed by treatment with a proton donor. This approach is one of the earliest reduction procedures in organic chemistry. Although its importance has decreased with the development of catalytic hydrogenation and metal hydride reduction, there remain a substantial number of dissolving metal reductions still in use due to their advantageous selectivity of reduction. Dissolving metal reductions of α, β-unsaturated carbonyl compounds have been discussed in several review articles[2-10].

Metals commonly utilized include the alkali metals, mainly lithium, sodium and potassium, and also calcium, zinc, magnesium, tin and iron. Alkali metals and calcium have been used in liquid ammonia[10], in low-molecular-weight aliphatic amines[11], in hexamethylphosphoramide[12], in ether or in THF containing crown ethers[13c], or in very dilute solutions in polyethers such as 1, 2-dimethoxyethane (DME)[11a,13a,b]. Reactions with metal solutions in liquid ammonia often use a cosolvent, such as ether, THF or DME, to increase solubility of the organic substrate in the reaction mixture. These same metals as well as zinc and magnesium have also been used as suspensions in various solvents including ether, toluene, xylene, etc. In all procedures a proton source (frequently ethanol, isopropanol, *t*-butanol or even water) is provided in the reaction medium, or together with the substrate, or during the workup procedure.

Sodium amalgam, aluminum amalgam, zinc, zinc amalgam, tin and iron have been added directly to solutions of the substrate in hydroxylic solvents such as ethanol, isopropanol, butanol, isoamyl alcohol, acetic acid, water or aqueous mineral acid. With hydroxylic solvents, and especially with relatively acidic ones, metal amalgams are often used rather than free metals to minimize the release of hydrogen gas side-product.

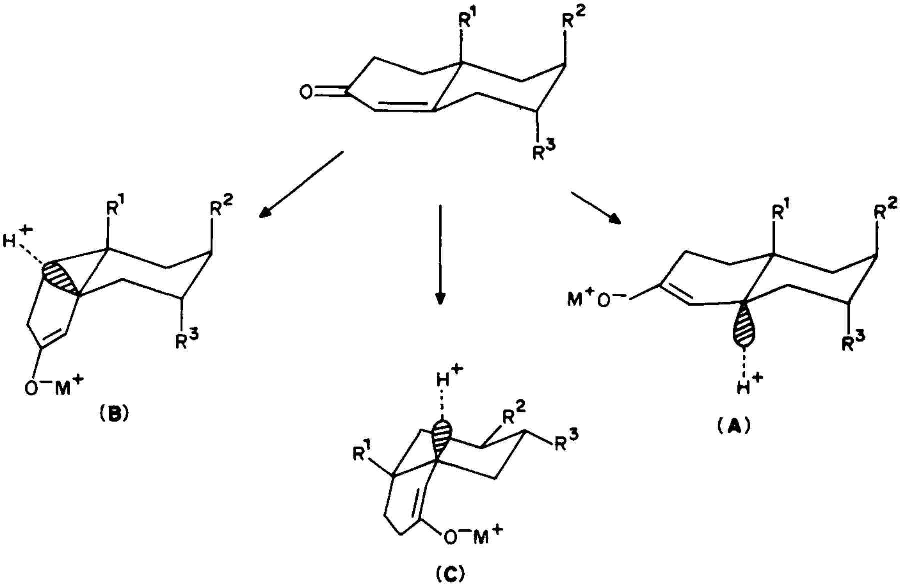
The dissolving-metal reductions are better classified as 'internal' electrolytic reductions in which an electron is transferred from the metal surface (or from the metal in solution) to the substrate. Reduction with low-valent metal ions may also be included in this general class (*vide infra*).

The generally accepted mechanism for dissolving-metal reduction of enones (Scheme 1)[10] involves reversible addition of an electron to a vacant orbital of the substrate (S), yielding a radical anion ($S^{-\bullet}$). The latter can be protonated to give a neutral radical, which may either dimerize or accept another electron and a proton. Alternatively, stepwise or simultaneous reversible addition of two electrons to S can give a dianion capable of accepting two protons. The sequence and timing of these steps should depend upon the substrate, the homogeneity and reduction potential of the medium, and the presence and nature of proton donors in the medium, among other factors.



SCHEME 1

The stereochemistry of reduction has been extensively studied. Metal-ammonia reduction of steroid and terpenoid enones with a β carbon at the fusion of two six-membered rings leads, in general, to the thermodynamically more stable isomer at that position[14]. Stork has formulated a more general rule, namely that the product will be the more stable of the two isomers having the newly introduced β-hydrogen axial to the ketone ring[15]. This rule has correctly predicted the stereochemical outcome of many metal-ammonia reductions, with very few exceptions. The rule is rationalized in terms of stereoelectronic effects in the transition state (either the radical anion or the dianion stage). For example, in reduction of octalones of the type shown in Scheme 2, only two (**A** and **B**) of three possible anionic transition states involving a half-chair conformation of the enone-containing ring would be allowed stereochemically[15].

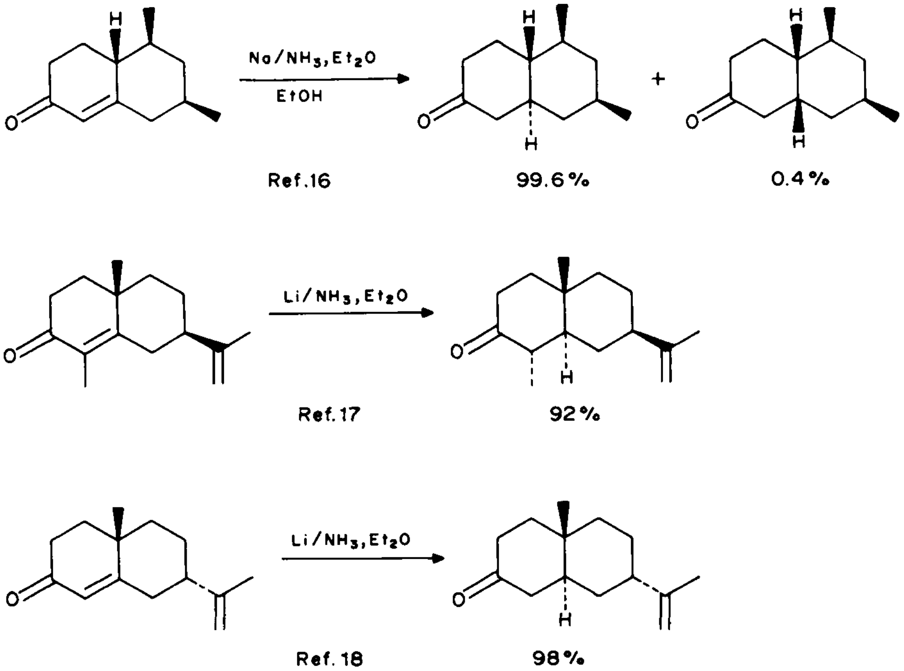


SCHEME 2

In these two conformers the orbital of the developing C—H bond overlaps with the remainder of the π-system of the enolate. The alternative conformer **C** is not allowed because it does not fulfill the overlap requirement. The *trans* transition-state **A** is generally more stable than the *cis* **B**, and the *trans*-2-decalone reduction product would be obtained, despite the fact that the *cis* isomer having a conformation related to **C** should be more stable when R^2 and/or R^3 are larger than a hydrogen atom. This rule of 'axial protonation' has been found to be widely applicable to metal-ammonia reductions of octalones, steroids and other fused-ring systems. Representative examples are given in Scheme 3[15-18].

Generally, the conditions employed in the workup of metal-ammonia reductions lead to products having the more stable configuration at the α-carbon atom, but products having the less stable configuration at this center have been obtained by kinetic protonation of enolate intermediates[19,20]. A more detailed discussion of stereochemistry in metal-ammonia reduction of α,β-unsaturated carbonyl compounds is given in Reference 10.

Scope and limitations. Before the introduction of metal-ammonia solutions for the reduction of α,β-unsaturated carbonyl compounds[10], sodium, sodium amalgam or zinc in protic media were most commonly employed for this purpose. Some early examples of

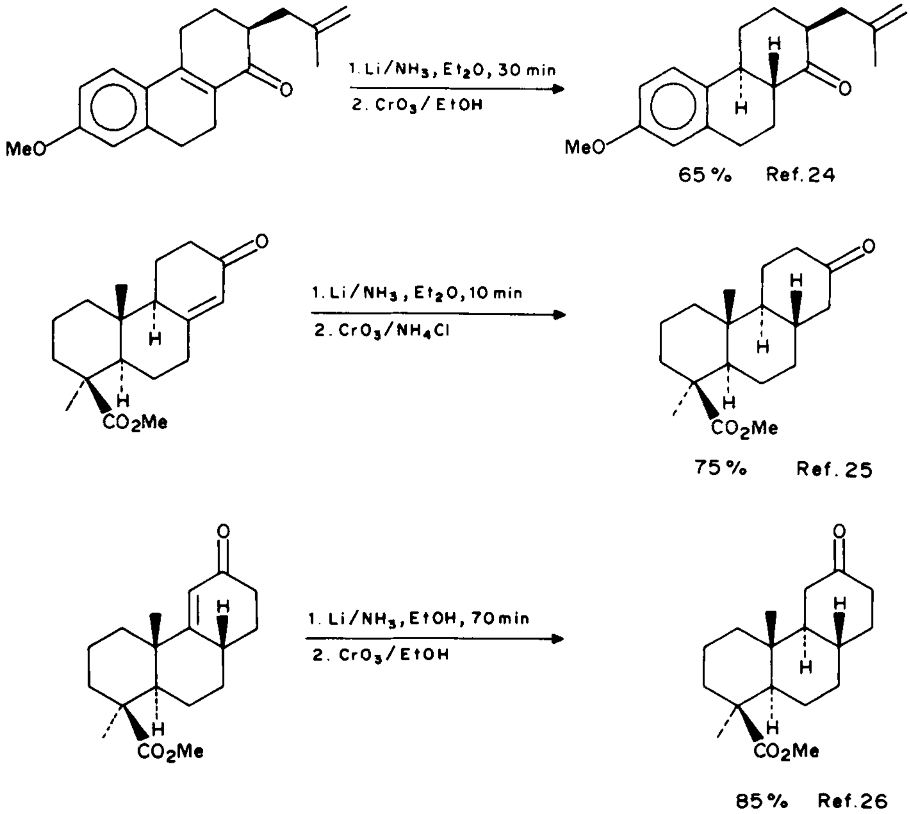


SCHEME 3

their use include the conversion of carvone to dihydrocarvone with zinc in acid or alkaline medium[21], and of cholest-4-en-3-one to cholestanone with sodium in alcohol[22,23]. Reductions using these earlier methods may be complicated by a variety of side-reactions, such as over-reduction, dimerization, skeletal rearrangements, acid- or base-catalyzed isomerizations and aldol condensations, most of which can be significantly minimized by metal-ammonia reduction.

Ketones ranging from simple acyclic varieties to complex polycyclic ones such as steroids, terpenoids and alkaloids have been reduced to saturated ketones, usually in good yield, by metal solutions, mainly in liquid ammonia. A few examples are given in Scheme 4[10,24–26]. The reduction is applicable to compounds with any degree of substitution on the double bond. Although only two equivalents of these metals are required for the conversion of an enone to a saturated ketone, it is often convenient to employ the metal in excess. Proton donors are often employed to prevent competing side-reactions, such as dimerization. The presence of proton donors in the medium may lead to the conversion of an α,β-unsaturated ketone to the saturated alcohol. Obviously, at least four equivalents of metal must be present for that type of reduction to take place.

Alcohols, such as methanol and ethanol, lead to the sole formation of saturated alcohols from unsaturated ketones when the former are present in excess during the reduction. Mixtures of ketone and alcohol are generally formed when one equivalent of these proton donors is employed[27]. These alcohols have acidity comparable to that of saturated ketones, and when they are present, equilibrium can be established between the initially formed metal enolate and the saturated ketone. The latter is then reduced to the saturated alcohol. Such reductions generally do not occur to a very significant extent when one equivalent of *t*-butanol[28] or some less acidic proton donor, such as triphenylcarbinol[27], is



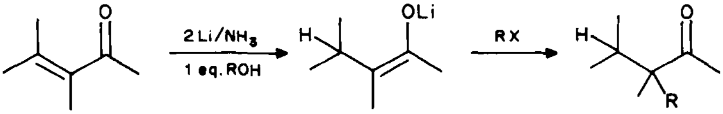
SCHEME 4

employed. The acidity of the ketone involved as well as the solubility of the metal enolate in the reaction medium are of importance in determining whether alcohols are formed.

Even though the reaction conditions may lead to formation of the metal enolate in high yield, further reduction may occur during the quenching step of the reaction. Alcohols such as methanol and ethanol convert metal enolates to saturated ketones much faster than they react with metals in ammonia[29,30], and quenching of reduction mixtures with these alcohols will usually lead to partial or complete conversion to alcoholic product rather than the saturated ketone. Rapid addition of excess solid ammonium chloride is the commonly employed quench procedure if ketonic products are desired[31].

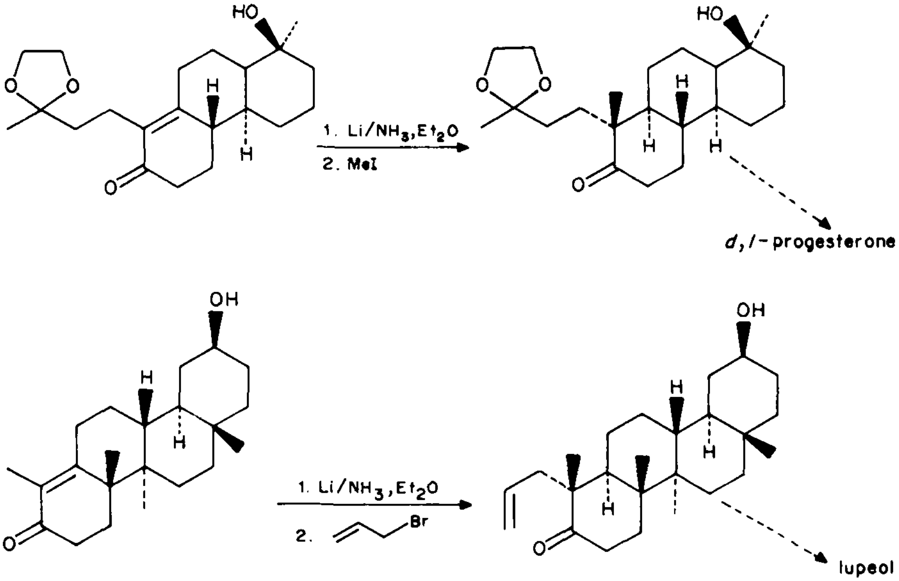
To prevent alcohol formation, other reagents that destroy solvated electrons before reaction mixture neutralization may be employed. These include sodium benzoate[32], ferric nitrate[33,34], sodium nitrite[35], bromobenzene[36], sodium bromate[37], 1,2-dibromoethane[4], and acetone[14].

Reduction-alkylation. The versatility of metal-ammonia reduction was considerably advanced by the discovery that the lithium enolates of unsymmetrical ketones generated during reduction can undergo C-alkylation with alkyl halides and carbonation with carbon dioxide[38,39]. These enolate trapping reactions allow regiospecific introduction of groups at the carbon atoms of unsymmetrical ketones via the appropriate enone precursors. This procedure has been widely employed for ketones of a variety of structural types[28,38–44]. The procedure usually involves generation of a specific lithium enolate of an unsymmetrical ketone by reduction of the corresponding α, β-unsaturated ketone with two equivalents of lithium in liquid ammonia that contains no proton donor or just a single equivalent of alcohol. This enolate is then reacted with excess alkylating agent (Scheme 5).



SCHEME 5

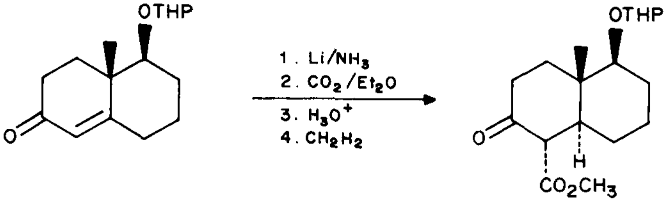
This reduction-alkylation sequence has been extensively used in the total synthesis of natural products. The two transformations shown in Scheme 6 represent key steps in the synthesis of *d, l*-progesterone[45] and lupeol[46].



SCHEME 6

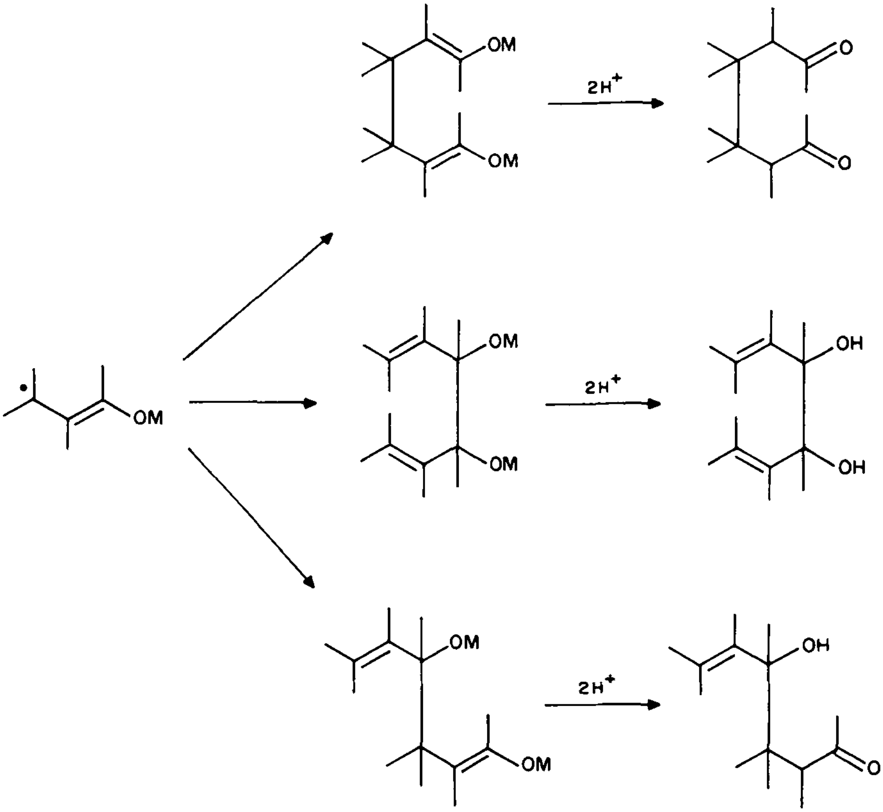
If the ammonia is removed and replaced by anhydrous ether, the intermediate lithium enolate can be converted to β-keto ester by carbonation, followed by acidification and treatment with diazomethane, as illustrated in Scheme 7[47].

Dimerization processes. Because of the intermediacy of radical anions and/or hydroxyallyl free radicals in dissolving-metal reductions of enones, dimerization processes involving these species may compete with simple reduction. Scheme 8 shows the three



SCHEME 7

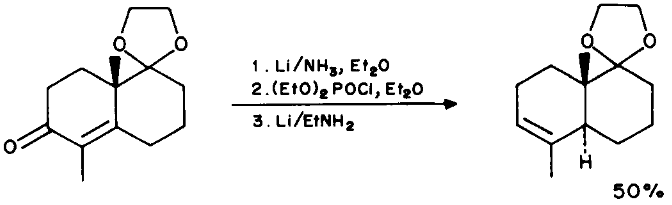
types of dimers that may be produced. 1,6-Diketones may be formed from coupling of the two radical anions at their β-positions; unsaturated pinacols are produced if coupling occurs at the carbonyl carbon atoms; and unsaturated γ-hydroxy ketones are produced by nonsymmetrical coupling of the β-carbon of one radical anion and the carbonyl carbon of a second such intermediate.



SCHEME 8

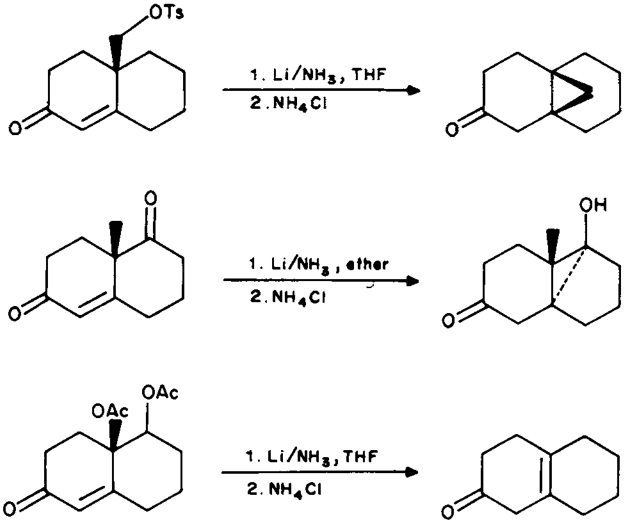
The dimerization products shown in Scheme 8 are generally the major ones obtained in electrochemical reductions[48-51] (*vide infra*) or reductions at metal surfaces[48,52], in which radical anion intermediates must diffuse to a surface before further electron transfer can occur. In metal-ammonia solutions, however, simple reduction is generally favored over dimerization. These solutions provide high concentrations of available electrons, favoring the probability of the radical ion or hydroxyallyl radical to accept a second electron.

Olefin synthesis. Appropriate quenching of a reductively formed lithium enolate with a carboxylic acid anhydride[53,54], chloride[55], methyl chloroformate[56] or diethyl phosphorochloridate yields the corresponding enol esters, enol carbonates or enol phosphates. These derivatives may be transformed into specific olefins via reductive cleavage of the vinyl oxygen function[57], as illustrated by the example in Scheme 9.



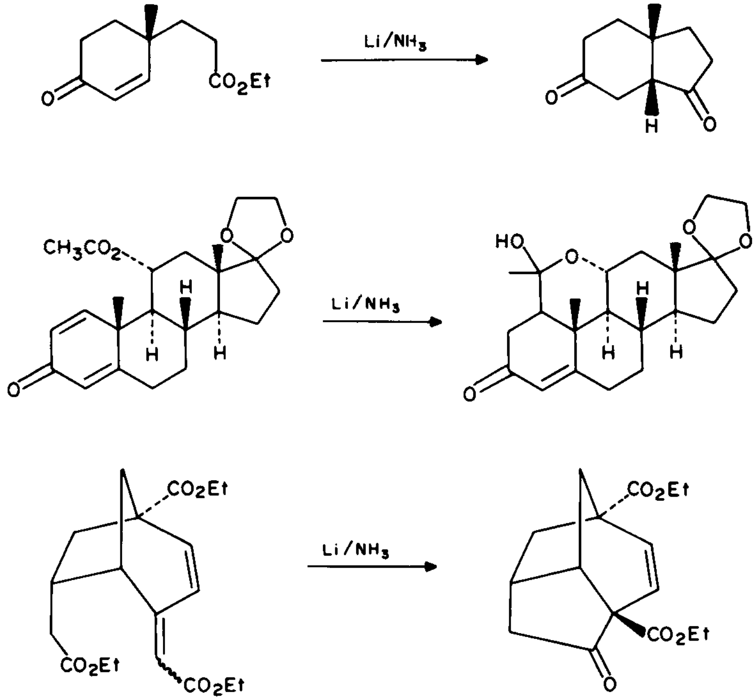
SCHEME 9

Intramolecular reactions. Dissolving-metal reduction of unsaturated ketones involve intermediates with carbanionic character at the β-position. Therefore, intramolecular displacements, additions and eliminations may occur during the reduction of polyfunctional enones. Many α,β-unsaturated carbonyl compounds have structural features which allow such intramolecular reactions. The examples given in Scheme 10 include intramolecular substitution of a tosylate leaving group[58], addition to ketone to form cyclopropanol[59], and elimination of an acetate group to give the unconjugated enone[60].



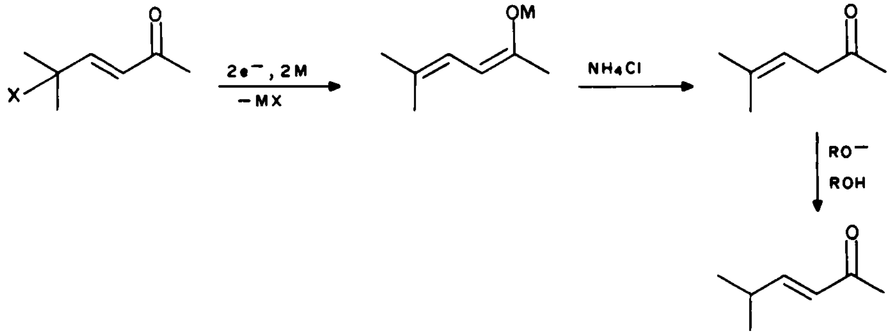
SCHEME 10

The examples given in Scheme 11 include synthesis of a perhydroindanedione skeleton via intramolecular addition to an ester group[61], a related formation of a stable steroidal hemiacetal[62], and lithium-ammonia conversion of a bicyclic unsaturated triester into a tricyclic keto diester[63].



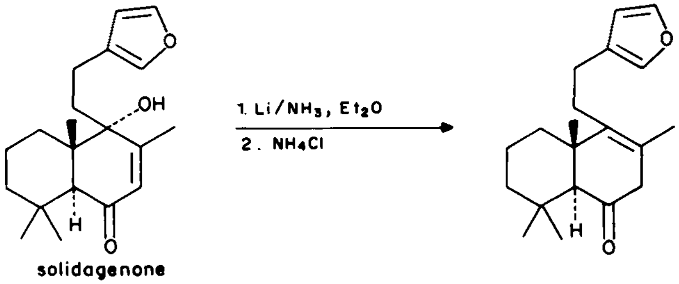
SCHEME 11

α,β-Unsaturated ketones with leaving groups at the γ-position normally undergo reductive elimination with metals in ammonia to give metal dienolates as an initial product (Scheme 12).



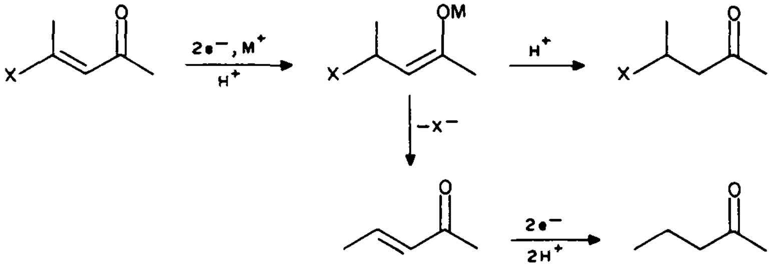
SCHEME 12

Quenching these enolates with ammonium chloride allows the isolation of the β,γ-unsaturated ketone. The latter can isomerize under basic conditions to the conjugated enone. Such processes have been reported with a broad variety of leaving groups, such as hydroxide anion[64,65], alkoxide[66], and acetate[60], as well as during fission of a lactone[67–69] or an epoxide ring[70]. An example involving elimination of hydroxide ion from solidagenone[65] is shown in Scheme 13.



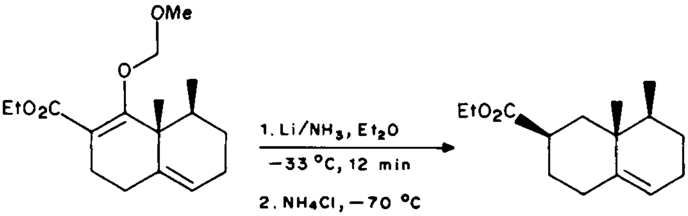
SCHEME 13

α,β-Unsaturated carbonyl compounds having a leaving group at the β position react with dissolving metals to give metal enolates, which may undergo elimination to yield new α,β-unsaturated carbonyl compounds that are susceptible to further reduction (Scheme 14)[43,71–77].



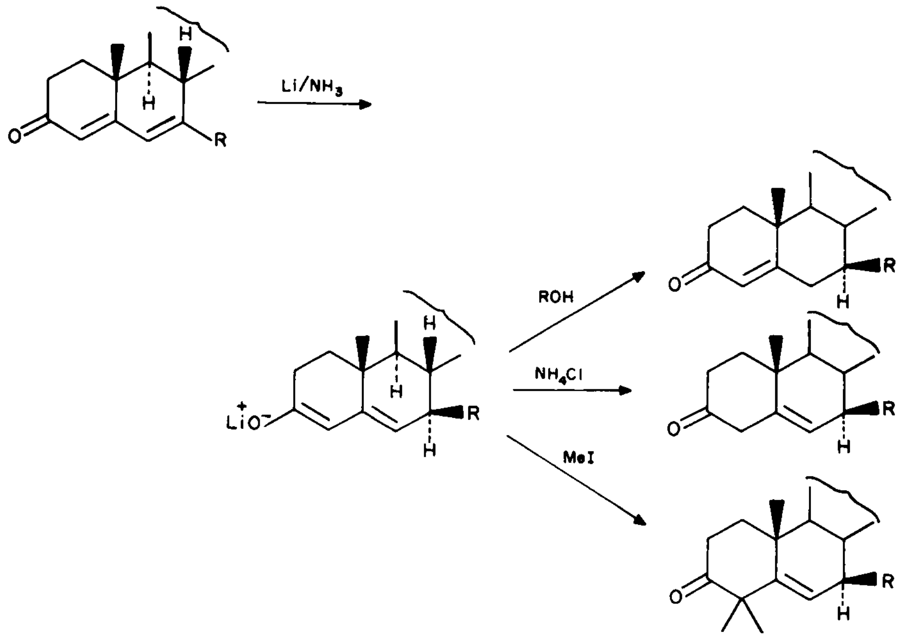
SCHEME 14

For example, β-alkoxy-α,β-unsaturated esters[72,73] and acids[78] have been found to undergo double reduction. This procedure was used as a key step in the total synthesis of eremophilane sesquiterpenes (Scheme 15)[72].



SCHEME 15

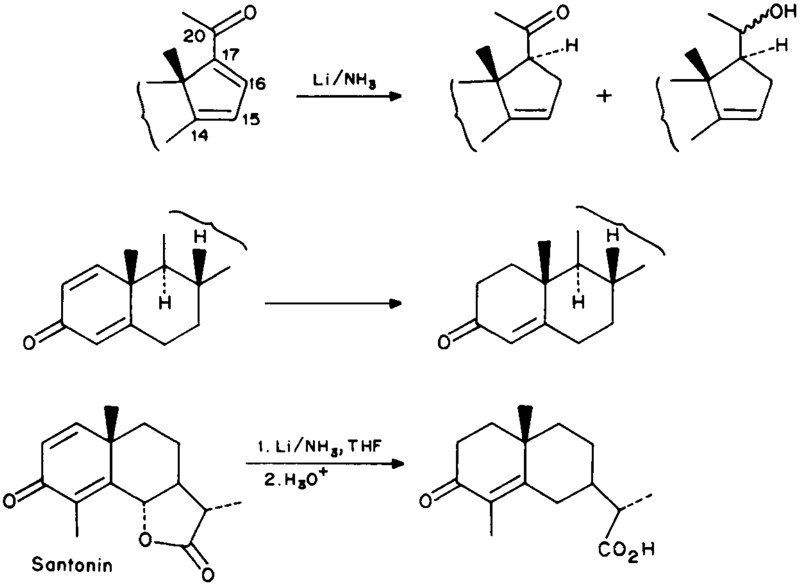
Both linear and cross-conjugated dienones are reduced by solutions of metals in liquid ammonia. For example, steroidal 4, 6-dien-3-ones (Scheme 16) and related compounds are reduced initially to 3, 5-dienolates[44,79–86]. While addition of ammonium chloride to the latter leads to formation of the nonconjugated 5-en-3-one system[83], addition of proton donors such as ethanol or water initiates isomerization leading to the more stable, conjugated 4-en-3-one skeleton[80,81]. Treatment of the dienolate with excess methyl iodide rather than a proton donor gives the 4, 4-dimethyl-5-en-3-one[44,87].



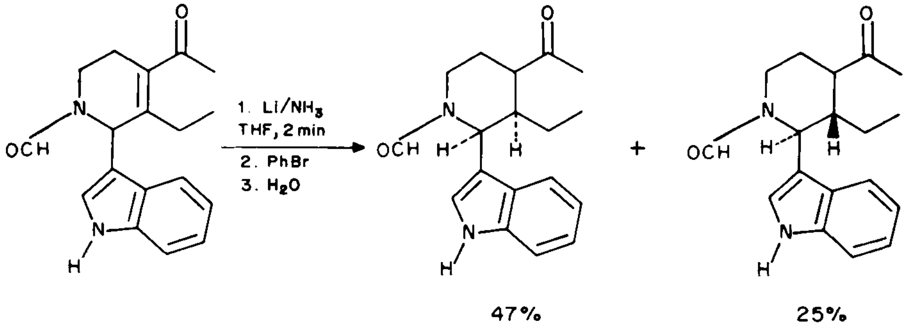
SCHEME 16

Linearly conjugated dienones may be completely reduced to saturated alcohols using excess lithium in liquid ammonia[88]. In variously substituted dienones, the less substituted double bond is often selectively reduced under these conditions. For example, treatment of steroidal 14, 16-dien-20-one with lithium in liquid ammonia (with or without propanol) leads mainly to reduction of the 16, 17 double bond (Scheme 17)[89,90]. Accordingly, the less substituted double bond of cross-conjugated steroidal dienones[4,44,91,92], santonin or related substrates is selectively reduced under these conditions (Scheme 17)[67–69,93].

Chemoselectivity. Although a host of organic functionalities are reduced by dissolving metals[2,3,5–7,9] it is often possible to reduce double bonds of α,β-unsaturated carbonyl systems without affecting other reducible groups. Internal, isolated olefins are normally stable to metal-ammonia solutions unless they have very low-lying antibonding orbitals[94] or special structural features that stabilize radical anion intermediates[95]. However, terminal olefins may be reduced by dissolving metals[96]. Mono- and polycyclic aromatic compounds undergo reduction with dissolving metals in liquid ammonia (Birch reduction)[2,3,5,8,97,98], but these reactions are generally slow unless proton donors are added. It is therefore possible to reduce α,β-unsaturated ketones selectively in the presence of aromatic rings[99–102]. Selective reduction preserving a reducible indole ring is illustrated in Scheme 18[103].

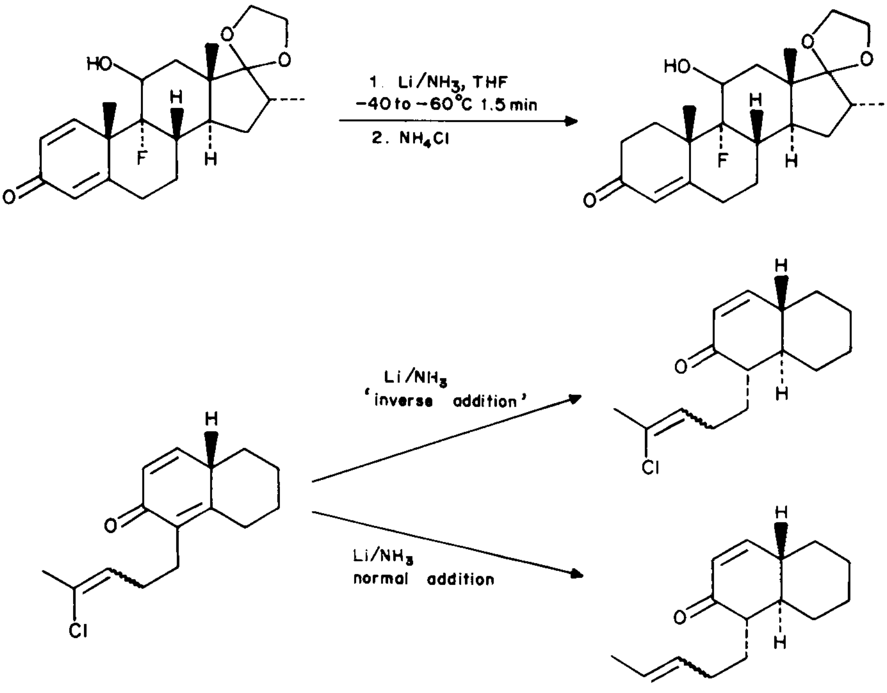


SCHEME 17



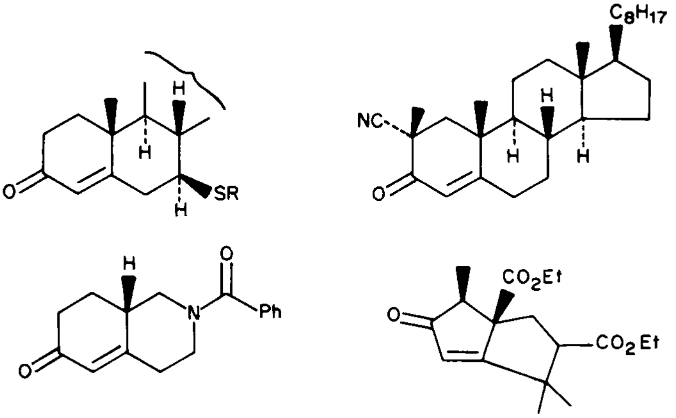
SCHEME 18

Ethynyl carbinols are reduced to allyl alcohols and eventually to olefins with metal-ammonia solutions containing proton donors[104]. However, by excluding proton donors, selective reduction of conjugated enones has been carried out despite the presence of ethynyl carbinol groups[34,105–107]. Similarly, selective reduction of conjugated enones containing allylic alcohols has also been achieved[34,105,107]. Carbon–halogen bonds of alkyl and vinyl halides are readily cleaved by metals in ammonia[5,8,9]. Yet, as shown in Scheme 19, fluoride substituent may be retained by limiting reaction times[92] and a rather sensitive vinyl chloride functionality is preserved by using an inverse addition technique[108].



SCHEME 19

Scheme 20 presents a number of enone-containing compounds that bear additional reducible functionalities, all of which were chemoselectively reduced at the enone site. For



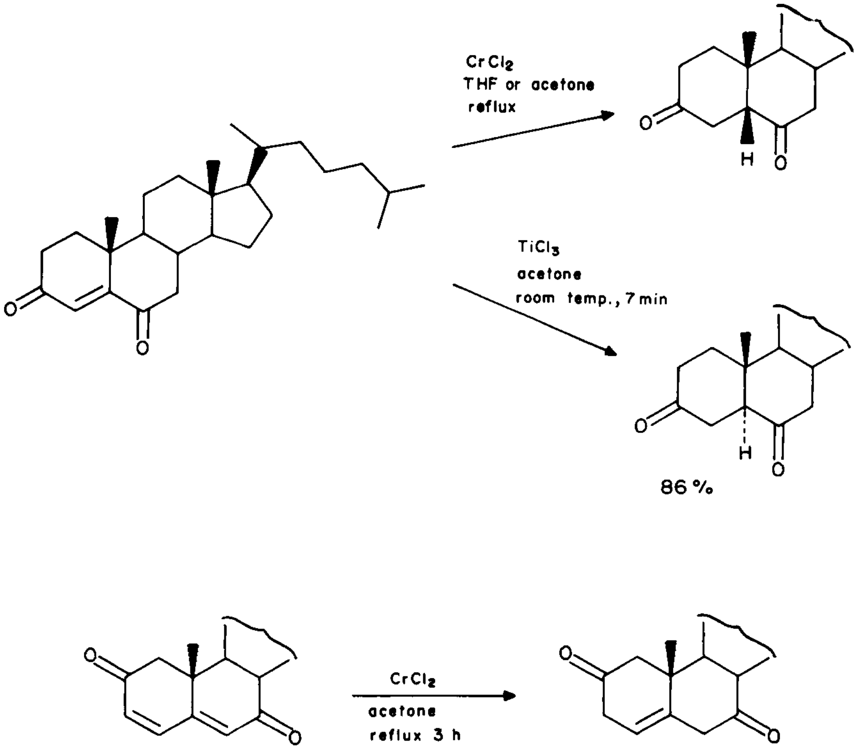
SCHEME 20

example, the C—S bond of many thioethers and thioketals are readily cleaved by dissolving metals[5,8,9,109]. Yet, there are examples of conjugate reduction of enones in the presence of a thioalkyl ether group[109,110]. Selective enone reduction in the presence of a reducible nitrile group was illustrated with another steroidal enone[111]. While carboxylic acids, because of salt formation, are not reduced by dissolving metals, esters[112] and amides[2,8] are easily reduced to saturated alcohols and aldehydes or alcohols, respectively. However, metal-ammonia reduction of enones is faster than that of either esters or amides. This allows selective enone reduction in the presence of esters[113] and amides[36,114,115] using short reaction times and limited amounts of lithium in ammonia.

B. Reduction with Low-valent Transition Metals

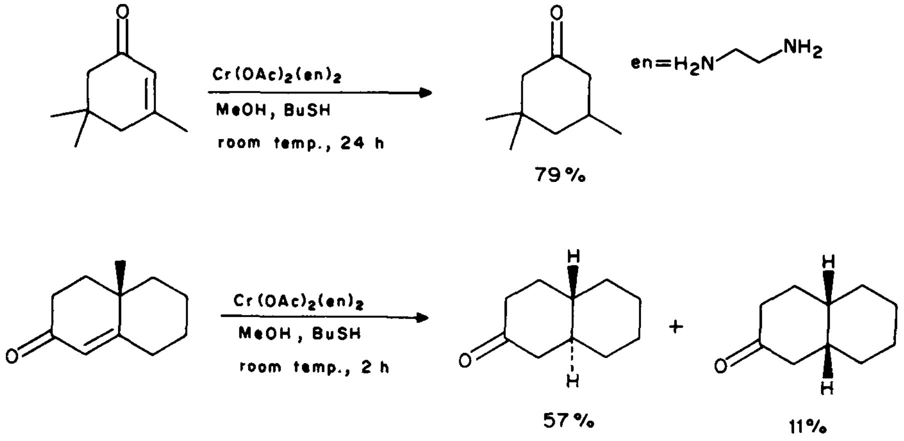
Low-valent species of early transition metals, such as chromium(II)[116], titanium(II), titanium(III)[117], vanadium, molybdenum and tungsten, are useful reducing agents[118]. Electron-deficient olefins and acetylenes are easily reduced by chromium(II) sulfate, *Z*-alkenes being more rapidly reduced than the corresponding *E*-isomers[119]. Titanium(III) species are weaker reducing agents, exhibiting higher chemoselectivity[120].

Several steroid enediones have been reduced by chromium(II) chloride[121]. Interestingly, reduction of cholest-4-ene-3,6-dione yields a different product than that obtained by titanium(III) reduction of the identical substrate (Scheme 21)[120c].



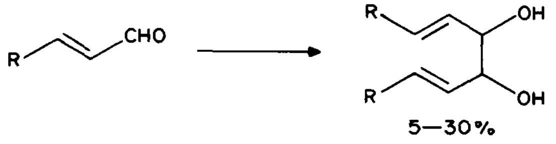
SCHEME 21

Solutions of chromium-bis(ethylenediamine)diacetate complex in methanol are capable of reducing simple α,β-unsaturated ketones to the corresponding saturated ketones. Useful yields are obtained, provided a proton donor (AcOH) and a good hydrogen donor (BuSH) are present in the reaction mixture (Scheme 22)[122].



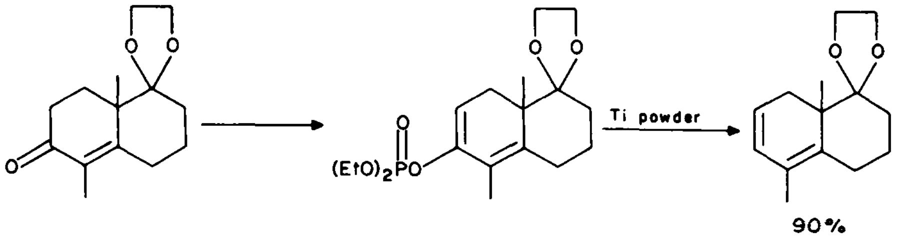
SCHEME 22

Reductive dimerization of α,β-unsaturated ketones is effected by either Cr(II) or V(II) chloride to give 1,4-diketones, and aliphatic α,β-unsaturated aldehydes are dimerized to the allylic glycals (Scheme 23)[123]. Interestingly, nonconjugated aldehydes are stable towards these reagents. Similar pinacolic couplings of aldehydes and ketones with Ti(II) reagents were developed by Corey[124].



SCHEME 23

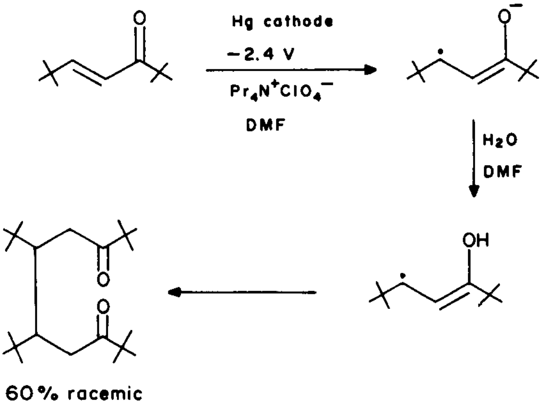
Highly reactive metallic titanium, prepared from $TiCl_3$ and potassium, was found useful for reduction of enol phosphate to alkenes, permitting regioselective synthesis of dienes from α,β-unsaturated ketones (Scheme 24)[125].



SCHEME 24

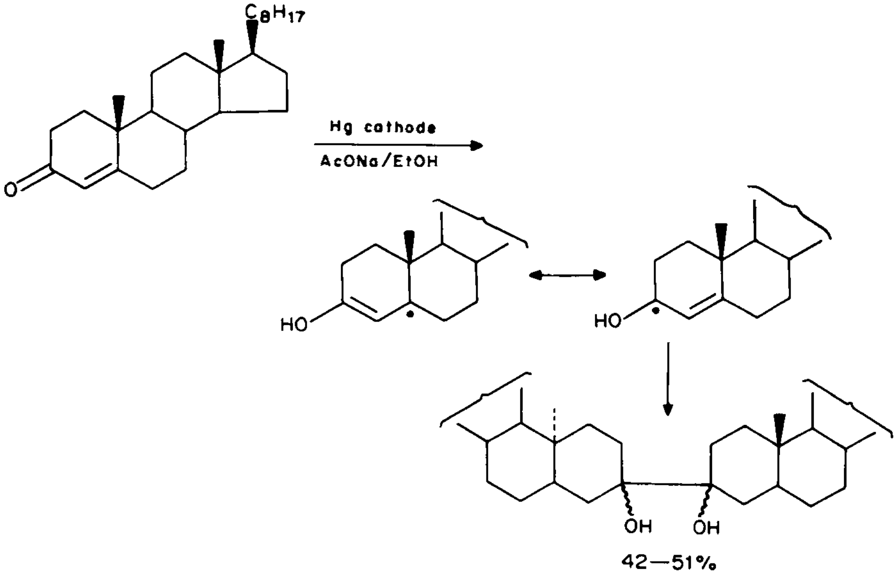
C. Electrochemical Reductions

The electrochemical reduction of α, β-unsaturated ketones and related compounds[5] in aprotic media in the absence of metal cations can, in some cases, lead to relatively stable anion radicals[12c,126]. However, in the presence of proton donors the latter are protonated to form hydroxyallyl radicals, which tend to dimerize more rapidly than they diffuse back to the electrode to undergo further reduction (Scheme 25)[12c].



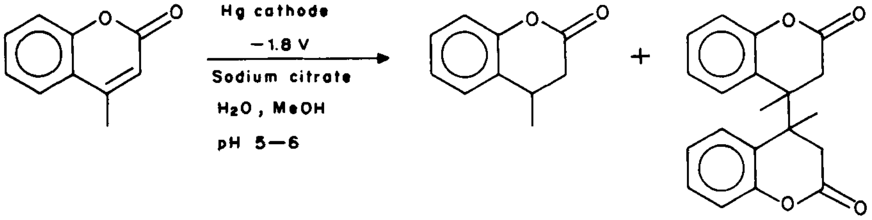
SCHEME 25

Although these allyl radicals prefer to dimerize by coupling at the β-position, if this position is sterically hindered, as in the case of cholest-4-en-3-one, coupling at the carbonyl carbon may be observed yielding a pinacol (Scheme 26)[127].



SCHEME 26

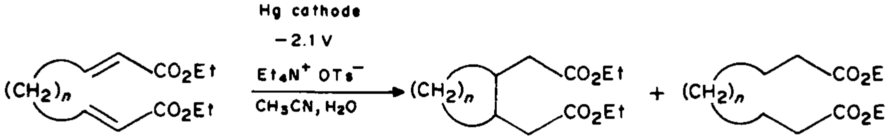
As noted above, such reductive dimerizations have been recorded when unsaturated carbonyl compounds are reacted with various metals, such as lithium, sodium, sodium amalgam, potassium, aluminum amalgam, zinc or magnesium[128,129]. Formation of monomeric reduction products is impeded in these reactions because the intermediate allylic radical must diffuse back to the electrode surface or metal particle for further reduction. A possible solution to this problem might be concurrent electrochemical generation of a soluble reducing agent that can intercept radical intermediates before their dimerization. For example, solutions of magnesium in liquid ammonia can be generated electrochemically[130c]. Similarly, tertiary amine salts, such as yohimbine hydrochloride, can participate in the electrochemical reduction of enones (Scheme 27)[130a,b], via concurrent reduction of the amine to a radical which transfers a hydrogen atom to the intermediate allyl radical.



with	$R_3\overset{+}{N}H\ Cl^-$	57 %	42%
without	$R_3\overset{+}{N}H\ Cl^-$	4 %	93%

SCHEME 27

Reductive dimerization of enones to form a new carbon–carbon bond at the β-position, known as hydrodimerization or electrohydrodimerization, has considerable synthetic utility[131]. For example, high yields of cyclic products are achieved when cyclization is kinetically favorable, leading to three- to six-membered rings from the corresponding unsaturated diesters (Scheme 28)[131d].



$n = 2$	41%	48%
3	100%	—
4	90%	—
6	—	43 %
8	—	50 %

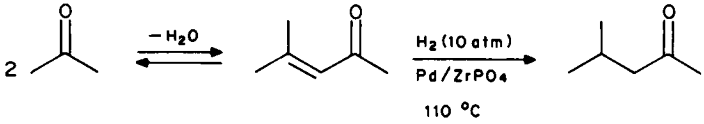
SCHEME 28

The product ratio in electrochemical reduction of benzalacetone is significantly altered by surfactants and various cations, which cause micellar and/or ion-pairing effects. Using these additives, it is possible to control the partitioning of the initially formed radical anion between the two main reaction pathways: either dimerization or further reduction to the saturated ketone[132]. Additionally, micellar surfactants allow the use of aqueous media without cosolvents.

III. CATALYTIC HYDROGENATION

Addition of molecular hydrogen to α,β-unsaturated carbonyl compounds has been extensively reviewed[5,133-135]. Enones can be converted to saturated ketones or to unsaturated or saturated alcohols. Usually, double bonds conjugated to the carbonyl moiety are reduced prior to nonconjugated ones. 1,2-Reduction to allylic alcohols via catalytic hydrogenation is quite rare, and this transformation is more conveniently performed with hydridic reducing agents, such as boron- and aluminum-hydrides (*vide infra*). Nevertheless, there are a number of reported cases where 1,2-reduction is preferred over 1,4-selectivity. Citronellal, for example, is reduced preferentially at the carbonyl function using nickel on silica-gel as a catalyst, while hydrogenation catalyzed by $Pd/BaSO_4$ yields the corresponding saturated aldehyde[136]. Reduction to the saturated alcohol is achieved by catalytic hydrogenation over nickel[137], copper chromite[138], or nickel–aluminum alloy in NaOH[139].

Enones are reduced to saturated ketones by catalytic hydrogenation, provided the reaction is stopped following the absorption of 1 mole of hydrogen[140]. A number of catalysts were found useful for this, including platinum[141], platinum oxide[142,143], Pt/C[140], Pd/C[140,144], Rh/C[140], tris(triphenylphosphine)rhodium chloride[145,146], nickel–aluminum alloy in 10% aqueous NaOH[147], and zinc-reduced nickel in an aqueous medium[148]. Mesityl oxide is formed from acetone and reduced in a single pot to methyl isobutyl ketone using a bifunctional catalyst comprised of palladium and zirconium phosphate (Scheme 29)[149].

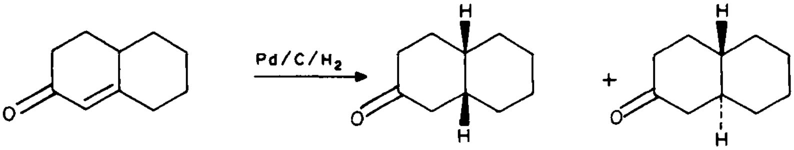


SCHEME 29

Both the ease and the stereochemical course of hydrogenation of α,β-unsaturated ketones are strongly influenced by various factors, particularly the nature of the solvent and the acidity or basicity of the reaction mixture. It is usually difficult to predict the product distribution in a particular reaction under a given set of conditions. Some efforts have been made to rationalize the effect of the various parameters on the relative proportions of 1,2- to 1,4-addition, as well as on the stereochemistry of reduction[150].

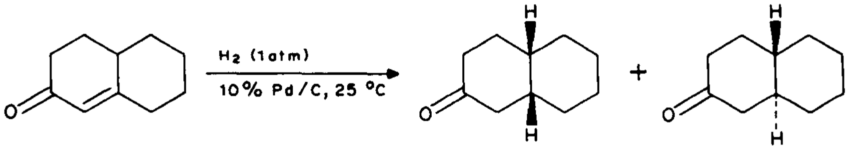
For example, the product distribution in β-octalone hydrogenation in neutral media is related to the polarity of the solvent if the solvents are divided into aprotic and protic groups. The relative amount of *cis*-β-decalone decreases steadily with decreasing dielectric constant in aprotic solvents, and increases with dielectric constant in protic solvents, as exemplified in Scheme 30 (dielectric constants of the solvents are indicated in parentheses)[151]. Similar results were observed in the hydrogenation of cholestenone and on testosterone[152]. In polar aprotic solvents 1,4-addition predominates, whereas in a nonpolar aprotic solvent hydrogenation occurs mainly in the 1,2-addition mode.

Acids and bases have a crucial effect on product stereochemistry in hydrogenation of ring-fused enone systems, as illustrated in Scheme 31[153].



DMF (38)	79 : 21
AcOEt (6)	57 : 43
diethyl ether (4.34)	58 : 42
hexane (1.89)	48 : 52
methanol (33.6)	41 : 59
propanol (21.8)	68 : 32
t-butanol (10.9)	91 : 9

SCHEME 30

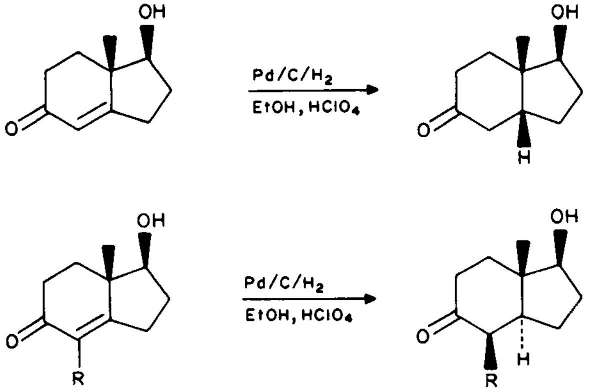


EtOH	53 : 47
EtOH, H_2O, HCl	93 : 7
EtOH, KOH	35—50 : 65—50

SCHEME 31

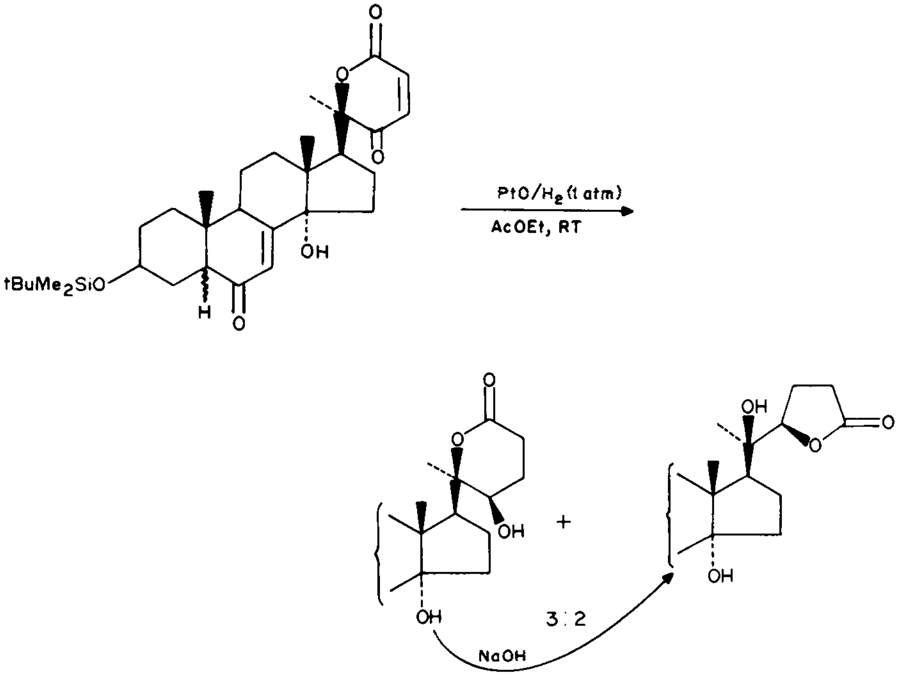
The increased amounts of *trans*-fused product obtained in basic solutions was suggested to arise from hydrogenation of the relatively flat enolate ion which adsorbs irreversibly onto the catalyst surface. Hydrogenation proceeds by hydride ion-transfer from the metal catalyst, followed by protonation. Conversely, in acidic medium, protonation occurs initially, followed by irreversible adsorption on the catalyst, and then transfer of a hydride ion[150]. Stereochemistry of reduction is also related to catalyst activity, catalyst concentration, pressure and stirring rate, as they all affect hydrogen availability at the catalyst surface. Under conditions of low hydrogen availability a reversible adsorption is favorable, and therefore the product stereochemistry is determined by the relative stability of the *cis*- and *trans*-adsorbed species. However, under conditions of high hydrogen availability, product stereochemistry is determined mainly by the nature of the initial adsorption[150,151]. Platinum catalysts, more than palladium varieties, give products determined by the initial adsorption.

Substrate structure has an important influence on stereoselectivity of hydrogenation. For example, hydrogenation of hydrindanone having a trisubstituted double bond gives mainly the *cis* product (Scheme 32)[154], whereas similar compounds with a tetrasubstituted olefin tend to give the *trans* isomer. This phenomenon has been rationalized in terms of preferred conformation of the adsorbed enone, which minimizes steric interactions[154,155].



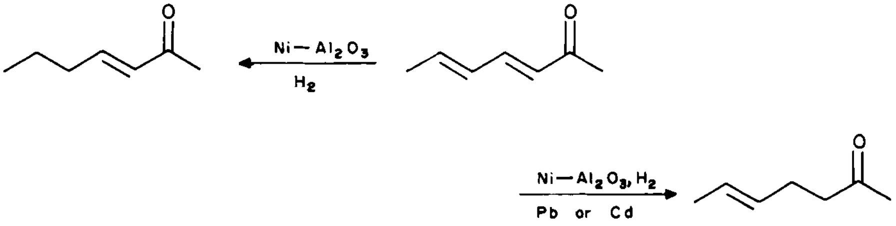
SCHEME 32

The key step in the synthesis of 2-deoxycrustecdysone from the corresponding 20-oxo steroid is the stereoselective catalytic hydrogenation of the α,β-unsaturated lactone shown in Scheme 33 to afford a 2:3 mixture of δ- and γ-lactones, respectively[156]. This crude product was converted into the thermodynamically more stable γ-lactone by treatment with aqueous NaOH.



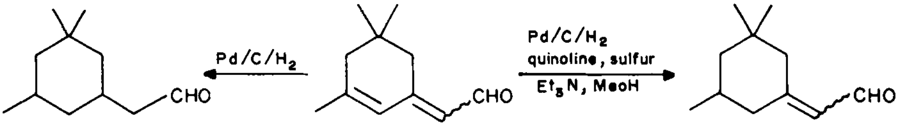
SCHEME 33

In the case of multiply unsaturated carbonyl compounds, regioselectivity is also sensitive to the nature of the catalyst, to reaction conditions and to the structure and degree of substitution of the hydrogenated double bonds. For example, hydrogenation of 3, 5-heptadien-2-one over nickel-on-alumina or nickel-on-zinc oxide occurs mainly at the γ,δ-double bond. But if the catalyst is modified by the addition of lead or cadmium, reduction occurs mainly at the α,β-double bond (Scheme 34)[157].



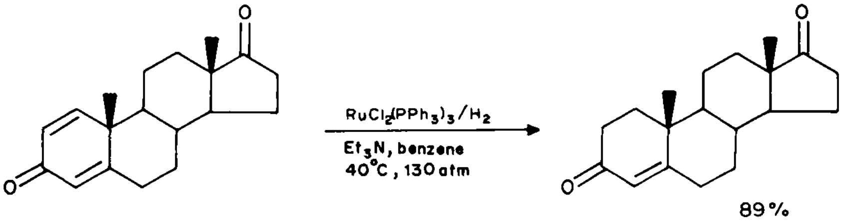
SCHEME 34

Selective reduction the γ,δ-double bond of the dienal shown in Scheme 35 was achieved by hydrogenation over palladium-on-carbon inhibited by quinoline and sulfur. Without inhibition, hydrogenation to the saturated aldehyde was observed[158].



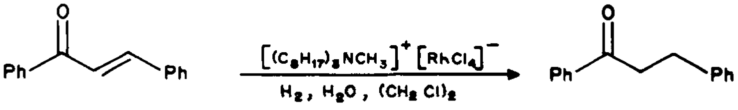
SCHEME 35

Homogeneous catalysts, such as $RhCl(PPh_3)_3$[146] and $RuCl_2(PPh_3)_3$[159], have proved efficient in the selective hydrogenation of enones and dienones. For example, the hydrogenation selectivity of 1, 4-androstadiene-3, 17-dione to 4-androstene-3, 17-dione is increased by elevated pressures, low temperatures and the presence of optimal amount of amines (Scheme 36)[159].



SCHEME 36

The solvated ion-pair $[(C_8H_{17})_3NCH_3]^+[RhCl_4]^-$, formed from aqueous rhodium trichloride and Aliquat-336 in a two-phase liquid system, hydrogenates α,β-unsaturated ketones and esters selectively at the C═C double bond (Scheme 37)[160]. The reduction of benzylideneacetone follows first-order kinetics in substrate below 0.2 M, and approaches second-order in hydrogen at partial pressures below 0.12 atm. The catalysis is also depends on the nature of the solvent, the phase-transfer catalyst and stirring rates.



SCHEME 37

The homogeneous water-soluble hydrogenation catalyst $K_3(Co(CN)_5H)$ is very active for hydrogenating conjugated dienes and α,β-unsaturated ketones under phase-transfer reaction conditions[161]. Thus, conjugated dienes are converted into monoenes, generally with overall 1,4-addition to yield *E*-olefins, and α,β-unsaturated ketones are reduced to saturated ketones in high yields. These conditions are not useful with α,β-unsaturated aldehydes, as they lead to polymerization of the starting material.

IV. REDUCTIONS WITH MAIN-GROUP METAL HYDRIDES

A. Boron Hydrides

Although $NaBH_4$ does not attack isolated olefins, C=C double bonds conjugated to strong anion-stabilizing groups may be reduced by this reagent[162–164].

Rationalization of the regioselectivity of borohydride reduction of α,β-unsaturated aldehydes and ketones has been attempted using the 'hard' and 'soft' acid-base concept[165] (*vide infra*, discussion of aluminum hydrides). It is assumed that the relatively 'soft' hydrides add preferentially to the enone system via a 1,4-mode while 'hard' reagents attack the carbonyl carbon. Borohydrides are considered softer than the corresponding aluminum hydrides. Replacement of a hydride group on boron by alkoxide makes it a harder reagent. Lithium salts are harder than sodium species. Thus, $LiAlH_4$ gives more 1,2-attack than $LiBH_4$, which, in turn, gives more than $NaBH_4$. $NaBH(OMe)_3$ yields more 1,2-reduction product than $NaBH_4$, and when production of alkoxyborates is prevented, 1,4-reduction predominates. This implies that slow addition of borohydride to a substrate solution should help to build up alkoxyborate species and increase the relative amount of 1,2-reduction. Generally, aldehydes undergo more 1,2-reduction than the corresponding ketones.

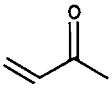
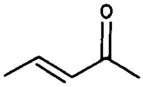
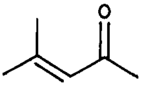
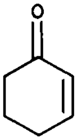
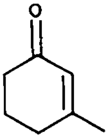
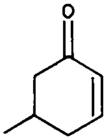
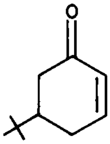
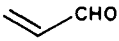
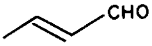
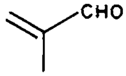
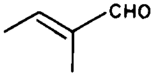
The reduction of α,β-unsaturated aldehydes and ketones by sodium borohydride leads, in general, to substantial amounts of fully saturated alcohols. In alcoholic solvents, saturated β-alkoxy alcohols are formed via conjugate addition of the solvent[166]. This latter process becomes the main reaction path when reduction is performed in isopropanol in the presence of sodium isopropoxide. In a base, a homoallylic alcohol can become the major product of borohydride reduction of an enone[166].

Analysis of the influence of substrate structure on $NaBH_4$ reduction has shown that increasing steric hindrance on the enone increases 1,2-attack (Table 1)[166].

$NaBH_4$ reduction of 3-substituted 5,5-dimethylcyclohex-2-enones in alkaline solution of water–dioxane occurs exclusively at the 1,2-positions. The rate of reduction is strongly dependent on the 3-substituent. A Hammett-type correlation revealed similar reaction characteristics to those of borohydride reduction of substituted acetophenones[167].

In order to study the factors determining the regioselectivity of sodium borohydride reduction of α,β-unsaturated ketones, reactions with 3-methylcyclohexenone, carvone and cholestenone were carried out in 2-propanol, diglyme, triglyme or pyridine[168]. Mixtures of 1,2- and 1,4-reduction products were obtained in the alcoholic and etheric

TABLE 1. The effect of the structure of α, β-unsaturated ketones and aldehydes on their reduction with $NaBH_4$ and $LiAlH_4$[a]

Substrate	$NaBH_4$ in 1:1 H_2O/EtOH	$LiAlH_4$ in ether
	86(57:43)	79(92:8)
	90(65:35)	85(99:1)
	89(92:8)	82(100:0)
	90(59:41)	97(98:2)
	90(70:30)	88(100:0)
	100(49:51)	99(91:9)
	100(42:58)	99(93:7)
	70(85:15)	70(98:2)
	91(92:8)	94(100:0)
	100(> 99: < 1)	98(100:0)
	95(> 99: < 1)	82(100:0)

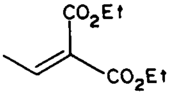
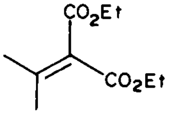
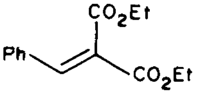
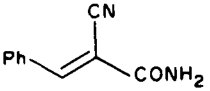
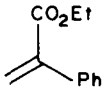
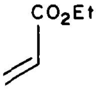
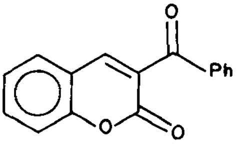
[a] The numbers represent the overall reduction yield (%), the numbers in parentheses represent the ratio of 1,2- to 1,4-attack.

solvents, whereas pure 1,4-reduction was observed in pyridine. Addition of triethyl amine to $NaBH_4$ in diglyme led to formation of triethylamine borine, Et_3NBH_3. Similarly, with pyridine, pyridine-borine could be isolated, leading to exclusive 1,4-reductions.

The results were interpreted in terms of steric requirements of the actual reducing species. It was suggested that attack of BH_4^- proceeds exclusively along the 1,4-reduction mode, whereas alkoxyborohydrides (formed as reaction products) prefer the 1,2-reduction mode. The pyridine-borine itself does not reduce enones under the reaction conditions, but it inhibits formation of alkoxyborohydrides[168]. The same trend was observed with aluminum hydride reductions. When $LiAlH_4$ was first reacted with pyridine to form lithium tetrakis(dihydro-*N*-pyridyl) aluminate, 1,4-reduction predominated[168].

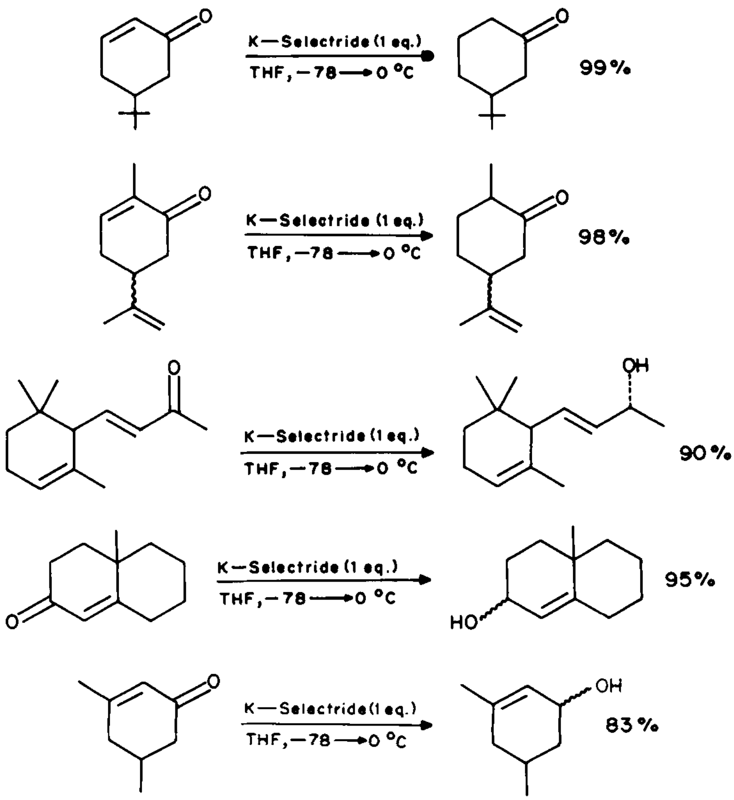
Low regioselectivity is observed in reduction of enones with a 2:1 mixture of sodium cyanoborohydride and zinc chloride in ether at room temperature[169]. A mixture containing 1,2- and 1,4-reduction products is obtained in a ratio that is greatly dependent upon substrate.

TABLE 2. Reduction of α,β-unsaturated carboxylic acid derivatives with $NaBH_4$

Substrate	Yield (%)
	59
	74
	69
	81
	80
	25
	79

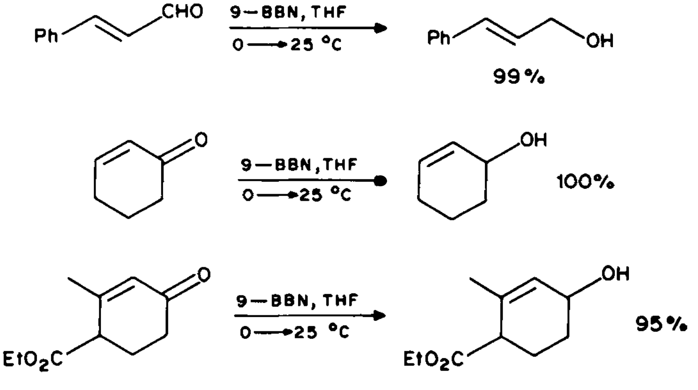
From the reduction in methanol of a series of substituted 2-aryl-(*Z*)- and (*E*)-cinnamates by $NaBH_4$ at room temperature, it was concluded that the facile reduction to give dihydrocinnamates proceeds through an early transition state of considerable polarity[162]. A few more examples are given in a related study (Table 2)[170].

Several organoborohydrides were found to effect the selective 1,4-reduction of enones. For example, lithium and potassium tri-*sec*-butylborohydrides (L- and K-Selectride) and lithium triethylborohydride were found useful for conjugate reduction of α, β-unsaturated ketones and esters. In general, β-unsubstituted cyclohexenones undergo exclusive 1,4-reduction to the corresponding ketone enolate, which can be protonated or alkylated in high yields. Ketones such as 5-*t*-butylcyclohex-2-en-1-one are cleanly reduced to the saturated ketone using K-Selectride at − 78 °C in THF (Scheme 38)[171]. This regioselectivity, however, is not general, but is a result of steric hindrance of the olefin, as well as the size of the ring. Thus alkyl substitution at the β-position completely suppresses the 1,4-reduction mode. While enones in 5- and 7-membered rings are reduced preferably in a 1,2-manner, 6-membered ring enones are reduced in a 1,4-mode. Trapping the intermediate enolate by an alkylating agent (e.g. MeI, allyl bromide) results in an efficient reductive alkylation. Accordingly, when the reduction of α, β-unsaturated esters is performed in dry ether solvents, the major reaction product arises from carbonyl condensation. However, addition of a proton source such as *t*-butanol results in 1,4-reduction.



SCHEME 38

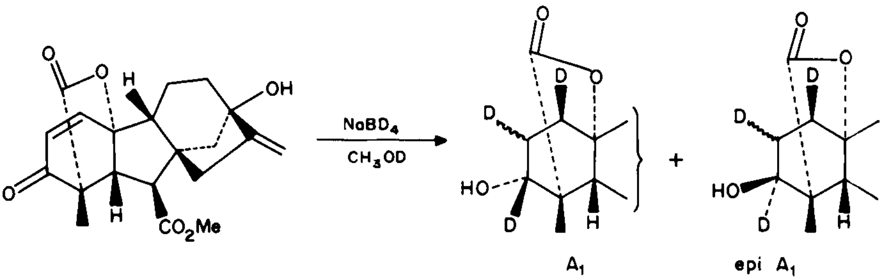
Reduction of α,β-unsaturated aldehydes and ketones with 9-borabicyclo[3.3.1]nonane (9-BBN) proceeds selectively and cleanly to form the corresponding allylic alcohols (Scheme 39)[172]. The reaction tolerates a large variety of functionalities, such as nitro, carboxylic acid, amide, nitrile, sulfide, disulfide, epoxide, etc. Hydroboration of the double bond is a much slower reaction, which does not interfere with carbonyl reduction. For example, 1,2-reduction of cyclohexenone at room temperature with excess of 9-BBN in THF is completed within 10 minutes, while hydroboration of the double bond requires 3 days.



SCHEME 39

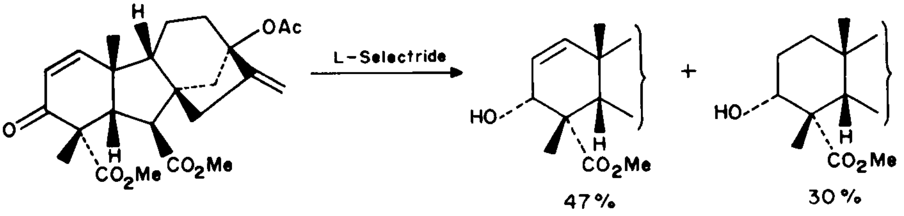
Borohydride reduction of α,β-unsaturated carbonyl compounds has been widely applied in natural product chemistry. A number of α,β-unsaturated ketone derivatives of gibberellins are reduced to the corresponding saturated alcohols by NaBH$_4$[173-176].

Sodium borodeuteride reduction of gibberellin A$_3$ 3-ketone affords gibberellin A$_1$ and its 3-epimer (Scheme 40)[173,174]. Attack of hydride proceeds stereospecifically from the β-face at C-1. Protonation at C-2 proceeds with limited selectivity. Thus, reduction of the above-mentioned gibberellin with either NaBH$_4$–CuCl in deuterated methanol or NaBH$_4$–LiBr followed by treatment with D$_2$O gave 2-deuteriogibberellin A$_1$ methyl ester together with some 3-epi-GA$_4$ with approximately 2:1 ratio of the 2β:2α deuterides.



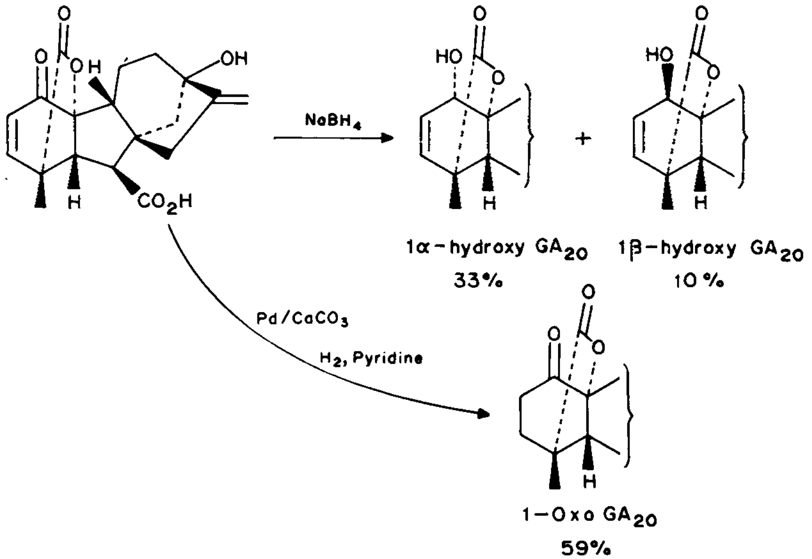
SCHEME 40

Using L-Selectride for the reduction of a similar gibberellin enone derivative resulted mainly in the 1,2-reduction product, affording the 3α-allylic and saturated alcohols in 47% and 30% yields, respectively (Scheme 41)[175].



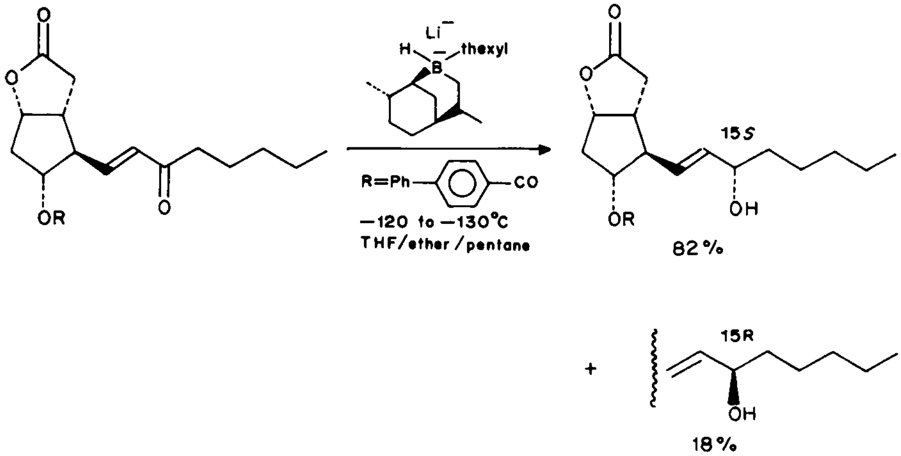
SCHEME 41

Substituted gibberellins, such as 1α- and 1β-hydroxy GA_5 and GA_{20}, were prepared from a single enone precursor by 1,2-reduction with $NaBH_4$ (Scheme 42). The reaction yielded 33% of 1α-hydroxy- and 10% of 1β-hydroxy-GA_5. Conversely, catalytic hydrogenation of the same enone with 10% $Pd/CaCO_3$ in pyridine afforded the 1,4-reduction product, 1-oxo-GA_{20}, in 59% yield[176].



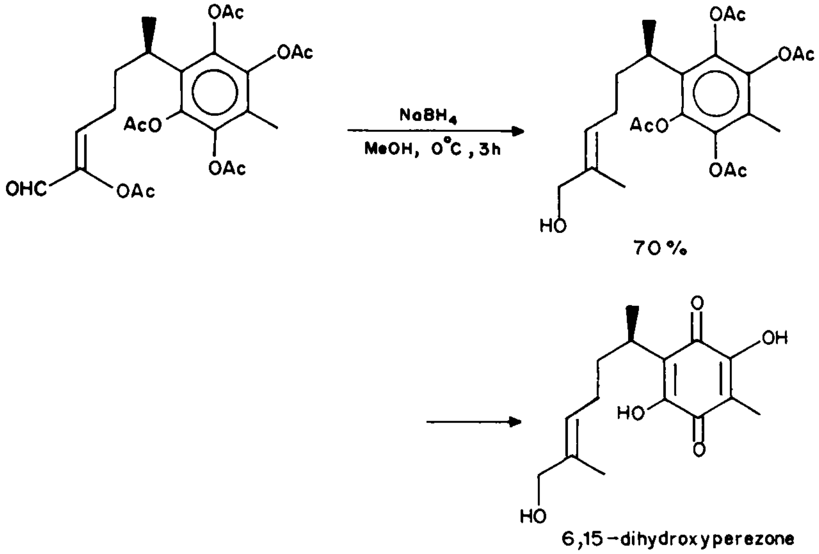
SCHEME 42

The stereoselective 1,2-reduction of the α,β-unsaturated ketone shown in Scheme 43 represents one of the key steps in Corey's approach to prostaglandin synthesis (Scheme 43)[177]. By using various boron and aluminum hydride reagents, mixtures of the corresponding 15*S* and 15*R* allylic alcohols were obtained in various ratios. Purest yields were obtained with highly hindered lithium trialkylborohydrides, such as diisobutyl-*t*-butylborohydride (74:26), tri-*sec*-butylborohydride (78:22), di-*sec*-butylthexylborohydride (80:20), the reagent indicated in Scheme 43 (82:18), etc. Even better stereoselectivity was achieved with *p*-phenylphenylurethane ($R = p\text{-}PhC_6H_4NHCO$) as a directing group. This derivative was reduced with thexyl-di-*sec*-butylborohydride and tri-*sec*-butylborohydride with 15*S*:15*R* ratios of 88:12 and 89:11, respectively[177].



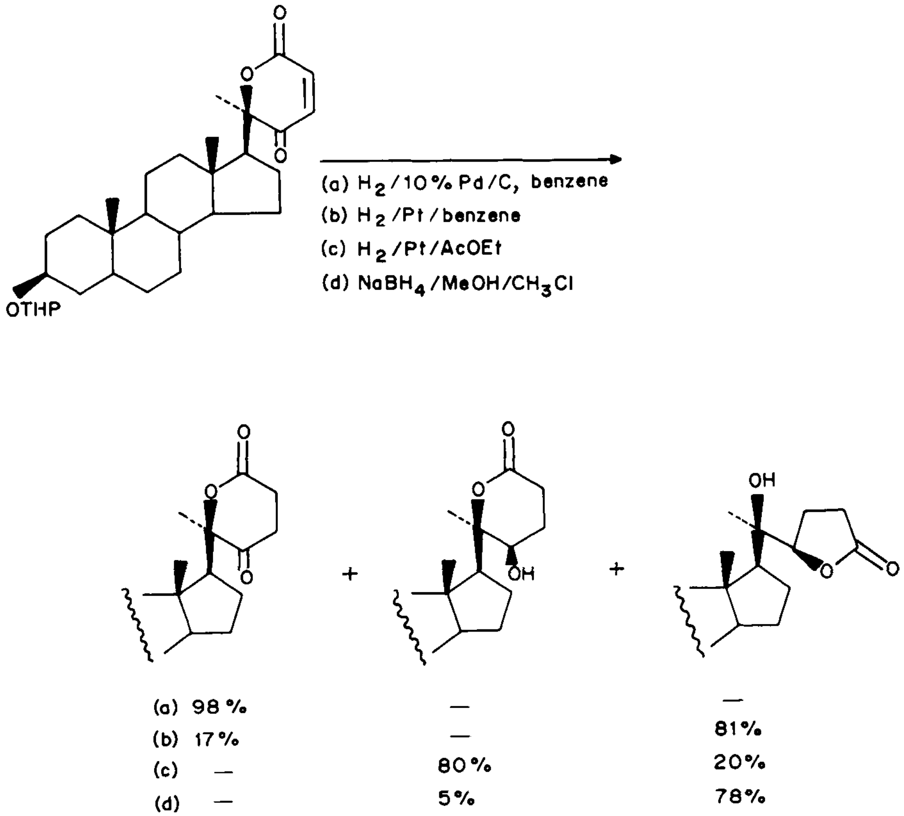
SCHEME 43

1, 2-Reduction of an α, β-unsaturated aldehyde with $NaBH_4$ represents one of the steps in the total synthesis of 6, 15-dihydroxyperezone (Scheme 44)[178].



SCHEME 44

Stereoselective reduction of an enono-lactone was a key step in the construction of the 20-hydroxyecdysone side-chain. Totally different mixtures of products were obtained when the reduction was carried out with sodium borohydride or by catalytic hydrogenation (Scheme 45)[156]. In all cases, the 1, 4-reduction mode is preferred. With borohydride, however, this process is followed by a subsequent reduction of the saturated ketone and base-catalyzed rearrangement of the δ-lactone into a γ-lactone.



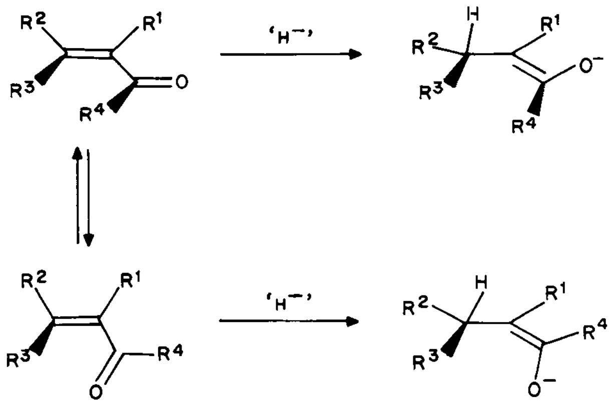
SCHEME 45

The conjugate reduction of acyclic α,β-unsaturated ketones can provide selectively regio- and stereochemically defined enolates that are unattainable by other methods. A knowledge of enone ground-state conformational preferences allows one to predict which enolate geometrical isomer will predominate in these reactions (Scheme 46)[179].

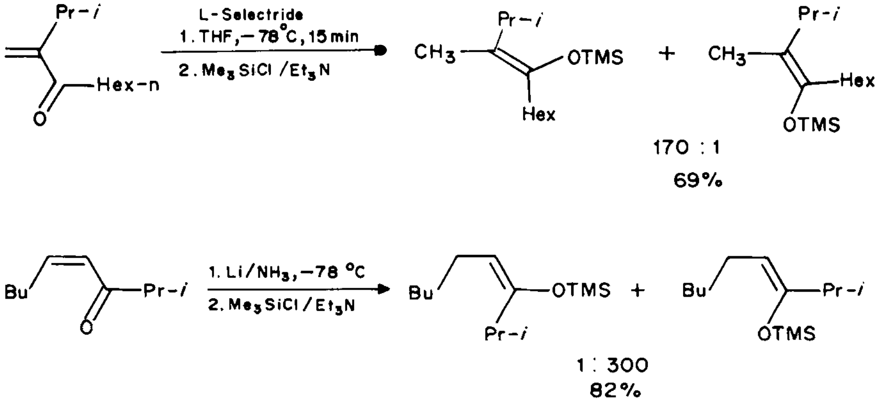
Thus, enones that exist preferentially as *s-trans* conformers will give rise to *E*-enolates whereas conjugate addition by hydride to *s-cis* enone will lead to *Z*-enolates. These can be trapped by trimethylsilyl chloride (TMSCl) to give the corresponding silyl enol ethers (Scheme 47)[179].

Sodium cyanoborohydride ($NaBH_3CN$) or tetrabutylammonium cyanoborohydride in acidic methanol or acidic HMPT reduces α,β-unsaturated aldehydes and ketones to the corresponding allylic alcohol (Scheme 48)[180]. This system is limited to enones in which the double bond is not further conjugated, in which case the allylic hydrocarbon is formed in substantial amounts. Thus, reduction of chalcone gives mainly 1,3-diphenylpropene (48%) as well as 26% of the allylic ether. Cyclic enones are also not good substrates, as competing 1,4-addition gives large fractions of saturated alcohols[180].

Lithium butylborohydride is prepared by reacting equimolar amounts of butyl lithium and borane-dimethylsulfide complex[181]. This reagent effectively reduces enones in



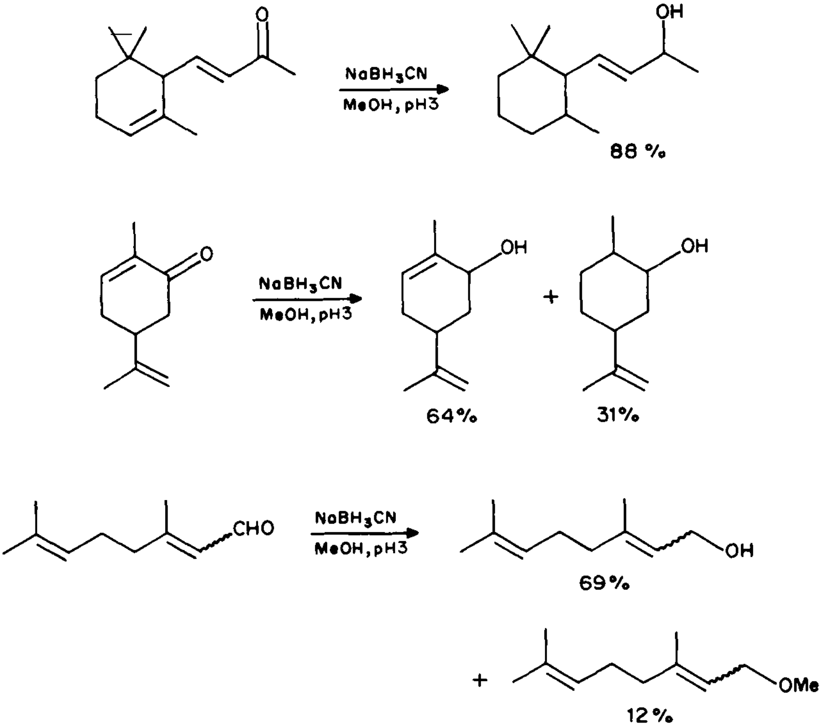
SCHEME 46



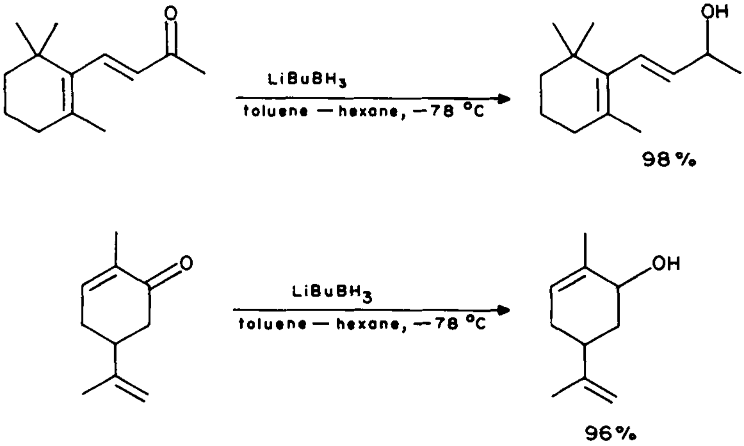
SCHEME 47

toluene–hexane mixtures at − 78 °C to give, in most cases, high yields of the corresponding allylic alcohols (Scheme 49)[181]. Conjugated cyclopentenones, however, give mixtures of 1,2- and 1,4-reduction products. Under identical reaction conditions, saturated ketones are reduced to alcohols. The latter process can take place in the presence of simple esters.

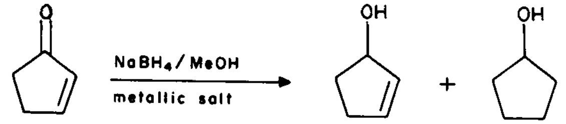
Regioselective 1,2-reduction of enones to the corresponding allylic alcohols is achieved with $NaBH_4$ in the presence of lanthanide ions, such as La^{3+}, Ce^{3+}, Sm^{3+}, Eu^{3+}, Yb^{3+} and Y^{3+}[182]. This procedure is complementary to those giving predominantly 1,4-selectivity, such as $NaBH_4$ in pyridine[168]. The general utility of $NaBH_4$–$CeCl_3$ selective reduction is illustrated by the conversion of cyclopentenone to cyclopentenol in 97% yield and only 3% of cyclopentanol, although conjugate reduction of cyclopentenone systems by most hydride reagents is usually highly favored (Scheme 50).



SCHEME 48



SCHEME 49

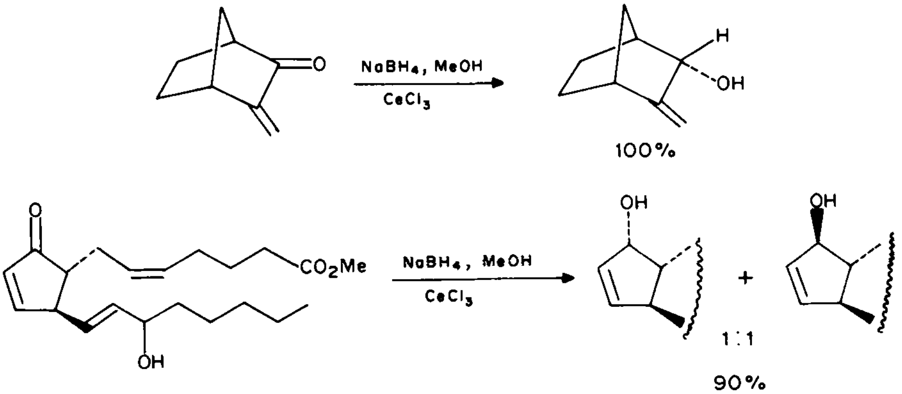


La^{3+}	90	:	10
Ce^{3+}	97	:	3
Sm^{3+}	94	:	6
Eu^{3+}	93	:	7
Yb^{3+}	89	:	11
Y^{3+}	86	:	14
Li^{+}	1	:	99

SCHEME 50

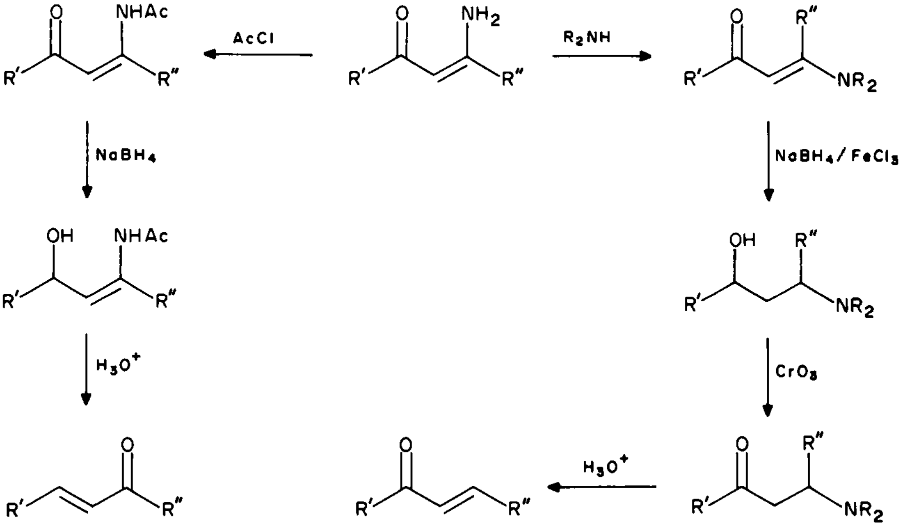
Thus, reaction of equimolar amounts of α, β-unsaturated ketones and either samarium or cerium chloride hexahydrate in methanol with sodium borohydride produced high yields of the corresponding allylic alcohols (Scheme 51)[182]. This approach was applied in the synthesis of 7, 7-dimethylnorbornadiene, whereas reduction of 4, 4-dimethylcyclopent-2-enone with sodium borohydride and cerium chloride in methanol afforded dimethylcyclopentenol in 93% yield[183].

A mechanistic study of the role of the lanthanide cations suggests that they catalyze decomposition of borohydride by the hydroxylic solvent to afford alkoxyborohydrides, which may be responsible for the observed regioselectivity. The stereoselectivity of the process is also modified by the presence of Ln^{3+} ions, in that axial attack of cyclohexenone systems is enhanced[182].



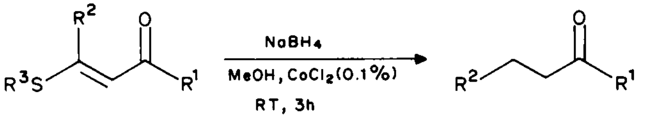
SCHEME 51

β-Dialkylamino conjugated enones are reduced to the corresponding γ-amino alcohols with $NaBH_4$ in the presence of $FeCl_3$. These aminoalcohols could be converted into conjugated enones by chromic acid oxidation and deamination (Scheme 52)[184]. On the other hand, β-acylamino conjugated enones are reduced by $NaBH_4$ to afford β, γ-unsaturated γ-acylamino alcohols, which are regioselectively hydrolyzed to conjugated enones.



SCHEME 52

Reduction of β-sulfenylated α,β-unsaturated ketones with $NaBH_4$ in the presence of catalytic amounts of $CoCl_2$ or $NiCl_2$ in methanol produces the corresponding desulfenylated, saturated ketones (Scheme 53)[185]. These substrates, however, were not affected by combinations of $NaBH_4$ and other metal salts, including $FeCl_2$, $FeCl_3$, CuI and $CuCl_2$.



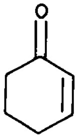
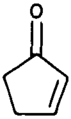
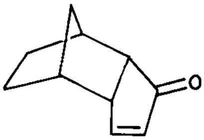
SCHEME 53

B. Aluminum Hydrides

The properties of complex metal hydrides, particularly those of aluminum, and their use in organic synthesis have been compared in a number of papers, review articles and monographs[186-190]. Useful tables, listing the most appropriate hydride reagents for selective reduction of various polyfunctional compounds, have been published[1,189-192]. Use of chiral metal alkoxyaluminum hydride complexes in asymmetric synthesis has also been reviewed[193].

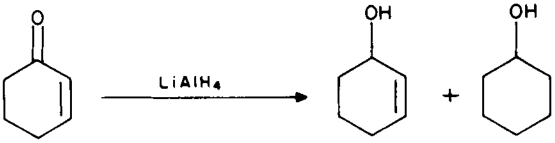
The two modes of reduction of α,β-unsaturated aldehydes and ketones, 1,2- and 1,4-addition of metal hydride to the enone system, lead respectively to either an allylic alcohol or a saturated ketone. It has been suggested that the relative importance of these paths depends upon substrate 'hardness' or 'softness', as defined in terms of the coefficients of the lowest unoccupied molecular orbital (LUMO) (*vide supra*, the discussion of borohydrides).

TABLE 3. Ratio of 1,4- to 1,2-reduction products

			
$LiAlH(OMe)_3$	5:95	10:90	24:76
$LiAlH_4$	22:78	86:14	100:0
$LiAlH(SMe)_3$	56:44	95:5	
$LiAlH(OBu\text{-}t)_3$	78:22	100:0	100:0
$LiAlH(SBu\text{-}t)_3$	95:5	100:0	

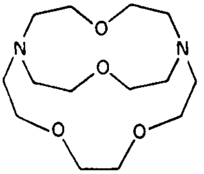
While 1, 2-addition is considered to be a mainly charge-controlled process, 1, 4-addition is a frontier orbital-controlled process[194]. These considerations predict, for example, that the 1, 4-addition of a given metal hydride to cyclopentenone should always be faster than a similar addition to cyclohexenone[195]. Moreover, in cases where the enone system is further conjugated to a phenyl ring, as in cinnamaldehyde, increased frontier-orbital control should render the enone more prone to 1, 4-addition[196]. Obviously, the course of reduction of conjugated carbonyl compounds is also highly influenced by the nature of the metal hydride. According to Pearson's concept of 'soft' and 'hard' acids and bases[197,198], hard metal hydrides add preferentially to the 2-position and soft metal hydrides to the 4-position of the conjugated enone system[194–196]. As shown in Table 3, these predictions agree well with representative experimental results[195,199].

Because of their electrophilic nature, Li^+ cations accelerate the reduction of carbonyl compounds by $LiAlH_4$ or $NaBH_4$, an effect that is significantly inhibited by Li^+-complexing agents, such as cryptands, crown ethers or polyamines, which decrease the rate of reduction[200]. In the case of α, β-unsaturated ketones, this slowdown is associated with altered regioselectivity. For example, $LiAlH_4$ reduction of cyclohexenones in the absence



THF	86 : 14	98%
ether	98 : 2	98%
THF, cryptand(1.2 eq)	14 : 86	85%
ether, cryptand (1.2 eq)	23 : 77	80%

cryptand =

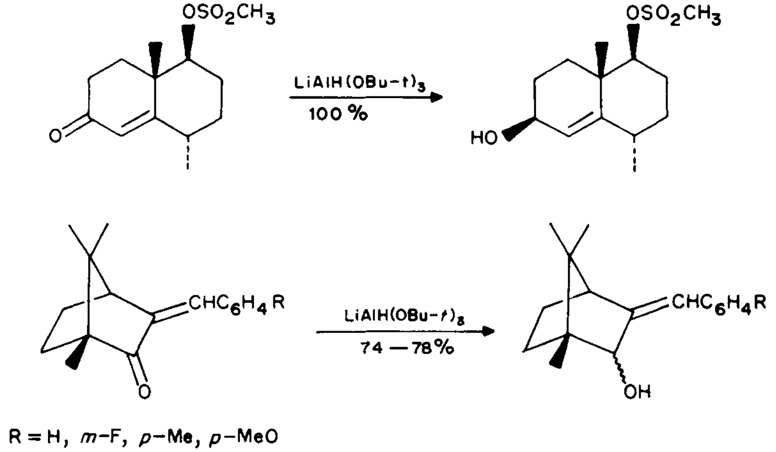


SCHEME 54

of the cryptand proceeds predominantly with 1,2-reduction. In the presence of the cryptand, 1,4-attack is favored. This selectivity is more pronounced with $LiAlH_4$ than with $NaBH_4$ (Scheme 54)[200] and is also highly dependent on solvent. In diethyl ether, 1,2-attack is essentially exclusive. However, when the cation is complexed, 1,4-addition again predominates.

This effect is explained in terms of Frontier Molecular Orbitals treatment[200]. The regioselectivity of reduction depends upon the relative values of the C_1 and C_3 atomic coefficients in the LUMO. The atom with the larger coefficient corresponds to the predominant site of attack. When Li^+ is complexed by the α-enone, the C_1 coefficient is larger than that of C_3, and C_1 attack is favored. In the absence of such complexation, the C_3 coefficient is larger, leading to 1,4-attack. The strength of carbonyl–Li^+ interaction is strongly dependent upon the solvent, the nature of the complexing agent and the interaction between the Li^+ ion and the reducing agent. Thus, in strongly coordinated solvents such as pyridine[168], 1,4-reduction predominates.

Steric and electronic factors in the enone substrate may also alter selectivity. For example, the high tendency of $LiAlH(OBu\text{-}t)_3$ to undergo 1,4-addition with simple enones is modified in the two examples given in Scheme 55[201].

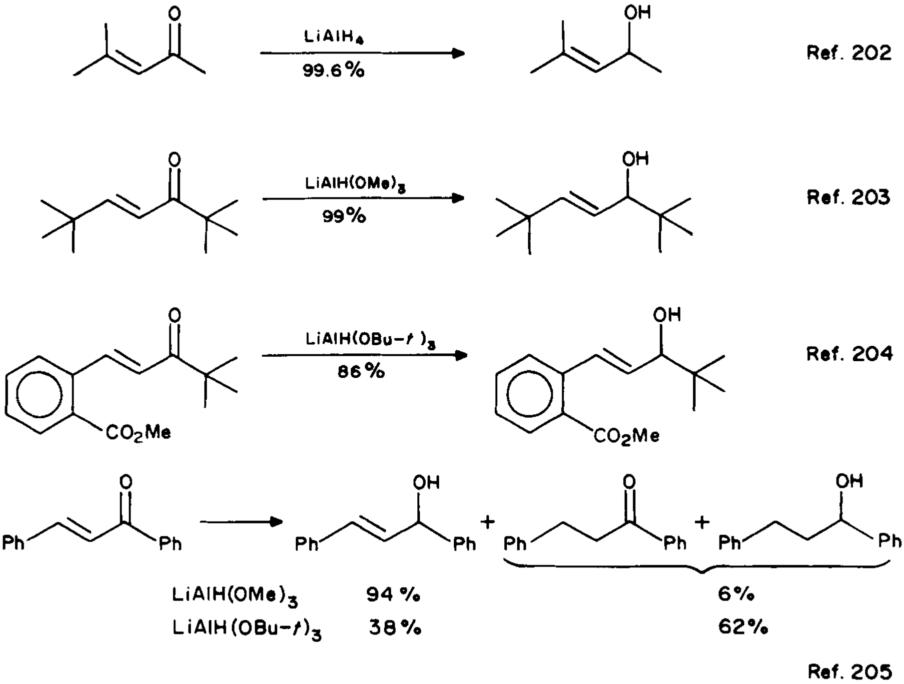


SCHEME 55

The ratio of 1,2- to 1,4-addition of aluminum hydride to an α,β-unsaturated ketone is highly dependent on the enone structure, solvent, relative initial concentrations of reactants, temperature, and softness or hardness of the hydride reagent. These reductions can be controlled to proceed with either 1,2- or 1,4-addition, with high selectivity[186]. The examples presented in Scheme 56[202–205] illustrate the prominent tendency of $LiAlH_4$ and $LiAlH(OMe)_3$ to yield 1,2- rather than 1,4-adducts, as compared to $LiAlH(OBu\text{-}t)_3$.

The reagent $NaAlH_2(OCH_2CH_2OCH_3)_2$ favors 1,2-addition to cyclic enones with greater selectivity than with either $LiAlH(OMe)_3$[195] or AlH_3[199]. Several examples are presented in Scheme 57[203,206–210].

In most of these examples, reductions are nonstereoselective. In some cases, however, such as in the reduction of 9-oxoisolongifolene to the allylic 9α- or 9β-alcohols (Scheme 58), reversal of stereochemistry occurs when $NaAlH_2(OCH_2CH_2OCH_3)_2$ is used instead of $LiAlH_4$ or $NaBH_4$[211]. While the latter two reagents lead to formation of the thermody-



SCHEME 56

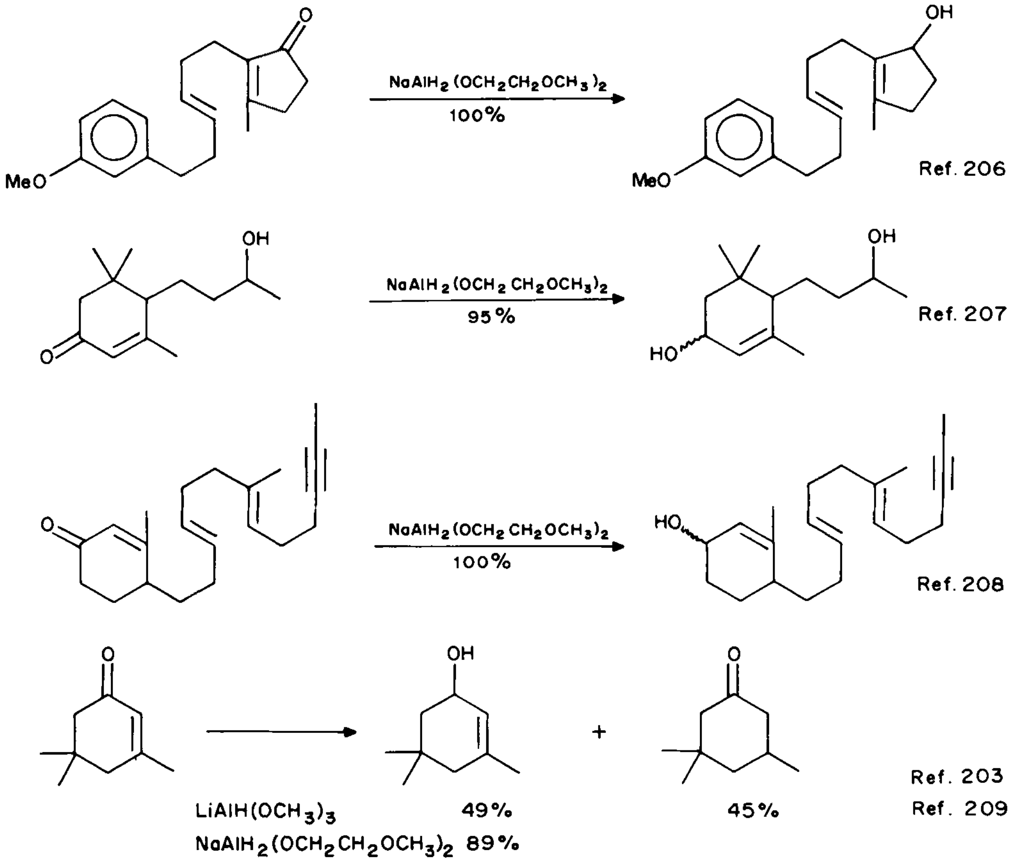
namically more stable α-alcohol as the major product, increased steric bulk of the former seems to favor the less stable β-isomer.

Sterically unhindered enones, such as cyclohexenone, are reduced by LiAlH(OBu-*t*)$_3$ to give predominantly the corresponding saturated ketone[195]. More sterically congested systems are cleanly reduced via the 1,2-mode to give the allylic alcohol, usually with high stereoselectivity (Scheme 59)[212–215].

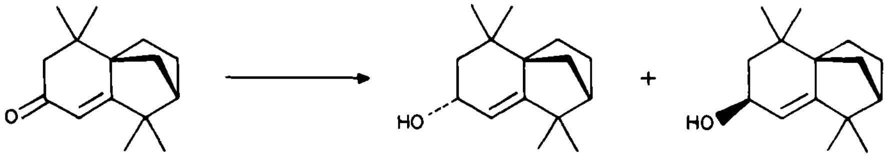
1,2-Reduction has been reported for other hydride reagents, such as diisobutylaluminum hydride[194,216,217], aluminum hydride[199] and 9-borabicyclononane (9-BBN)[218], as illustrated by the example in Scheme 60.

1,4-Reduction of enones can be effected with high selectivity with AlH(OBu-*t*)$_2$, AlH(OPr-*i*)$_2$, AlH(NPr$^i_2$)$_2$ or HBI$_2$, forming saturated ketones in 90–100% yield. AlH(NPr$^i_2$)$_2$ exhibited the lowest selectivity, as no 1,4-reduction of mesityl oxide or isophorone is observed with this reagent. The same reagent with methyl vinyl ketone or cyclohexenone led to mixture of products. *Trans*-chalcone also undergoes quantitative 1,4-reduction with the above-mentioned hydrides[217]. Similarly, reduction of 9-anthryl styryl ketone or anthracene-9,10-diyl-bis(styryl ketone) with LiAlH(OBu-*t*)$_3$ affords the saturated ketone as the sole product[219]. Hydrides such as LiAlH(OBu-*t*)$_3$ and LiAlH(SBu-*t*)$_3$ favor 1,4-reduction in cyclopentenones[195,196,199,220–223]. An example is given in Scheme 61, where steric factors allow only *exo* approach of the bulky hydride[224,225].

Scheme 62 illustrates an interesting two-step selective reduction of an enone system, first with sodium hydride and NaAlH$_2$(OCH$_2$CH$_2$OCH$_3$)$_2$ and then with the same reagent in the presence of 1,4-diazabicyclo[2.2.2]octane. Specific reduction, however, is not achieved with NaBH$_4$, LiBH$_4$, LiBH(*s*-Bu)$_3$ or 9-BBN[226].

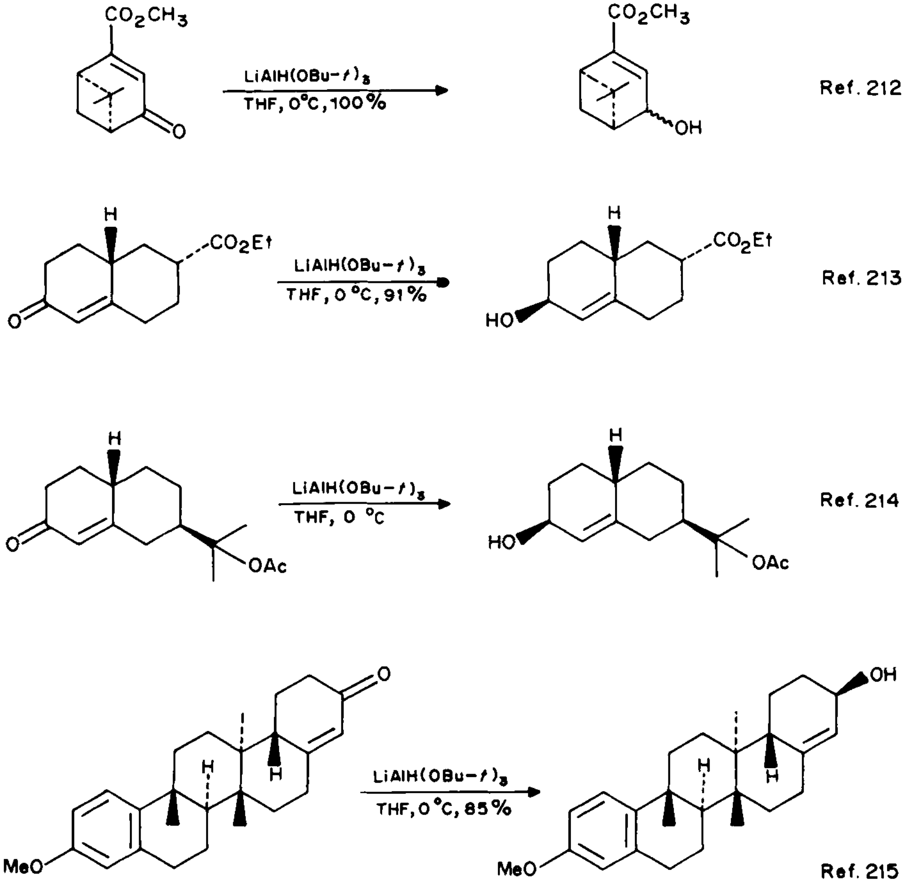

MeO
O
$NaAlH_2(OCH_2CH_2OCH_3)_2$
100%
MeO
OH
Ref. 206
OH
O
$NaAlH_2(OCH_2CH_2OCH_3)_2$
95%
OH
HO
Ref. 207
O
$NaAlH_2(OCH_2CH_2OCH_3)_2$
100%
HO
Ref. 208
O
OH
+
O
$LiAlH(OCH_3)_3$ 49%
$NaAlH_2(OCH_2CH_2OCH_3)_2$ 89%
45%
Ref. 203
Ref. 209

SCHEME 57

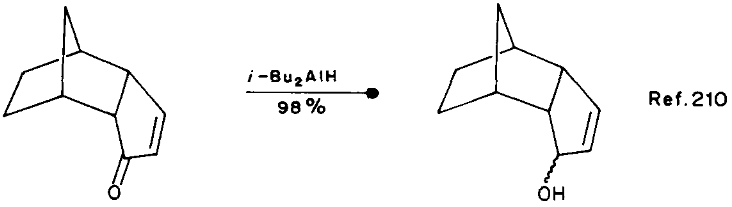


$LiAlH_4$	76 : 24
$NaBH_4$	76 : 24
$NaAlH_2(OCH_2CH_2OCH_3)_2$	18 : 82

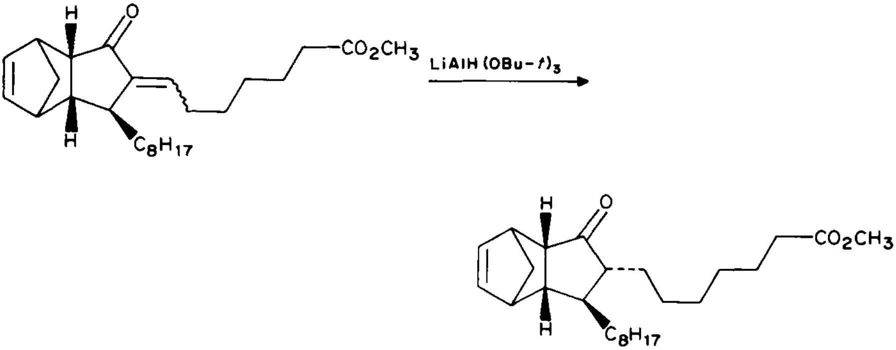
SCHEME 58



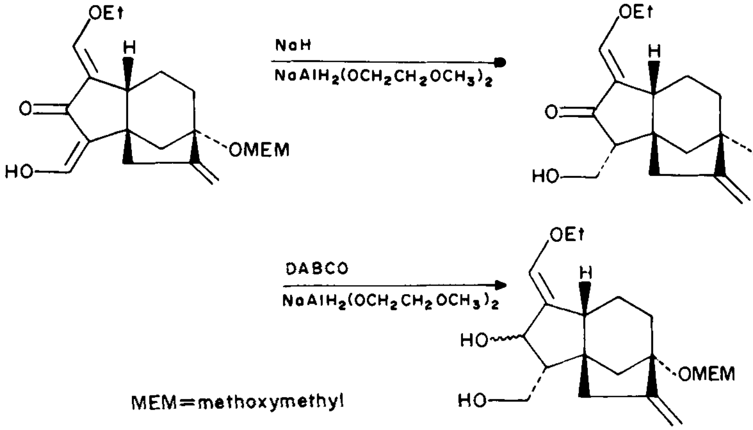
SCHEME 59



SCHEME 60

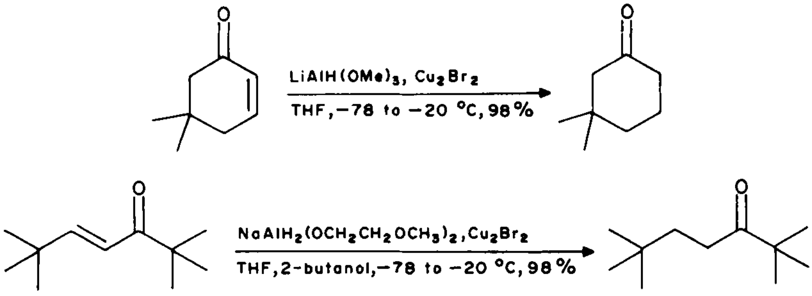


SCHEME 61



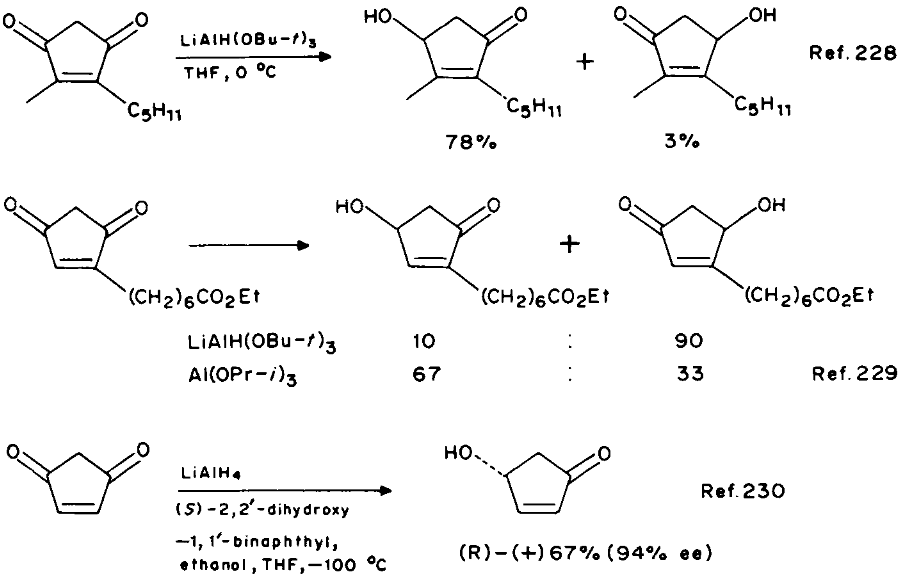
SCHEME 62

Both $LiAlH(OMe)_3$ and $NaAlH_2(OCH_2CH_2OCH_3)_2$ are convenient reducing agents for low-temperature, copper-mediated 1,4-reduction, as shown by the examples in Scheme 63[203,227].



SCHEME 63

Aside from the nature of the hydride reagent, steric effects and lower reactivity of the enone substrate affect the course of reduction in polyfunctional molecules. Several examples of partial reduction of cyclopentenedione systems are given in Scheme 64[228-230].

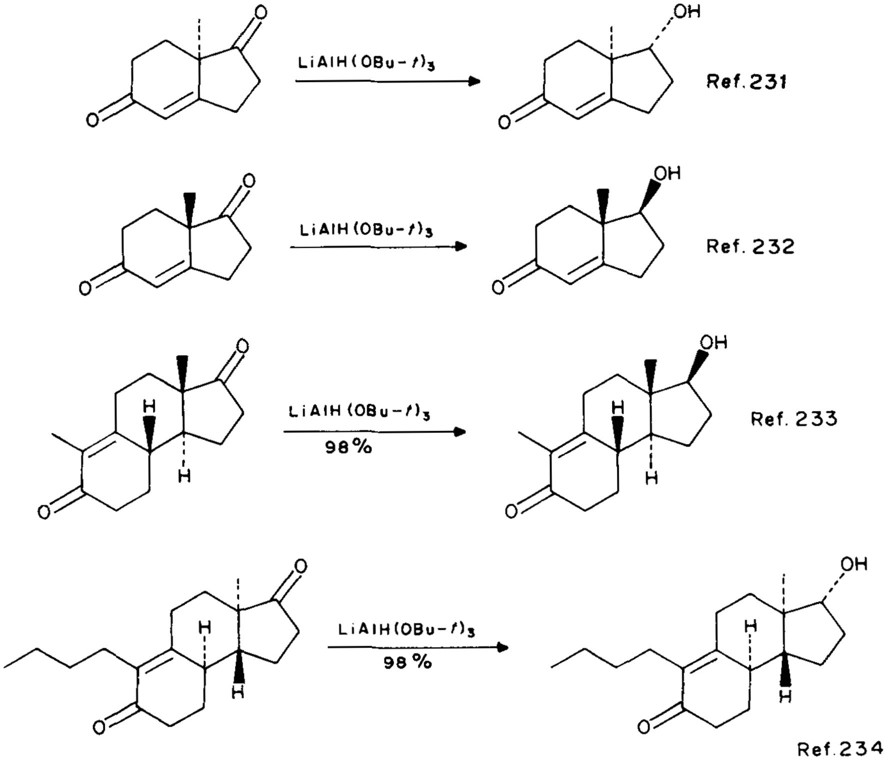


SCHEME 64

There are a number of cases where a less reactive enone group remains intact while a more reactive saturated ketone present in the same substrate is selectively reduced, as shown in Scheme 65[231-234].

Alternatively, there are a number of examples of simultaneous reduction of both saturated and unsaturated ketones or of preferential reduction of the unsaturated one (Scheme 66)[235-237].

Reduction of enol ethers or enol esters of 1,3-diketones followed by acid-catalyzed allylic rearrangement of the reduction product (see p. 85 in Reference 5) is a useful route to

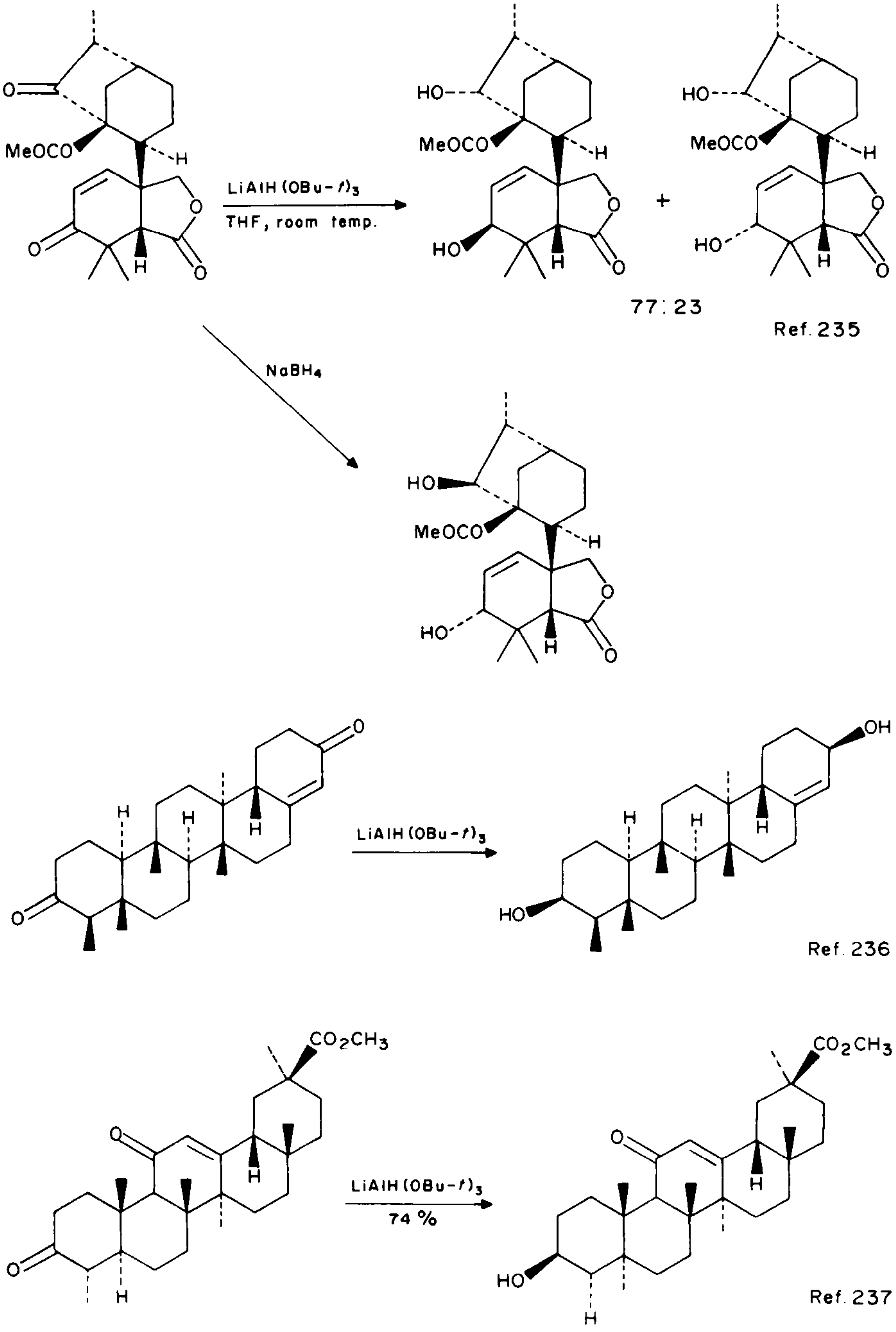


SCHEME 65

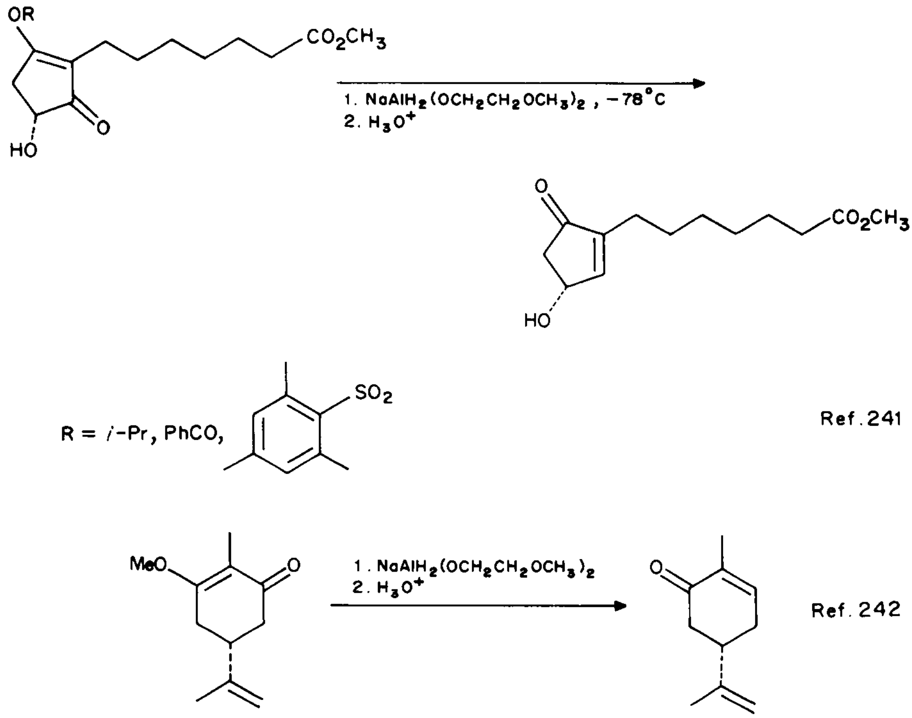
α,β-unsaturated ketones. Aliphatic[238,239] and alicyclic[240] enones have thus been prepared in good yields at low temperatures with $NaAlH_2(OCH_2CH_2OCH_3)_2$ (Scheme 67)[241,242].

Reduction of α,β-unsaturated aldehydes can afford either an unsaturated or saturated primary alcohol, or a mixture of both, depending on reaction conditions. For example, while addition of cinnamaldehyde to $NaAlH_2(OCH_2CH_2OCH_3)_2$ in benzene gives 97% 3-phenylpropanol, inverse addition (of the reducing agent to solution of the substrate) yields 94% cinnamyl alcohol[243,244]. Reduction with $LiAlH_4$ is similarly dependent on the addition sequence. The more sterically hindered hydride LiAlH(OBu-*t*)$_3$ is highly selective for 1,2-reduction of aldehydes, even under conditions of normal addition. For example, it reduces cinnamaldehyde cleanly to cinnamyl alcohol, without affecting the olefinic bond[245–247]. Similar behavior is exhibited by $NaAlH_2(OCH_2CH_2OCH_3)_2$, which reduces 2-butenal to 2-butenol in 97% yield[244]. On the other hand, hydrides such as $LiAlH(OMe)_3$[187,245,246] and $NaAl_2H_4(OCH_2CH_2NMe_2)_3$[248] usually yield the saturated primary alcohol. Other examples of 1,2-reduction of α,β-unsaturated aldehydes with these reagents are given in Scheme 68[249–251].

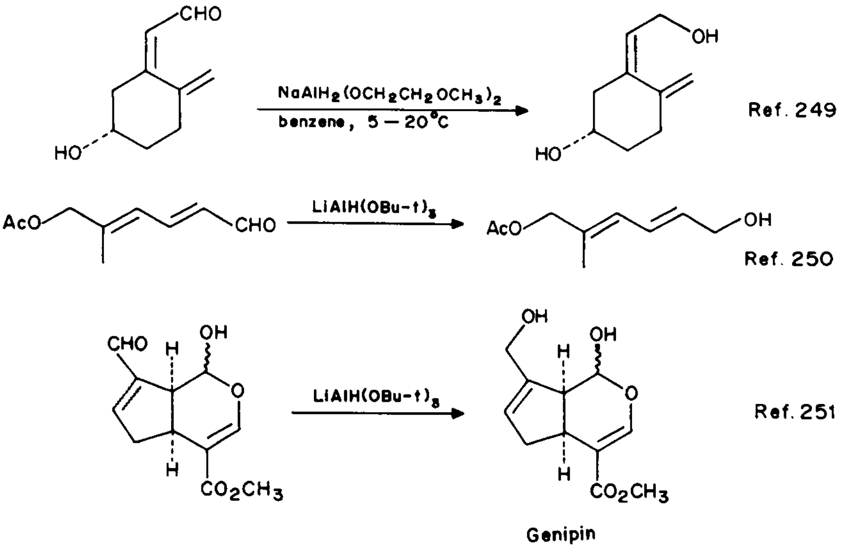
Regioselectivity of enone reduction with diisobutylaluminum hydride (DIBAH) is very susceptible to minor structural changes in the substrate. While five-membered exocyclic enones provide the allylic alcohols which are the normal products for this reagent, reduction of chromones possessing exocyclic six-membered enones yield saturated


LiAlH(OBu-t)3
THF, room temp.
77 : 23
Ref. 235
NaBH4
LiAlH(OBu-t)3
Ref. 236
LiAlH(OBu-t)3
74 %
Ref. 237

SCHEME 66

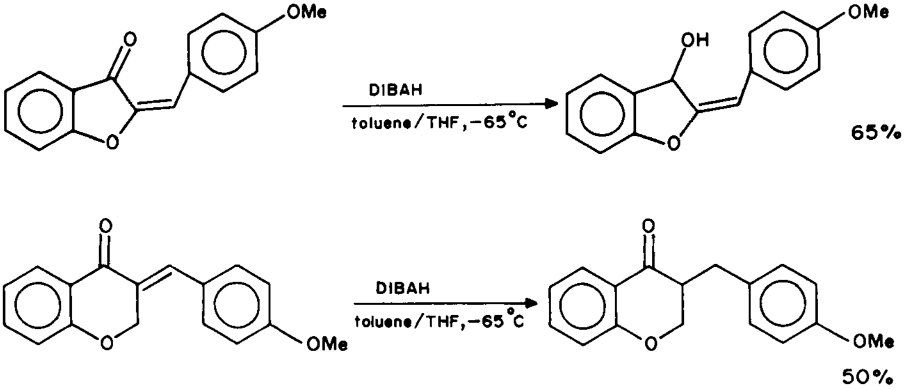


SCHEME 67



SCHEME 68

ketones (Scheme 69)[252]. This was explained by the strict coplanarity of the enone function in the five-membered structure, whereas the enones giving rise to saturated ketones are slightly twisted. Reduction of isoflavones with DIBAH under these conditions provides the corresponding isoflavan-4-ones in very high selectivity[252].



SCHEME 69

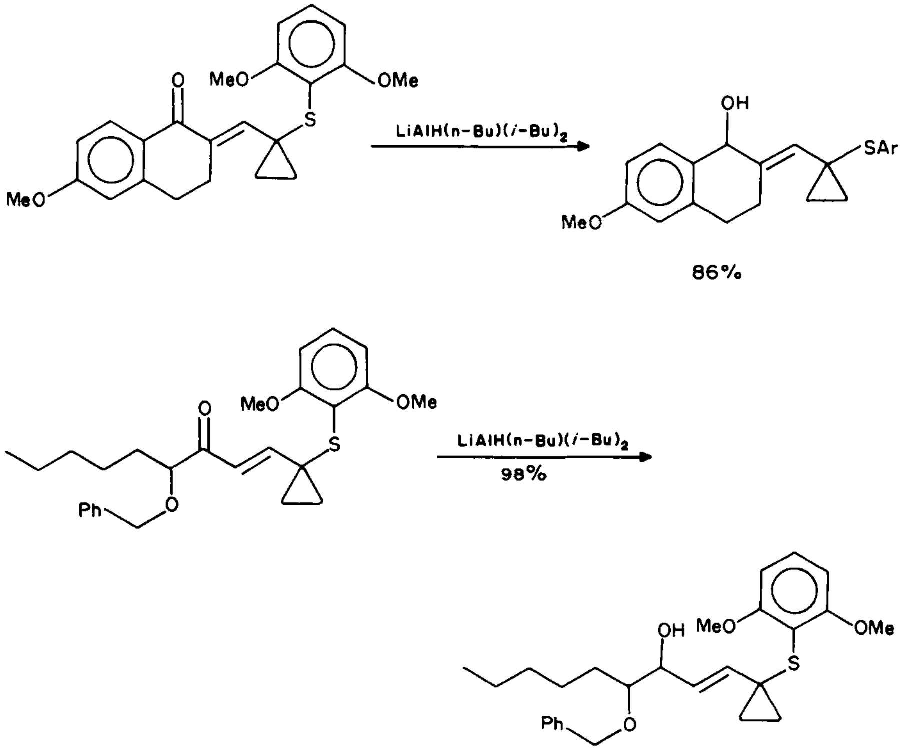
The 'ate' complex LiAlH(n-Bu)(*i*-Bu)$_2$ is prepared from DIBAH and butyllithium in either THF or toluene–hexane. This reagent is more effective for selective 1,2-reduction of enones to the corresponding allylic alcohol than is DIBAH alone[253]. The reagent also reduces esters, lactones and acid chlorides to the corresponding alcohols, and epoxides to the respective alcohols. α,β-Unsaturated ketones derived from dehydration of aldol products from 1-(arylthio)cyclopropanecarboxaldehydes and ketones were selectively reduced by this 'ate' complex or by DIBAH itself, yielding the allylic alcohols with minor amounts of the 1,4-reduction product (Scheme 70)[254]. Yields were typically higher with this reagent than with DIBAH.

Enones may be deoxygenated with $LiAlH_4/AlCl_3$ to give the corresponding olefinic hydrocarbons. The reactive species seem to be $AlHCl_2$ or AlH_2Cl, which act as both Lewis acids and hydride donors. The reaction involves initial 1,2-reduction to form the allylic alcohol, followed by substitution of the allylic hydroxyl group by hydride (mainly via an S_N2' mechanism) to form the corresponding mixture of alkenes (Scheme 71)[255].

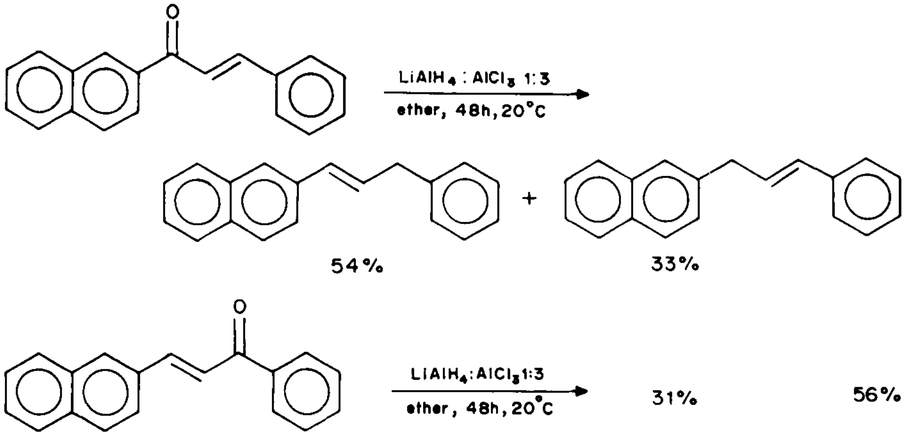
This technique has been applied to the deoxygenation of natural products. By using mixtures of $LiAlH_4$ and $AlCl_3$, flavanone and chalcones were transformed into flavan and diarylpropenes, respectively (Scheme 72)[256].

Conjugate reduction is the major pathway of enone reduction with a mixture of $LiAlH_4$ and excess CuI in THF[257]. It has been shown that the active reducing agent in this mixture is an H_2AlI species and not the copper hydride. Enones of *cis* geometry are reduced much more slowly than the corresponding *trans* compounds, and no reduction was observed with cyclohexenone and 3,3,5-trimethylcyclohexenone. These results suggest that the mechanism involves coordination of the metal to the carbonyl, forming a six-center transition state (Scheme 73)[257].

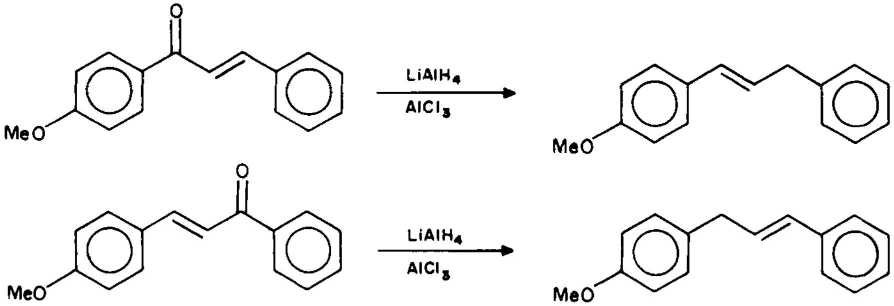
Enones with two alkyl groups at the β-position are reduced very sluggishly under these conditions. Other metal salts, such as HgI_2, $TiCl_3$ and $HgCl_2$, premixed with $LiAlH_4$ in THF, similarly give rise to 1,4-reduction. Yields and selectivities were found to be much lower than with CuI. H_2AlI was found to react in the exact same manner as $LiAlH_4$–CuI, and the series H_2AlI, $HAlI_2$, H_2AlBr, $HAlBr_2$, H_2AlCl and $HAlCl_2$ was therefore



SCHEME 70

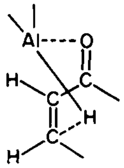


SCHEME 71



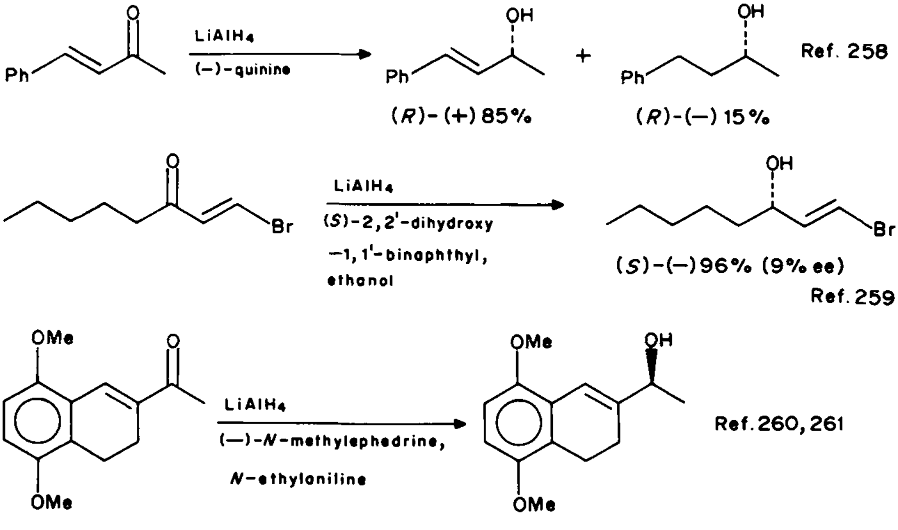
SCHEME 72

prepared. Of these, the iodo compounds exhibited the highest reactivity. HAlI$_2$ reduces enones at a slower rate than H$_2$AlI, probably due to steric factors.



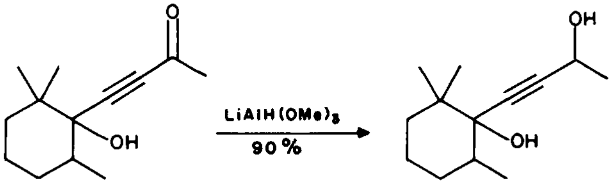
SCHEME 73

Chiral lithium alkoxyaluminumhydride complexes can be used to obtain optically active allylic alcohols (Scheme 74)[258-261]. These reagents are more selective than the polymer-supported LiAlH$_4$ and LiAlH$_4$–monosaccharide complexes[262].



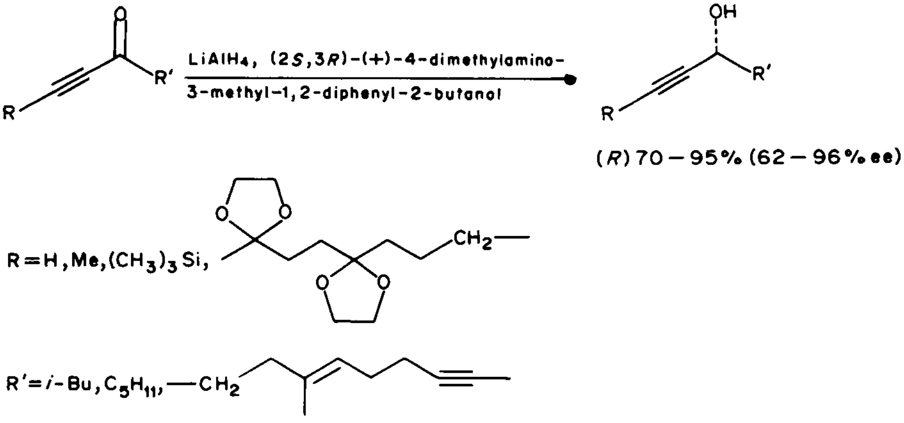
SCHEME 74

α,β-Acetylenic ketones are selectively reduced to the corresponding propargylic alcohols with $LiAlH(OMe)_3$ (Scheme 75).



SCHEME 75

Asymmetric 1,2-reduction of acetylenic ketones is an effective method for preparing optically active propargylic alcohols in high yield and high enantioselectivity. Common chiral reductants for this purpose include the Mosher–Yamaguchi reagent[263–265], the Vigneron–Jacquet complex[266–268] and $LiAlH_4$/2,2′-dihydroxy-1,1′-binaphthyl/methanol (*R* and *S*) complexes[269], as well as the $LiAlH_4$-*N*-methylephedrine/*N*-ethylaniline complex[260]. For example, reduction of simple acetylenic ketones (Scheme 76) with $LiAlH_4$/(2*S*,3*R*)-(+)-4-dimethylamino-3-methyl-1,2-diphenyl-2-butanol results in propargylic (*R*)-alcohols in 62–95% enantiomeric excess. These chiral building blocks were used in the synthesis of tocopherol, prostaglandins and 11α-hydroxyprogesterone[264,265].

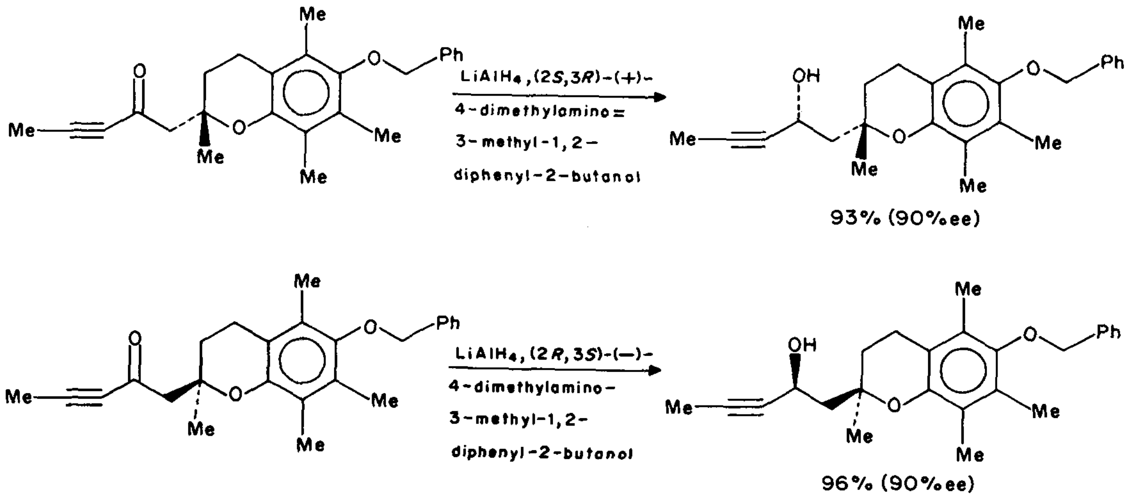


SCHEME 76

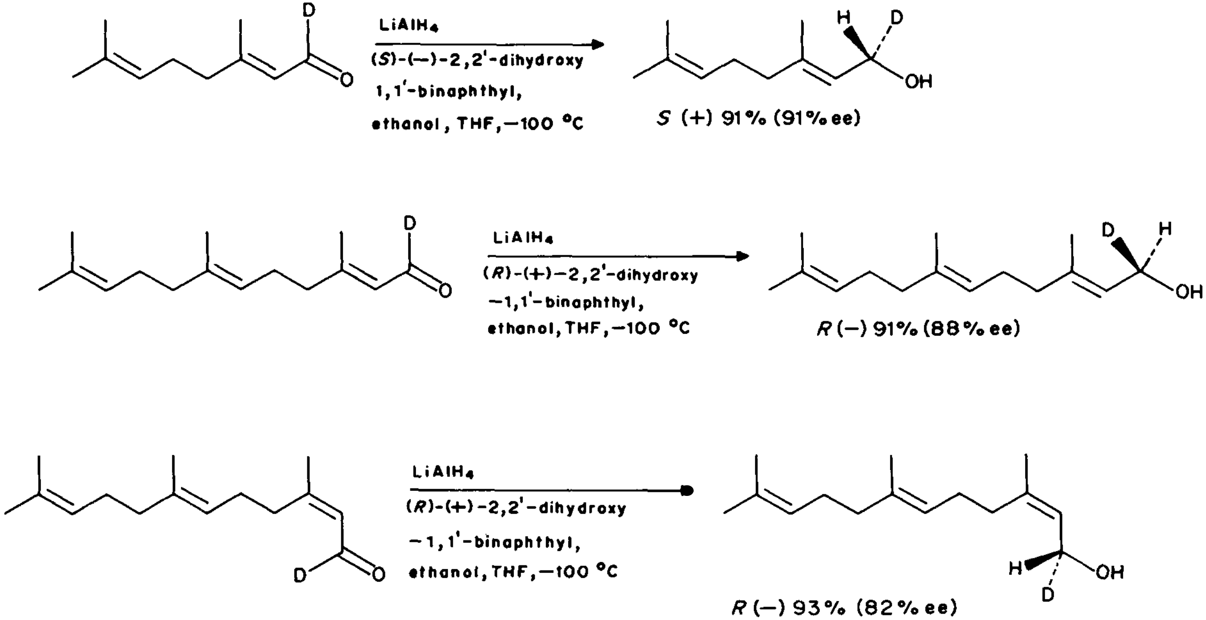
This method can also be used for diastereoselective reduction of optically active acetylenic ketones, as shown in Scheme 77[263].

Enantioselective formation of propargylic alcohols is carried out via reductions with the Vigneron–Jacquet complex[266–268]. However, Landor's chiral $LiAlH_4$–monosaccharide complexes are less selective for this purpose[270–272].

Asymmetric reduction of geranial-d1, neral-d1 and related linear terpenic aldehydes can be achieved with $LiAlH_4$–dihydroxybinaphthyl complex with 72–91% enantiomeric excess (Scheme 78)[273].

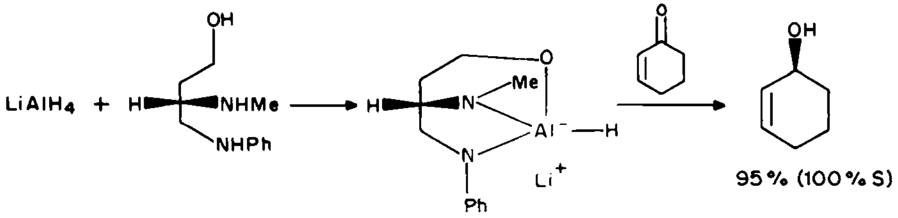

Me
O
Me
Ph
O
Me
Me
Me
LiAlH₄, (2S,3R)-(+)-
4-dimethylamino=
3-methyl-1,2-
diphenyl-2-butanol
OH
Me
O
Me
Ph
O
Me
Me
Me
93% (90%ee)
Me
O
Me
Ph
O
Me
Me
Me
LiAlH₄, (2R,3S)-(−)-
4-dimethylamino-
3-methyl-1,2-
diphenyl-2-butanol
OH
Me
O
Me
Ph
O
Me
Me
Me
96% (90%ee)

SCHEME 77


D
O
LiAlH₄
(S)-(−)-2,2'-dihydroxy
1,1'-binaphthyl,
ethanol, THF, −100 °C
H
D
OH
S (+) 91% (91% ee)
D
O
LiAlH₄
(R)-(+)−2,2'-dihydroxy
−1,1'-binaphthyl,
ethanol, THF, −100 °C
D
H
OH
R (−) 91% (88% ee)
D
O
LiAlH₄
(R)-(+)-2,2'-dihydroxy
−1,1'-binaphthyl,
ethanol, THF, −100 °C
H
OH
D
R (−) 93% (82% ee)

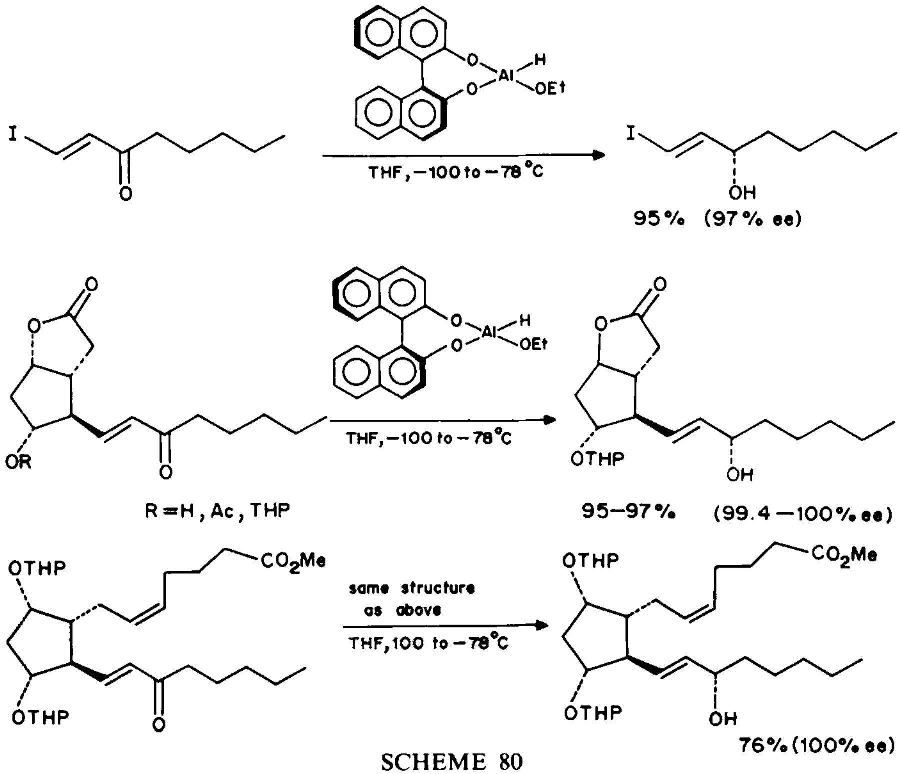
SCHEME 78

Asymmetric reduction of prochiral α,β-unsaturated ketones with chiral hydride reagents derived from $LiAlH_4$ and (*S*)-4-anilino- and (*S*)-4-(2,6-xylidino)-3-methylamino-1-butanol gives (*S*)- and (*R*)- allylic alcohols, respectively, in high chemical and optical yields (Scheme 79)[274].



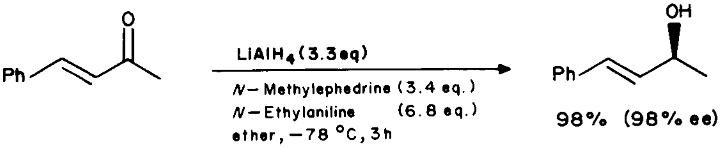
SCHEME 79

A modified aluminum hydride is prepared by treating $LiAlH_4$ in THF with equimolar amounts of ethanol and optically pure *S*-(−)-2,2′-dihydroxy-1,1′-binaphthyl. Allylic alcohols of very high optical purity are obtained in high yield by reduction of α,β-unsaturated ketones with this reagent[275]. Of particular interest are the attractive opportunities provided by this reagent in prostaglandin synthesis. For example, some of the chemical transformation shown in Scheme 80[275] are more effective in both terms of chemical and optical yields than standard microbiological reduction[276].



SCHEME 80

Asymmetric reduction of α,β-unsaturated ketones is achieved with LiAlH$_4$, partially decomposed by (−)-*N*-methylephedrine and ethylaniline (Scheme 81)[260]. This reagent converts open chain enones into the corresponding optically active allylic alcohols in high chemical (92–100%) and optical yields (78–98% ee).



SCHEME 81

C. Silicon Hydrides

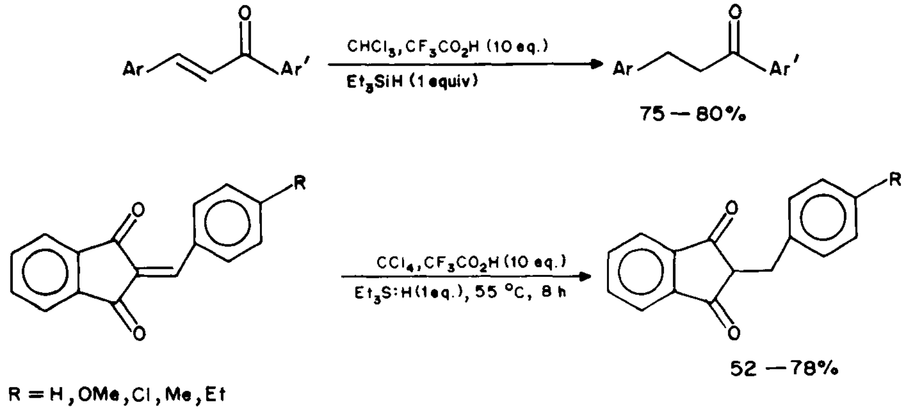
The hydrogen in the Si—H bond is slightly hydridic in nature, as would be expected from the relative electronegativities of silicon (1.7) and hydrogen (2.1). Therefore, silanes may function as hydride transfer agents toward highly electrophilic species such as carbonium ions. The hydridic nature of the Si—H bond may be significantly increased upon interaction with strong anionic ligands, such as fluoride and alkoxides (*vide infra*). In addition, the average bond energy of the Si—H and C—H bonds (70 and 99 kcal mol^{-1}, respectively) suggests that Si—H bonds should be susceptible to hydrogen atom abstraction by carbon radicals. Thus, the dehalogenation of alkyl halides with hydridosilane under homolytic conditions is explained in terms of a radical-chain mechanism[277]. Alternatively, silanes readily transfer a hydride ligand to a variety of transition-metal complexes via oxidative addition, allowing for highly selective transition metal-catalyzed reduction processes (*vide infra*, Section IV, B).

A useful reduction method involving hydridosilane in strongly acidic media, 'ionic hydrogenation', is useful for reduction of a number of organic functional groups[278]. The ionic hydrogenation reaction is based on the principle that the carbonium ion formed by protonation of the double bond reacts with a hydride donor to form the hydrogenated product. Reduction conditions generally involve reflux in strongly acidic media in the presence of the silane. Obviously, reduction is possible only when the substrate can produce carbonium ions under the given conditions. A hydrogenation pair most useful for many reduction processes is comprised of trifluoroacetic acid and a hydridosilane, which exhibits the following order of reactivity[278]:

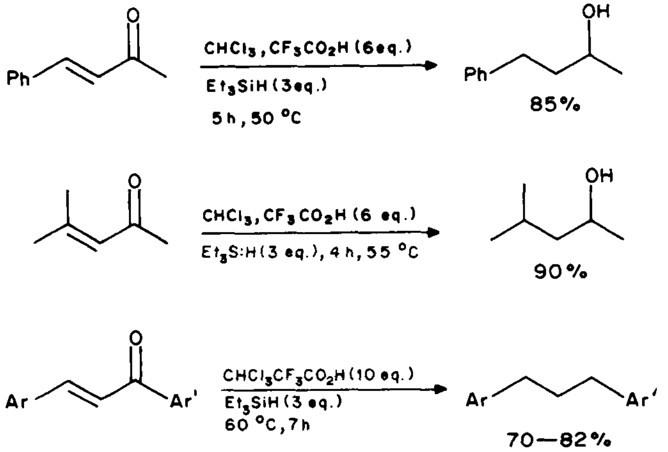
$$\mathrm{Et_3SiH > Octyl_3SiH > Et_2SiH_2 > Ph_2SiH_2 > Ph_3SiH > PhSiH_3}$$

These reducing systems tolerate carboxylic acid derivatives, nitriles, nitro groups, sulfonic esters, aromatic rings and, occasionally, olefins, alkyl halides, ethers and alcohols as well. Reduction may be chemoselective in compounds containing many functionalities, with the functional groups most easily capable of stabilizing a carbonium ion being reduced most readily. Thus, for example, aliphatic alkenes are reduced only when they are branched at the alkene carbon atom. With α,β-unsaturated ketones, the reduction can be directed almost exclusively to the C—C double bond. Thus, using only one equivalent of silane, enones are reduced to saturated ketones (Scheme 82)[279].

With excess silane, further reduction of the saturated ketone to the corresponding saturated alcohol occurs in high yields. In case of chalcones, excess silane may affect complete reduction and deoxygenation to yield the corresponding alkane (Scheme 83)[279,280].



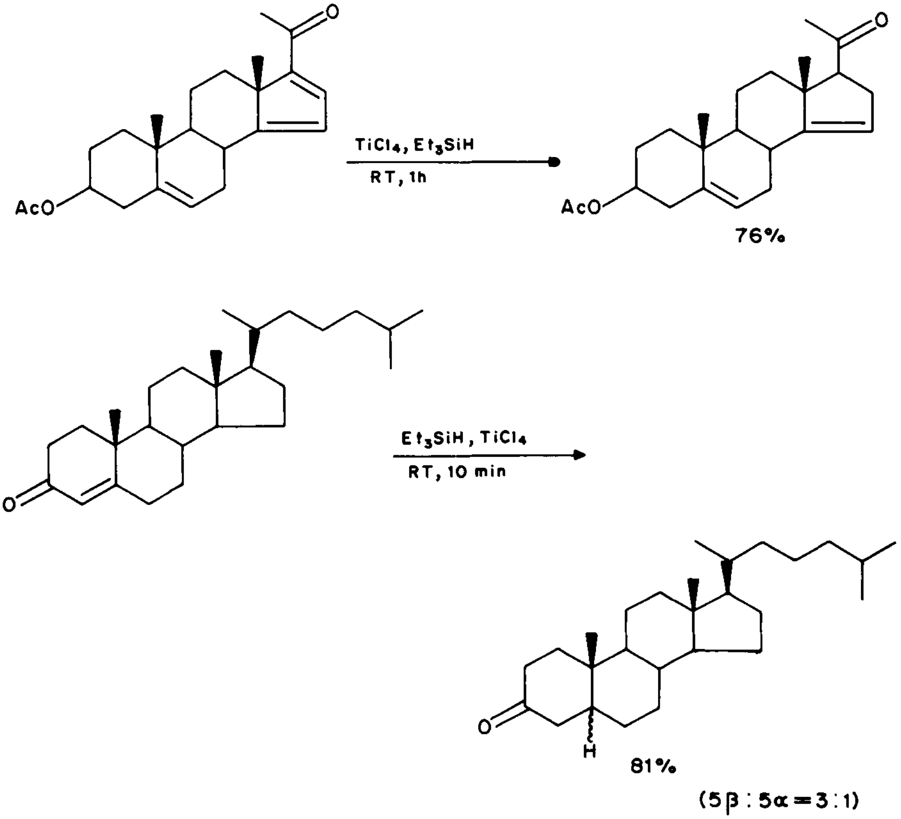
SCHEME 82



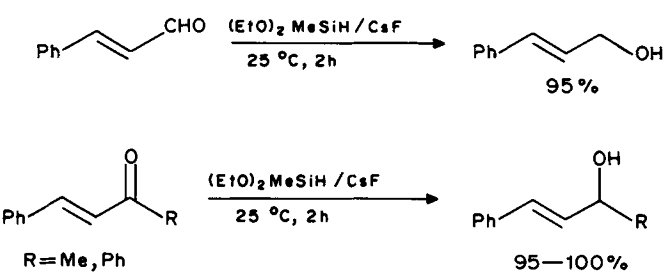
SCHEME 83

The reaction of conjugated enones and dienones with trimethyl- and triethylsilane in the presence of $TiCl_4$ followed by aqueous workup produces the corresponding saturated ketones. This Lewis acid catalysis is particularly useful for conjugated reduction of sterically hindered systems (Scheme 84)[281]. α, β-Unsaturated esters are not reduced under these conditions.

Anionic activation of Si—H bonds[282] by fluorides, such as KF or CsF, or by potassium phthalate, $KHCO_3$, KSCN, etc., yields powerful hydridic reagents that reduce the carbonyl group of aldehydes, ketones and esters[283]. It was postulated that the active species in these reactions is a pentacoordinated or even hexacoordinated hydridosilane. 1, 2-Reductions of α, β-unsaturated aldehydes and ketones occur with very high selectivity to give allylic alcohols (Scheme 85)[283]. The analogous activation of hydridosilanes by fluoride ions is also achieved under acidic conditions with boron trifluoride etherate, in which the latter compound is consumed and fluorosilanes are formed[284].

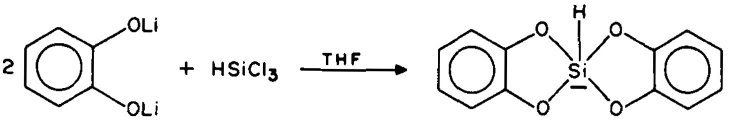


SCHEME 84



SCHEME 85

Effective anionic activation of trichlorosilane can be carried out with either catechol or 2, 2'-dihydroxybiphenyl in THF yielding bis(diolato)hydridosilicates (Scheme 86)[285]. Such reagents exhibit reducing power that is reminiscent of the complex aluminum hydrides. Even tertiary amines are useful activators of trichlorosilane, enhancing its hydridic character[286].

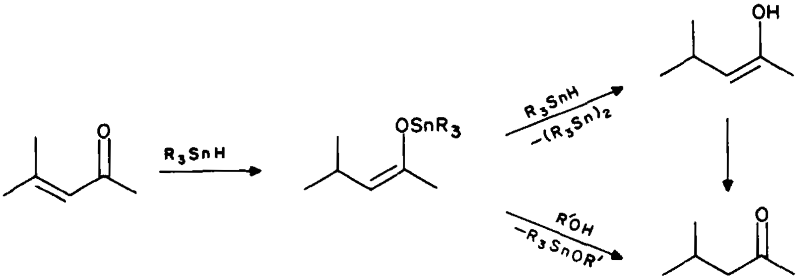


SCHEME 86

D. Tin Hydrides

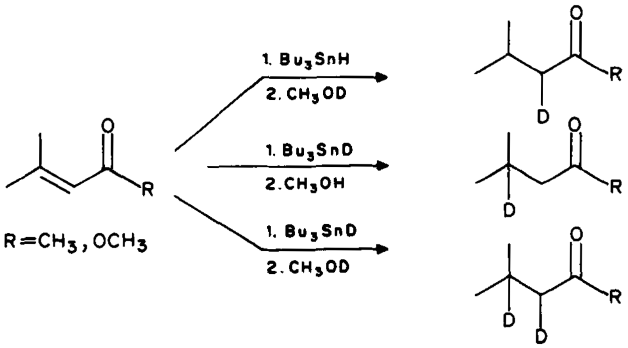
The special characteristics of organotin hydrides as reducing agents are rationalized by the fact that the tin–hydrogen bond is both weaker and less polar than the B—H or Al—H bonds[287]. These characteristics are manifested in reactions that proceed by either a free radical chain or polar mechanism, depending on the substrate, catalyst and reaction conditions.

α,β-Unsaturated aldehydes and ketones are readily reduced by organotin hydrides under rather mild conditions, but the reaction is often obscured by subsequent transformation of the adducts[288]. On heating or under UV irradiation, the organotin monohydrides add mainly at the 1,4-positions of the enone system to form the enol stannane. The latter may be hydrolyzed or cleaved by a second equivalent of tin hydride, resulting in overall reduction of the double bond (Scheme 87)[287,288].



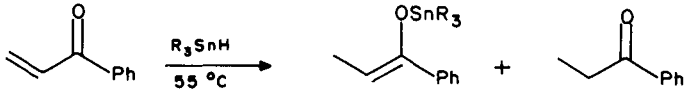
SCHEME 87

The protonolysis pathway was demonstrated in reactions carried out in deuteriated methanol (Scheme 88)[289].



SCHEME 88

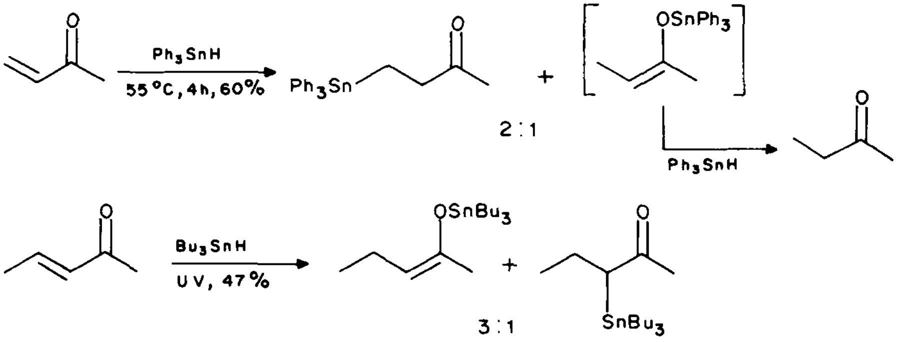
Enolate cleavage by a second equivalent of tin hydride is illustrated in Scheme 89[288l]. With Bu_3SnH the reaction proceeds no further, whereas the more electrophilic Ph_3SnH leads to hydrostannolysis of the tin enolate.



Bu_3SnH(1eq.), 6h	95 : 5
Bu_3SnH(1.3eq.), 20h	85 : 15
Ph_3SnH(1.3eq.), 3h	70 : 30
Ph_3SnH(2eq.), 4h	0 : 100

SCHEME 89

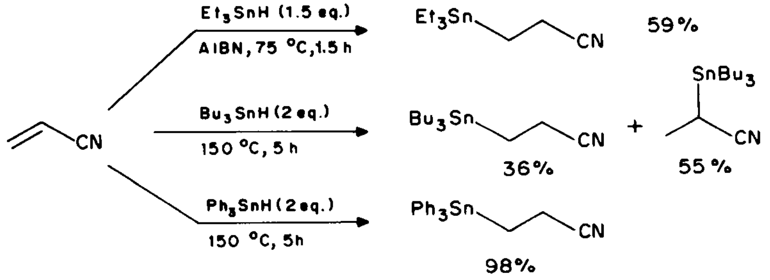
Sterically nonhindered enones may produce mixtures of products, including carbon-stannylated species. For example, methyl vinyl ketone gives rise to significant quantities of the inverted 1,4-adduct, where tin binds at the 4-position, leading to β-stannyl ketone. In the case of methyl propenyl ketone, addition occurs at position 3 and 4, producing α-stannyl ketone (Scheme 90)[288j].



SCHEME 90

In this class of reagents, diphenylstannane exhibited the highest regioselectivity, affording essentially pure 1,4-reduction. Other hydrides, such as Bu_3SnH or Ph_3SnH, give mixtures of 1,2- and 1,4-reduction products and they usually require free radical initiation[290].

In the case of α,β-unsaturated esters and nitriles, hydrostannation may proceed via either a polar or radical mechanism. Compounds containing a terminal multiple bond form the α-stannyl derivative according to a polar mechanism, while β-adducts are formed according to the radical pathway[291]. Other conditions being equal, triarylstannanes are more active than trialkylstannanes in radical processes. In general, α,β-unsaturated nitriles undergo the polar addition more actively than do the corresponding esters. However, with acrylonitrile, the homolytic mechanism is significant as well[292]. With trialkylstannanes under the action of azobis(isobutyronitrile) or UV irradiation or with triphenylstannane on heating, β-adducts are formed exclusively. Mixtures of α- and β-adducts are produced on thermal addition of trialkylstannanes (Scheme 91)[292]. Expectedly, the α/β ratio increases with solvent polarity.



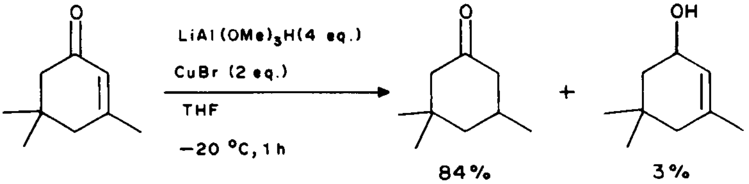
SCHEME 91

Hydrostannation of α-acetylenic esters generally produces a mixture of products. For more details, see Reference 287.

V. REDUCTIONS WITH STOICHIOMETRIC AMOUNTS OF TRANSITION-METAL HYDRIDES

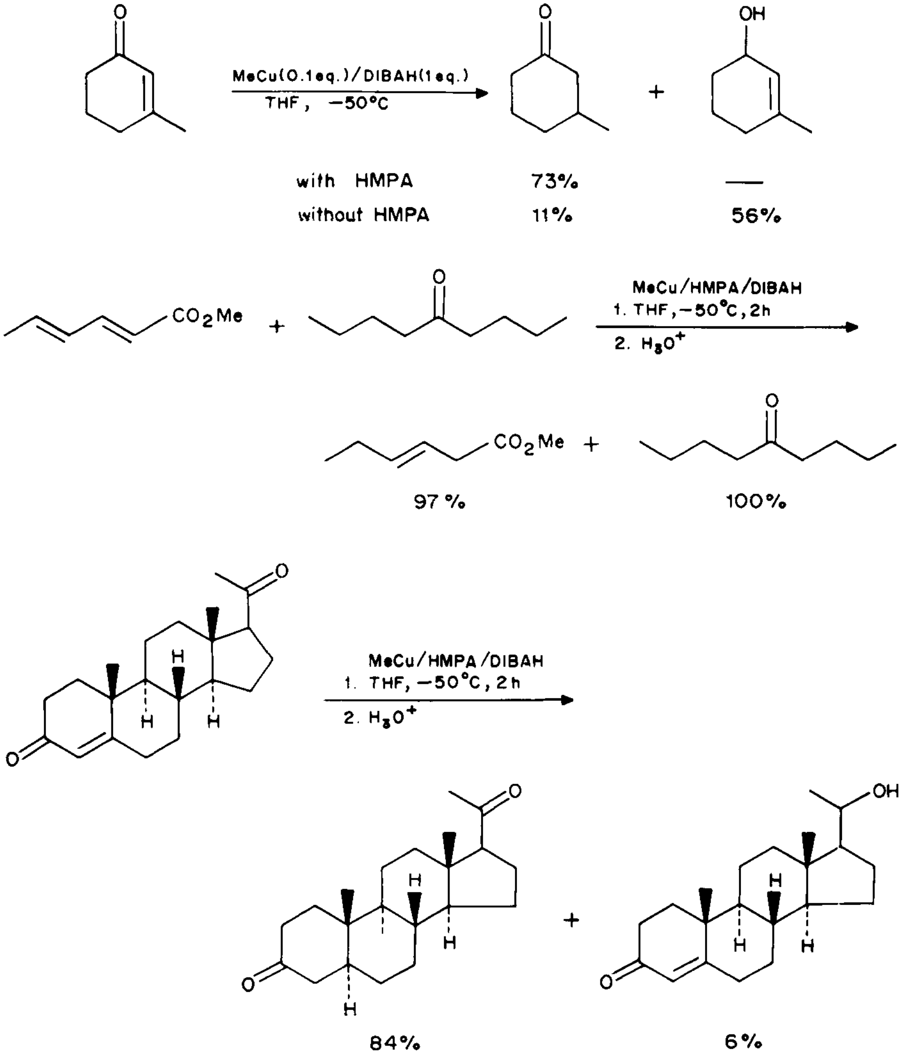
A. Copper Hydrides

The known preference of organo-copper reagents to engage in 1,4-addition to α,β-unsaturated carbonyl compounds[293] prompted an extensive search for analogous hydrido-copper reagents that would undergo conjugate addition to enones. Indeed, reaction of cuprous bromide with either two equivalents of lithium trimethoxyaluminum hydride or one equivalent of sodium bis(2-methoxyethoxy)aluminum dihydride ('Vitride' by Eastman or 'Red-Al' by Aldrich) in THF produces a heterogeneous mixture capable of 1,4-reduction of α,β-unsaturated ketones and esters[294]. The exact composition of these reagents is not yet known. Reductions usually take place between −20 and −78 °C to give moderate yields of the saturated carbonyl compound along with varying amounts of the 1,2-reduction product (Scheme 92). The use of lithium trimethoxyaluminium deuteride with CuBr produces the saturated ketone deuteriated at the β-position. Addition of D_2O before the aqueous workup leads to deuterium incorporation at the α-position. Because these reagents react with other functional groups (saturated ketones and aldehydes and alkyl bromides being reduced almost as rapidly as enones), their chemoselectivity is limited. The reagent has also been used for the conjugate reduction of α,β-unsaturated nitriles[295].



SCHEME 92

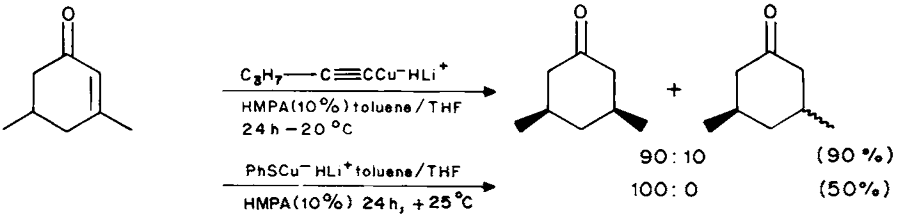
Combination of $LiAlH_4$ and catalytic amounts of CuI in HMPA/THF (1:4) is useful for 1,4-reduction of α,β-unsaturated ketones, aldehydes and esters[296]. Reactions carried out at −78 °C for 1 hour resulted predominantly in the 1,4-reduction product, but traces of the saturated and allylic alcohols were also formed[296]. It was claimed that the ratio between $LiAlH_4$ and CuI (10:1) as well as the presence of HMPA generates a hydridocuprate species which acts as the actual reducing agent. In contrast, in a previously reported work using either $LiAlH_4$ or AlH_4 and CuI (in a 4:1 ratio) in THF, it was suggested that the active reductant is H_2AlI[257] (*vide supra*). An improved system based on diisobutylaluminum hydride (DIBAH) as the hydride donor and MeCu as the catalyst effects clean conjugate reduction of a variety of α,β-unsaturated carbonyl compounds without 1,2-reduction products. The presence of HMPA, probably acting as a ligand, was found to be of crucial importance for this reducing system, as shown in Scheme 93[297]. Other coordinating solvents including pyridine, DMF and DMSO did not lead to comparable regioselectivity. Chemoselectivity is demonstrated by the selective 1,6-



SCHEME 93

reduction of methyl sorbate in the presence of a saturated ketone, and the conjugate reduction of the enone of progesterone with only minor reduction of the saturated ketone in this molecule.

A series of heterocuprate complexes Li^+HRCu^-, with R representing a nontransferable ligand such as 1-pentynyl, *t*-BuO$^-$ or PhS$^-$, was generated in toluene from DIBAH and CuI by addition of RLi. These reagents were used for clean 1,4-reduction of α,β-unsaturated ketones and esters[298]. Yields, however, were quite low in several cases due to the strong basicity of these reagents. Although HMPA was found to facilitate 1,4-reduction in substrates where the β-carbon is highly substituted, enone reduction in multifunctional compounds resulted in low yields (Scheme 94). In a related, independent study, the hydridocuprate complex was prepared by addition of RLi (R = alkyl or alkynyl) to a suspension of CuH in ether or in THF. These reagents were used for clean conjugate reduction of α,β-unsaturated carbonyls[299], however with poor chemoselectivity, as saturated aldehydes and ketones were reduced under these conditions to the corresponding alcohols, and various tosylates and bromides were reductively cleaved.



SCHEME 94

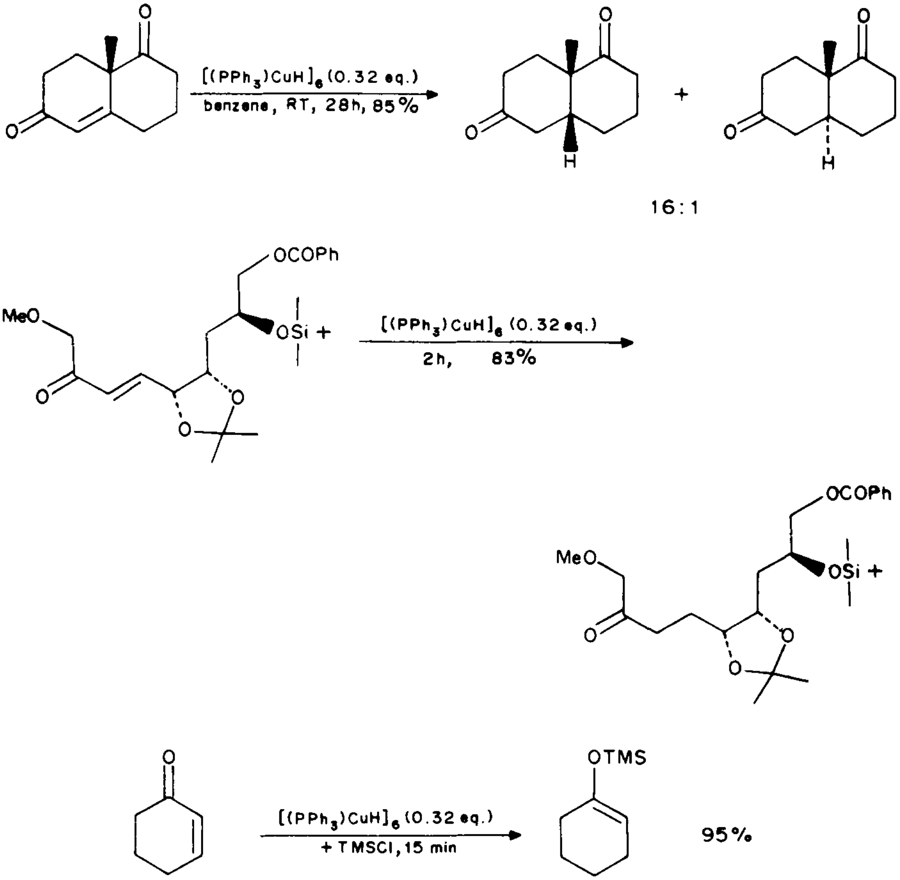
Polyhydrido-copper complexes, such as $LiCuH_2$, Li_2CuH_3, Li_3CuH_4, Li_4CuH_5 and Li_5CuH_6, were prepared[300] by $LiAlH_4$ reduction of $Li_nCu(CH_3)_{n-1}$. Reduction of α,β-unsaturated carbonyl compounds with any of these hydrides in ether or in THF produced mixtures of 1,4- and 1,2-reduction products. These reagents also reduce ketones, alkyl halides, alkyl tosylates and aryl halides.

The stable, well-characterized copper(I) hydride cluster $((PPh_3)CuH)_6$[301] is a useful reagent for conjugate reduction of α, β-unsaturated carbonyl compounds[302]. This hydride donor is chemically compatible with chlorotrimethylsilane, allowing formation of silyl enol ethers via a reductive silation process (Scheme 95).

B. Iron Hydrides

Iron hydrides were also used for selective 1,4-reduction of enones[287b]. For example, tetracarbonylhydridoferrate, $NaHFe(CO)_4$, which is prepared directly by refluxing pentacarbonyl iron with sodium methoxide in methanol, reduces benzalacetone to benzylacetone. Addition of this reagent to an ethanolic sotution containing both an aldehyde and a ketone results in reductive alkylation of the ketone. The reaction probably involves base-catalyzed aldol condensation of the aldehyde and the ketone, followed by elimination of water to give the corresponding α, β-unsaturated ketone. The latter is then reduced by the tetracarbonylhydridoferrate, to afford the saturated ketone[303]. Interestingly, $NaHFe(CO)_4$ in THF reduces α,β-unsaturated carbonyl compounds to the corresponding saturated alcohols with high stereospecificity. For example, (+)- and (−)-carvones are reduced to (−)- and (+)-neodihydrocarveol, respectively[304].

The binuclear hydride $NaHFe_2(CO)_8$[305,306], which is prepared by addition of AcOH to a slurry of $Na_2Fe_2(CO)_8$ in THF, is also useful for clean conjugate reductions. This reagent



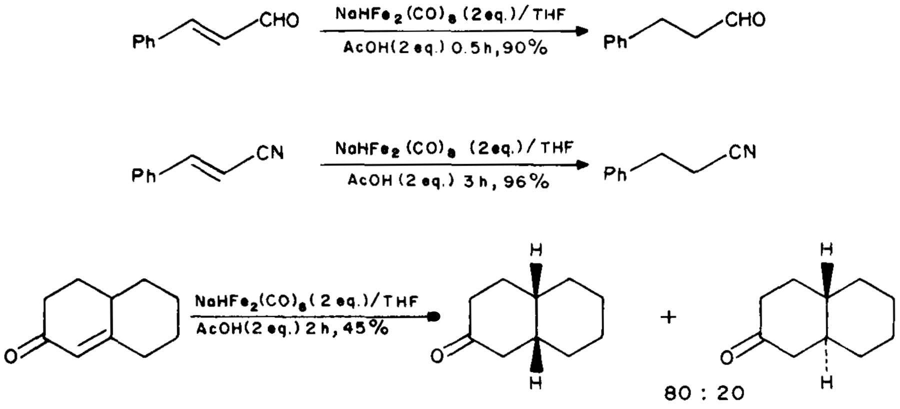
SCHEME 95

is capable of selective 1, 4-reduction of α, β-unsaturated ketones, aldehydes, esters, nitriles, amides and lactones in good yields (Scheme 96). Reductions are generally performed at − 50 °C in a THF solution of $NaHFe_2(CO)_8$ and HOAc. Usually, two or more equivalents of the reagent are required for the reduction of 1 equivalent of substrate.

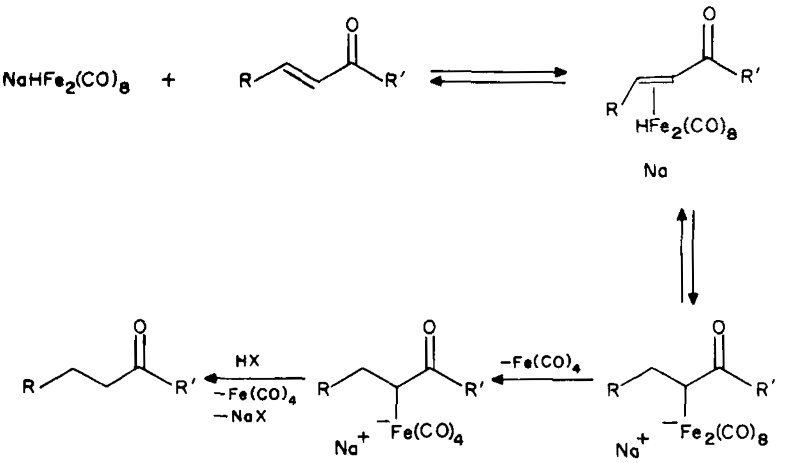
According to a detailed mechanistic study[306], the reaction involves concerted, reversible, regiospecific addition of $NaHFe_2(CO)_8$ to the C=C double bond of the enone, affording the corresponding binuclear iron enolate. Cleavage of the latter to the mononuclear iron enolate represents the rate determining step. Finally, protonolysis of this iron enolate by acetic acid provides the saturated ketone (Scheme 97).

C. Other Transition-metal Hydrides

The intermetallic hydride $LaNi_5H_6$ was found to be an effective reagent for conjugate reduction of enones. Reduction of the resulting saturated carbonyl compound occurs very slowly with this reagent, giving high yields of the 1, 4-reduction product[307].



SCHEME 96



SCHEME 97

α,β-Unsaturated carbonyl compounds are reduced selectively and in good yields (55–80%) to the corresponding saturated derivatives by the hydridochromium complex $NaHCr_2(CO)_{10}$ in THF at 66 °C. This latter complex is prepared by stirring chromium-hexacarbonyl with potassium graphite (C_8K) in dry THF with subsequent addition of water[308].

Excess hydridocobaltcarbonyl reduces α,β-unsaturated ketones and aldehydes in moderate yield and good regioselectivity. The reaction involves complexation of the double bond to cobalt, followed by migratory insertion of hydride into the enone, forming an oxa-allyl cobalt complex[309]. Poor chemoselectivity is one of the major drawbacks of this reaction, as simple olefins are rapidly hydroformylated to the corresponding aldehyde under the reaction conditions (25 °C, 1 atm of CO).

α,β-Unsaturated ketones and esters are selectively 1,4-reduced by $Et_4N[\mu\text{-}HMo_2(CO)_{10}]$ and HOAc in refluxing THF[310]. Benzalacetone is quantitatively reduced to benzylacetone under these conditions. However, reduction of cinnamaldehyde gives a mixture of dihydrocinnamaldehyde (3%), cinnamyl alcohol (85%) and phenylpropane (12%).

VI. COMPOSITE REDUCING SYSTEMS

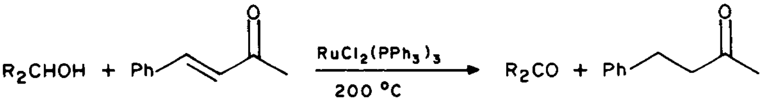
Composite reducing systems are comprised of at least two components, namely a relatively inactive source of hydride ions and a transfer agent to deliver the hydride selectively from that donor to a target functionality. This family of reducing systems will therefore selectively transfer a hydride ion to various electrophilic functional groups, including α,β-unsaturated carbonyl compounds. The acceptor properties of the latter make them excellent ligands for low-valent, electron-rich transition metals and, obviously, good substrates for selective reduction with nonreactive hydride donors.

Such multiple-component reducing systems offer high flexibility because they involve a large number of independent variables that can be tailored to various synthetic tasks, especially in comparison to metal hydride reduction which utilizes a single reagent. Thus, appropriate modification of the hydride donor, judicious selection of a transition metal transfer agent and, in some cases, use of a cocatalyst provide an opportunity for creating a wide variety of reducing systems that exhibit improved chemoselectivity, as well as regio- and stereocontrol.

A. Transfer Hydrogenation Using Alcohols as Hydrogen Donors

Catalytic transfer of hydrogen from an organic donor to a variety of unsaturated organic acceptors is widely documented[311]. This approach has also been applied to the reduction of α,β-unsaturated carbonyl compounds, utilizing a catalyst and an organic compound with a low enough oxidation potential to be oxidized under the reaction conditions by the unsaturated carbonyl substrate[311]. With respect to enone reduction, the most commonly used hydrogen donors are primary or secondary alcohols. Temperatures for catalytic transfer hydrogenation are usually in the range 100–200 °C, depending upon the hydride source.

When α,β-unsaturated ketones are heated with a primary or secondary alcohol in the presence of $RuCl_2(PPh_3)_3$ or $RuHCl(PPh_3)_3$ at 200 °C, hydrogen is transferred selectivity to the olefinic double bond (Scheme 98)[312–314]. The competing equilibrium that reduces the saturated ketone back to the alcohol may be suppressed by use of a primary alcohol such as benzyl alcohol or, more conveniently, by the use of boiling ethylene glycol, since saturated ketones are readily separated from insoluble glyoxal polymers[315]. Polyvinyl alcohol can also be used as convenient hydrogen donor[316]. α,β-Unsaturated ketones give higher yields than the corresponding aldehydes, which undergo self-condensation. α,β-Unsaturated esters undergo transesterification side-reactions with the donor alcohol.



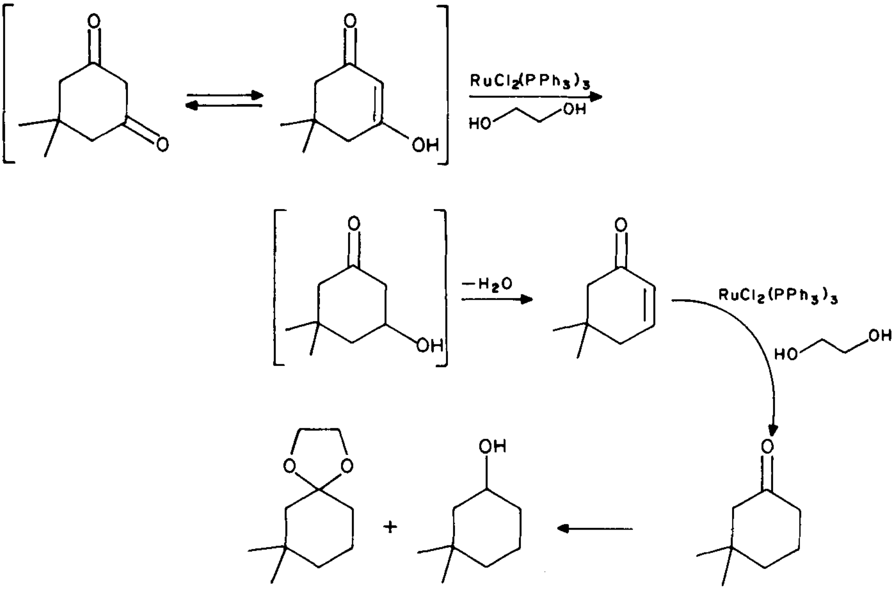
SCHEME 98

Studies on the role of a Ru(II) catalyst as well as the mechanism of hydrogen transfer in enone reduction with benzyl alcohol at 170–190 °C revealed that $RuCl_2(PPh_3)_3$ is converted by the primary alcohol into $RuH_2(CO)(PPh_3)_3$, which then hydrogenates benzylideneacetone[317]. The kinetic data are compatible with the expression:

$$\text{reaction rate} = k_{obs}[Ru][enone][alcohol]$$

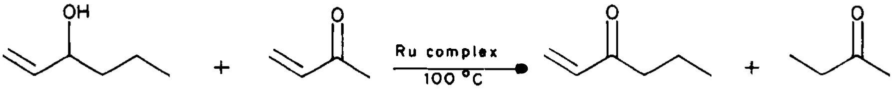
The rate-determining step of this reaction is generally assumed to be hydrogen transfer from the alcohol to a ruthenium species[317].

Transfer hydrogenation catalyzed by $RuCl_2(PPh_3)_3$ has been applied to the synthesis of cyclododecane-1,2-dione in 53% yield from the corresponding 1,2-diol using benzylideneacetone as the hydrogen acceptor[318]. 5,5-Dimethylcyclohexa-1,3-dione reacts via its enol tautomer on heating with ethylene glycol in the presence of $RuCl_2(PPh_3)_3$ to give 3,3-dimethylcyclohexanol, 3,3-dimethylcyclohexanone and its corresponding ketal (Scheme 99)[319].

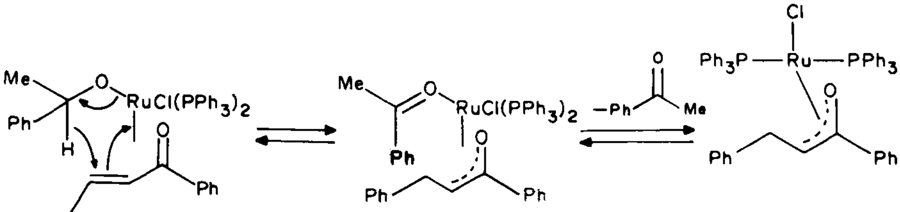


SCHEME 99

Vinyl ketones, such as methylvinyl ketone, are not reduced in the presence of $RuCl_2(PPh_3)_3$ on heating with common primary or secondary alcohols, but they are reduced on heating with allylic alcohols, such as hex-1-en-3-ol, using hydrated $RuCl_3$, $RuCl_2(PPh_3)_3$, $RuHCl(PPh_3)_3$, $RuH(OAc)(PPh_3)_3$ or, most efficiently, $Ru_3O(OAc)_7$ (Scheme 100)[320]. Surprisingly, other ketones, including acetophenone or benzylideneacetone, are not reduced under these conditions.



SCHEME 100



SCHEME 101

As in hydrogen transfer between alcohols and saturated ketones, the rate-determining step in the corresponding reaction with α, β-unsaturated ketones is hydrogen abstraction from the α-carbon atom. It has been suggested that the hydrogen atom is transferred directly to the β-carbon of the enone, yielding an η^3-oxaallyl complex which, following protonation, yields the saturated ketone (Scheme 101)[312].

Unsaturated esters also undergo trasnfer hydrogenation under $RuCl_2(PPh_3)_3$ catalysis to the saturated esters, but significant transesterification reaction with the reacting alcohol also occurs[313]. Simple olefins are reduced, in general, very slowly under the reaction conditions, although $RuCl_2(PPh_3)_3$ is reported to catalyze hydrogen transfer from indoline to cycloheptene in refluxing toluene, to give cycloheptane and indole[321], and other Ru(II) complexes catalyze hydrogen transfer from alcohols to diphenylacetylene to yield *cis*-stilbene[322].

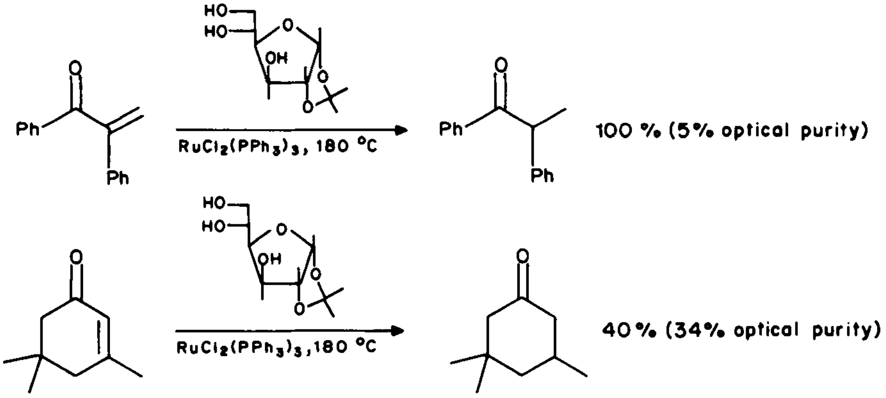
Transfer hydrogenation of a prochiral olefin in the presence of a chiral catalyst may lead to a chiral saturated product. For example, tiglic acid ($MeCH{=}C(Me)CO_2H$) is hydrogenated at 120 °C by either isopropanol in the presence of $Ru_4H_4(CO)_8((-)\text{-diop})_2$[323] (diop = 2, 3-*O*-isopropylidene-2, 3-dihydroxy-1, 4-bis(diphenylphosphino)-butane) or by benzyl alcohol in the presence of $Ru_2Cl_4(diop)_3$ at 190 °C[324]. The optical purities reported for the resulting saturated acids, however, do not exceed 10–15%, a lower figure than that obtained by catalytic hydrogenation with hydrogen gas.

Prochiral α, β-unsaturated esters can also be asymmetrically hydrogenated by benzyl alcohol or 1-phenylethanol and catalytic $Ru_2Cl_4(diop)_3$[324], but the optical purities of the resulting esters are even lower than those obtained from hydrogenating the corresponding acids. Enantioselectivity is also observed in transfer hydrogenation of α, β-unsaturated ketones, such as $PhCH{=}CHCOMe$, by racemic 1-phenylethanol in the presence of Ru(II) chloro complexes containing optically active tertiary phosphines, including diop and neomenthyldiphenylphosphine. Thus the optical purity of 1-phenylpropan-1-ol enriched in the *S*-(−)-isomer is 11% when reacted under these conditions with benzylideneacetone[325].

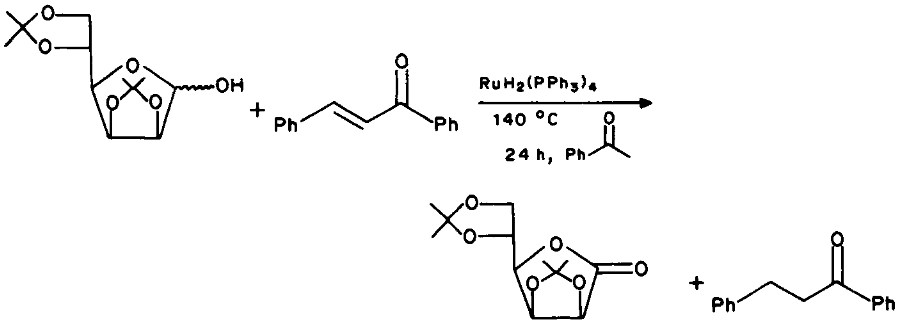
Asymmetric hydrogen transfer from optically active monosaccharides, such as 1, 2-α-D-glucofuranose, to prochiral enones is catalyzed by $RuCl_2(PPh_3)_3$ in diphenyl ether at 180 °C or by $RuH_2(PPh_3)_4$ in toluene at 100 °C (Scheme 102)[326].

Catalytic hydrogen transfer from sugars with free anomeric hydroxyl groups was studied with 2, 3; 5, 6-di-*O*-isopropylidene-D-mannofuranose and $RuH_2(PPh_3)_4$. In an excess of enone acceptor, these sugars were converted in high yields into the corresponding lactones (Scheme 103)[327].

The 1, 4-reduction of styryl ketones by 1-phenylethanol using $RhH(PPh_3)_4$ catalyst can be carried out at 50 °C, a relatively low temperature for transfer hydrogenation. An electron-withdrawing group present in the enone system increases the initial rate of reduction, suggesting a transfer of hydrogen to the enone by an intermediate with hydride-ion character[328]. Isotope labeling of the alcohol donors shows that hydrogen is regioselectively transferred from the carbinol carbon to the β-carbon of the enone, with the

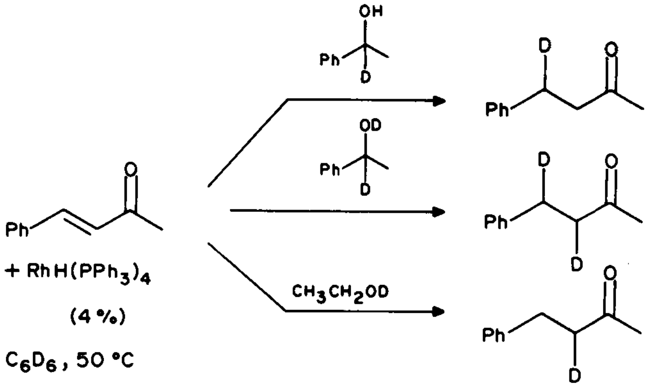


SCHEME 102



SCHEME 103

hydroxylic proton being transferred to the α-position (Scheme 104). Cleavage of an O—H bond is the rate-determining step in this reaction[329].



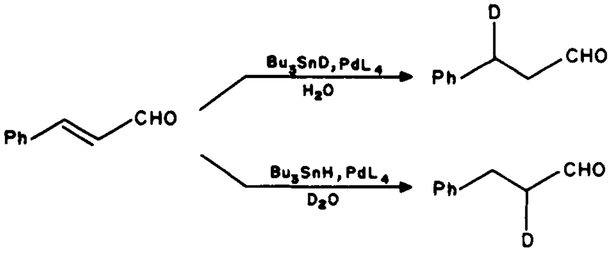
SCHEME 104

High catalytic activities, with turnovers of up to 900 cycles/min, is displayed in the transfer hydrogenation of α,β-unsaturated ketones, such as benzylideneacetone and chalcone, using isopropanol and catalytic amounts of [Ir(3,4,7,8-Me_4-phen)COD]Cl (phen = 1,10-phenanthroline; COD = 1,5-cyclooctadiene) in a weakly alkaline medium[330]. Other Ir-chelated complexes are also active catalysts in this reaction, with over 95% selectivity for the 1,4-reduction mode.

B. Transition Metal-catalyzed Reductions with Group-14 Metal Hydrides

Group-14 metal hydrides, especially those of silicon and tin, are satisfactory nonreactive hydride donors, as in the absence of a catalyst they are, generally, poor reducing agents. Transition-metal complexes are attractive transfer agents because they insert readily into Si—H or Sn—H bonds and they also bind specifically to various functional groups.

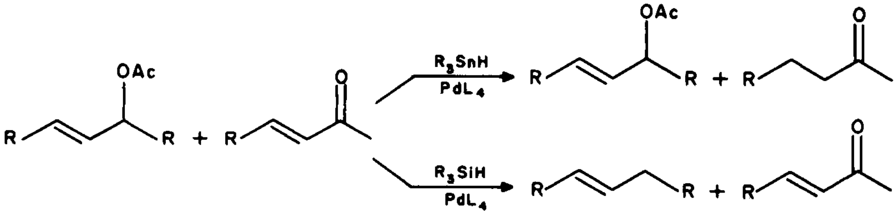
Indeed, a combination of tributyltin hydride, Pd(0) catalyst and a weak acid, such as ammonium chloride, forms an effective, yet mild tool for conjugate reduction of α,β-unsaturated aldehydes and ketones[331]. Similar results are obtained with other acidic cocatalysts, such as zinc chloride, acetic acid and tributyltin triflate[332]. With this system, reductions occur with high regioselectivity, providing a useful approach for deuterium incorporation into either the β- or α-position by using either tributyltin deuteride or D_2O, respectively (Scheme 105)[331].



SCHEME 105

The above-described reducing system comprising tributyltin hydride and a soluble palladium(0) catalyst also allows chemoselective reductive cleavage of allylic heterosubstituents, even in the presence of aldehydes, benzylic acetate and benzylic chloride groups. These latter functions are normally as reactive as the allylic structure when using standard hydride reducing agents[333].

Silicon hydrides offer even greater selectivity in these reductions[334]. Their superiority over tin hydrides is manifested by the greater stability of the palladium catalyst in the reaction solution, and the absence of diene side-products, frequently formed via the competing Pd-catalyzed elimination processes. Moreover, the difference in reactivities between tin and silicon hydrides can be exploited for functional-group differentiation. In the presence of Pd(0), tributyltin hydride, for example, reduces rapidly α,β-unsaturated ketones and aldehydes but silicon hydrides are unable to do so. Thus, the treatment of a mixture of an allylic acetate and an unsaturated ketone with tin hydride and Pd(0) catalyst results in total conjugate reduction of the latter and nonreacted allylic acetate (Scheme 106)[334]. In contrast, employment of silicon hydride provided complementary chemoselectivity: allylic reduction was completed before reduction of the Michael acceptor could be detected.



SCHEME 106

When using either tin or silicon hydrides, allylic substitution occurs with absolute inversion of configuration at the carbon, implying that hydride is initially transferred to palladium and from there to the allylic ligand via migratory insertion[333,334c]. This behavior is reminiscent of the proposed mechanism of the palladium-catalyzed conjugate reduction of enones (*vide infra*).

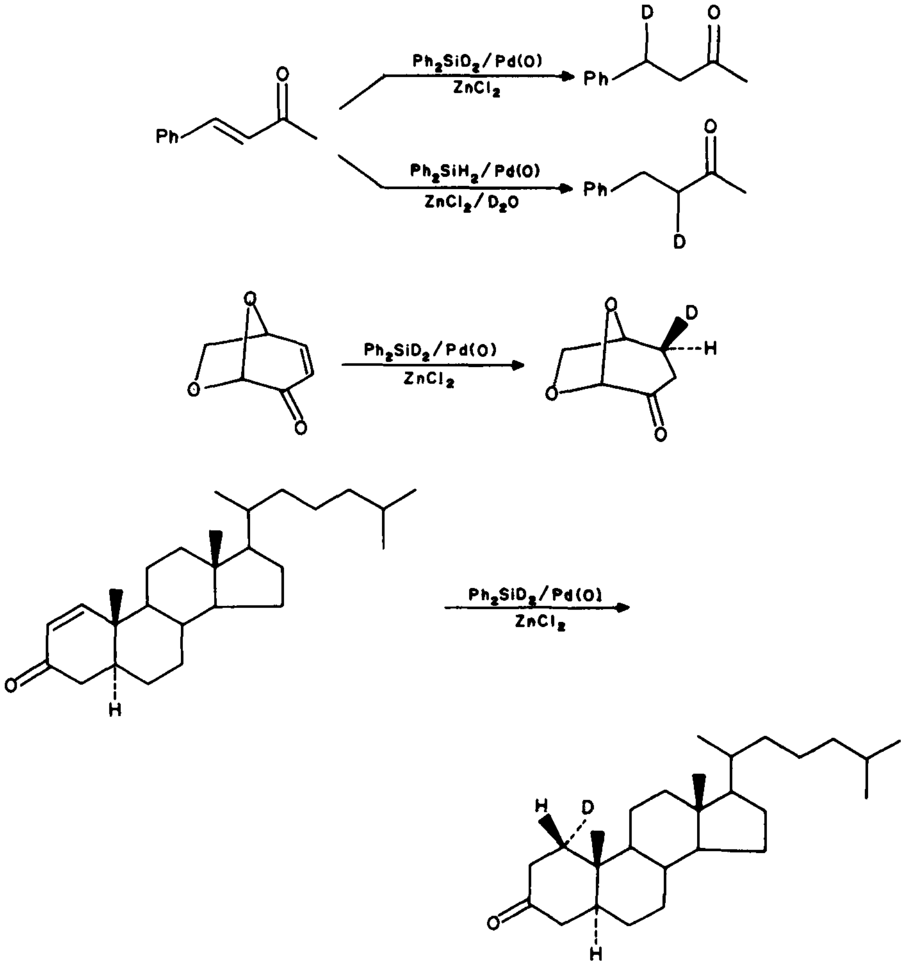
The useful flexibility characteristic of these multicomponent reducing systems is well illustrated by the silicon hydride/Pd(0) mixture. As mentioned above, this combination is essentially useless for reduction of electron-deficient olefins. However, addition of catalytic amounts of zinc chloride fundamentally alters the situation and creates a new three-component mixture that enables rapid conjugate reduction of α,β-unsaturated ketones and aldehydes[335]. In fact, soluble palladium complexes of various oxidation states were equally efficient catalysts, an obvious practical advantage of this approach. The generality of the method with respect to the substrate, its experimental simplicity and its easy applicability to large-scale work make it a method of choice for conjugate reduction of unsaturated ketones and aldehydes.

The reaction was found to be both regio- and stereoselective. In all cases where diphenyldideuteriosilane was used to reduce unsaturated ketones, deuterium was stereoselectively introduced at the less-hindered face of the substrate and regioselectively at the β-position (Scheme 107). Conversely, when reductions were carried out in the presence of traces of D_2O, deuterium incorporation occurred at the α-position[335].

Interestingly, this method is highly selective for unsaturated ketones and aldehydes, as reduction of corresponding α,β-unsaturated carboxylic acid derivatives, such as esters, amides and nitriles, is very sluggish under the conditions used. Thus, benzylideneacetone was selectively and cleanly reduced in the presence of methyl cinnamate, cinnamonitrile or cinnamamide[335].

Based on deuterium-incorporation experiments and ^1H NMR studies, a multistep catalytic cycle was postulated (Scheme 108) in which the first step is rapid, reversible coordination of the Pd(0)-phosphine complex to the electron-deficient olefin, resulting in complex I. Oxidative addition of silicon hydride to palladium in that complex forms hydrido-palladium olefin complex II. Migratory insertion of hydride into the electrophilic β-carbon of the coordinated olefin produces intermediate palladium enolate III which, via reductive elimination of the silicon moiety and enolate ligand, completes the catalytic hydrosilation cycle, resulting in silyl enol ether IV. The latter is prone to acid-catalyzed hydrolysis, yielding the saturated ketone[335].

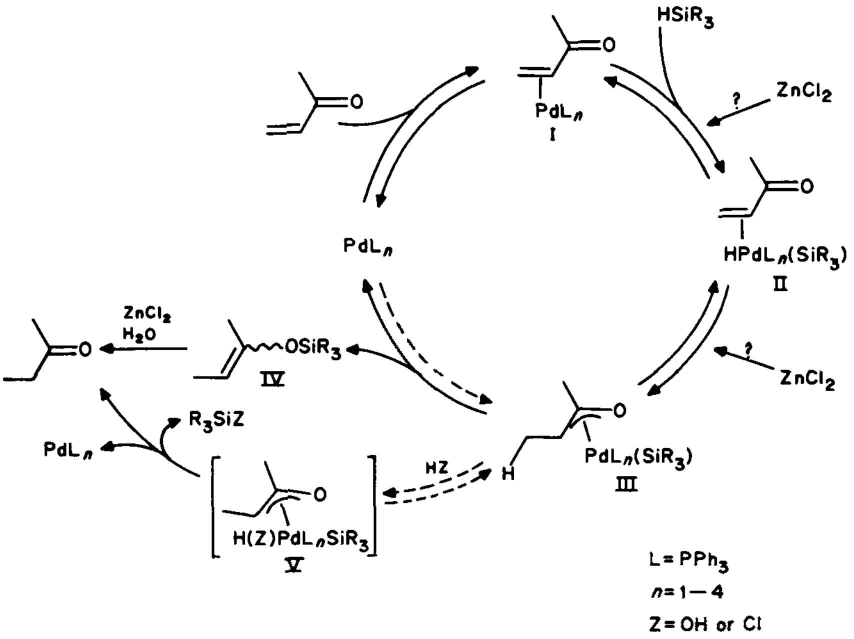
The role of the Lewis acid cocatalyst is not yet fully understood. One may envision a number of points at which intervention of a Lewis acid could promote the reaction. It seems that in addition to its obvious role in catalyzing hydrolysis of the silyl enol ether, $ZnCl_2$ polarizes the substrate, thereby facilitating migratory insertion of hydride into the olefin (II to III in Scheme 108).



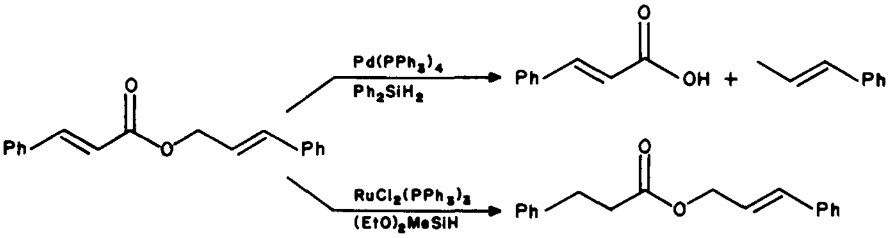
SCHEME 107

Combination of silicon hydrides with catalytic amounts of a ruthenium(II) complex in tetrahydrofuran, chloroform or benzene has afforded a new reducing system capable of efficient reduction of α,β-unsaturated carboxylic acids, esters, amides, etc[336]. Addition of a weak proton source, such as a sterically-hindered phenol, significantly increases reaction rates. The ruthenium mixture was found to exhibit the same regioselectivity observed with the above-described palladium systems.

The order of reactivity of this Ru/silane combination to various functional groups differs greatly from that of its Pd/silane/$ZnCl_2$ analog. While the latter is very useful for allylic reductions and essentially useless for unsaturated esters, the Ru-based system exhibits exactly opposite reactivity. A convincing demonstration of this complementary chemoselectivity is illustrated by the reduction of cinnamyl cinnamate (Scheme 109), a substrate containing both an allylic carboxylic and an α,β-unsaturated ester[336]. Each of



SCHEME 108

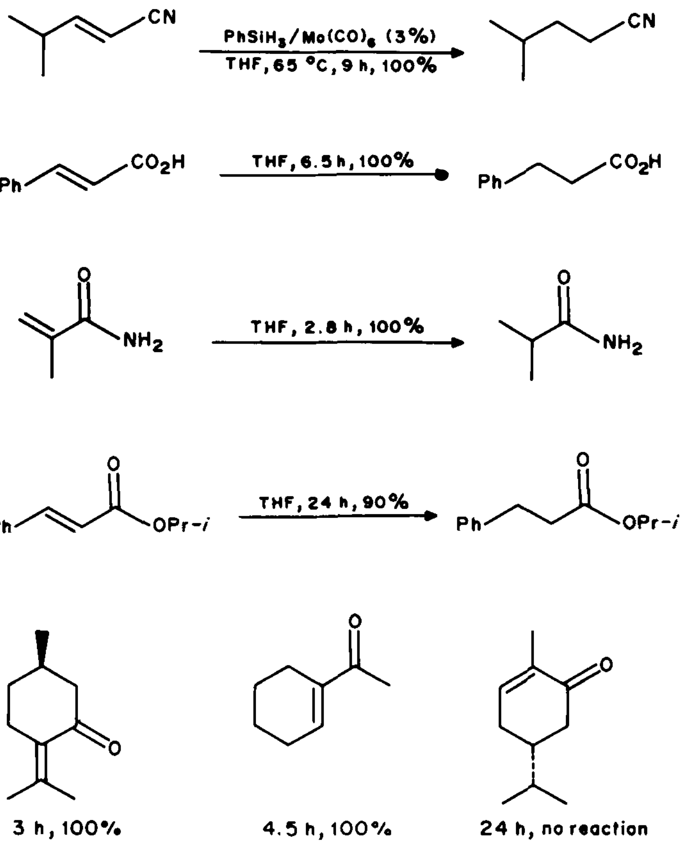


SCHEME 109

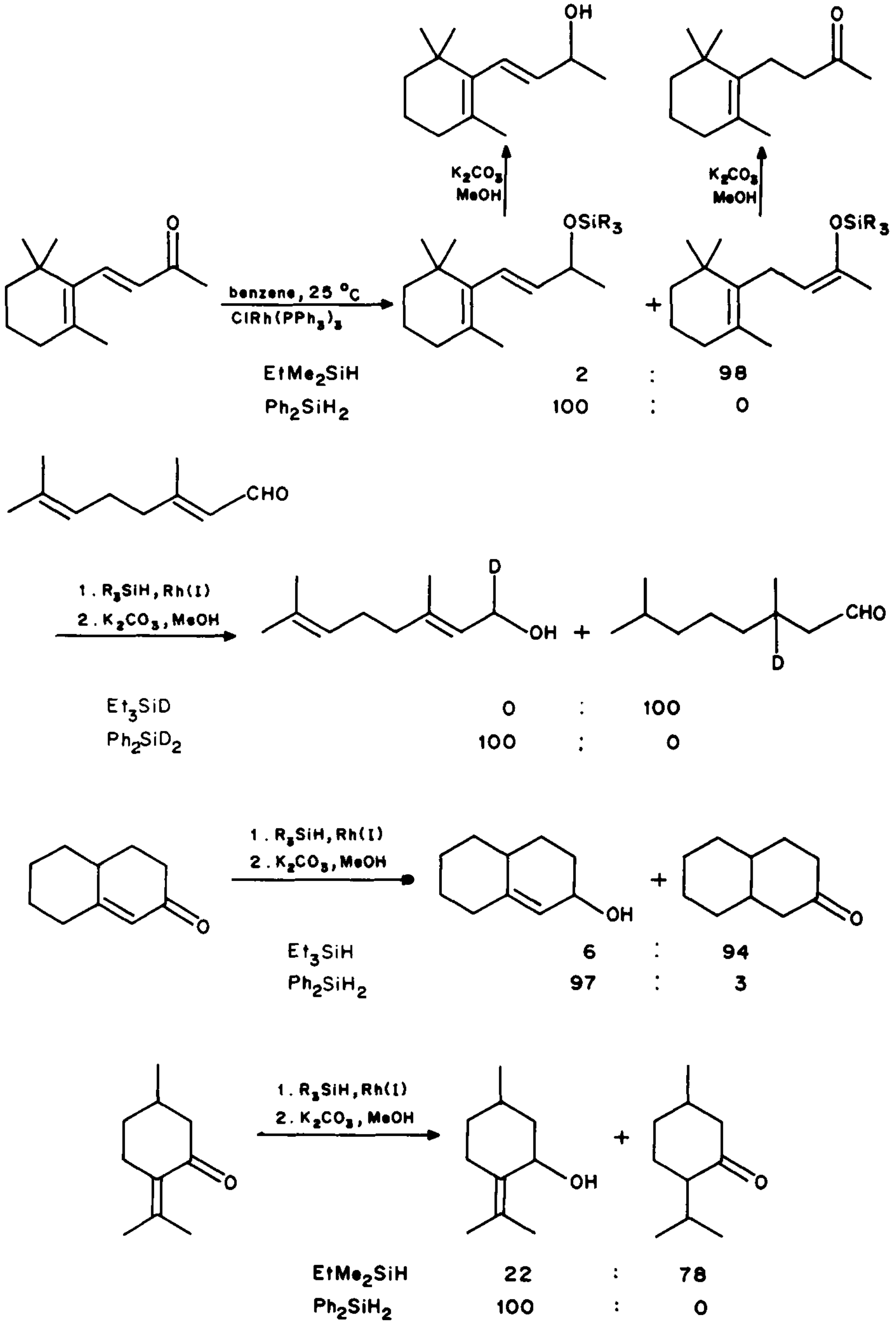
these can be reduced separately by silicon hydride and the appropriate transition-metal catalyst.

Early transition-metal complexes, including those of group 6, have been rarely used to catalyze transfer hydrogenation[337] and hydrogenation with hydrogen gas[338] and, in particular, little is known about hydrosilation with these catalysts. Under mild thermal conditions, catalytic amounts of Mo(CO)$_6$ and phenylsilane engender a powerful reducing system, suitable for conjugate reduction of α, β-unsaturated ketones, carboxylic acids, esters, amides, etc. The mixture is especially useful for conjugate reduction of unsaturated nitriles, usually difficult to reduce with other media (Scheme 110)[339]. Although the reaction also works with mono- and dihydridosilanes, the general order of silane reactivity is: $PhSiH_3 > Ph_2SiH_2 > Me(EtO)_2SiH >$ PMHS, $PhMe_2SiH$, Et_3SiH.

Of special interest are the relative rates of reduction of various cyclic enones, such as carvone, acetylcyclohexene and pulegone (Scheme 110). While the enone system in carvone is frozen in its transoid form, in acetylcyclohexenone it is flexible and may adopt either transoid or cisoid conformation. Acetylcyclohexenone is completely reduced while essentially no reaction observed with carvone, demonstrating the clear preference of the cisoid form and indicating that the molybdenum atom interacts simultaneously with both the olefinic bond and the carbonyl of the enone system. Accordingly pulegone, which is frozen in the cisoid form, is reduced much faster than the other two compounds. A similar phenomenon was observed in enone hydrogenation catalyzed by arene-chromium tricarbonyl complex, where the cisoid conformation is also markedly preferred[338c]. With Pd(0) catalyst, however, enones behave as monodentate ligands and reductions of the above-mentioned substrates proceed at comparable rates[335]. These reactivity characteristics may be utilized for chemoselective differentiation between similar enones. For example, benzylideneacetone is quantitatively reduced to benzylacetone in the presence of carvone[339]. Allylic heterosubstituents and α-halo carbonyl compounds are also reduced very efficiently under these conditions[340].



SCHEME 110

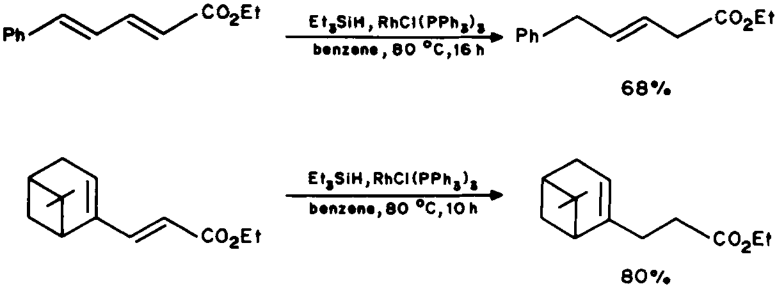

OH
O
K₂CO₃
MeOH
K₂CO₃
MeOH
O
OSiR₃
OSiR₃
benzene, 25 °C
ClRh(PPh₃)₃
+
EtMe₂SiH 2 : 98
Ph₂SiH₂ 100 : 0
CHO
1. R₃SiH, Rh(I)
2. K₂CO₃, MeOH
D
OH
+
CHO
D
Et₃SiD 0 : 100
Ph₂SiD₂ 100 : 0
1. R₃SiH, Rh(I)
2. K₂CO₃, MeOH
O
OH
+
O
Et₃SiH 6 : 94
Ph₂SiH₂ 97 : 3
1. R₃SiH, Rh(I)
2. K₂CO₃, MeOH
O
OH
+
O
EtMe₂SiH 22 : 78
Ph₂SiH₂ 100 : 0

SCHEME 111

Highly regioselective reduction of α,β-unsaturated ketones and aldehydes to give either the corresponding saturated carbonyls or allylic alcohols as the predominant product is effected by hydrosilation catalyzed by tris(triphenylphosphine)chlororhodium (Wilkinson catalyst), followed by methanolysis of the resulting adducts[341]. Regiospecific deuteriation is also achieved by using deuteriosilanes. Product distribution is mainly dependent upon the structure of the hydrosilane employed. In general, monohydridosilanes afford the 1,4-adduct (silyl enol ether), which may be hydrolyzed to the corresponding saturated carbonyl compound. Diaryl or dialkyl dihydridosilane produce mainly silyl ether (1,2-adduct), which may be hydrolyzed to the corresponding allylic alcohol.

Other factors controlling the regioselectivity of this method include the enone structure, the hydridosilane/substrate ratio, the solvent and temperature. Although regioselectivity here is generally satisfactory (Scheme 111)[341], in some cases mixtures of 1,2- and 1,4-reduction products are obtained, even under maximally optimized conditions. The reaction is usually complete within 30–120 minutes at 0–80 °C in benzene, or in the absence of solvent, using 1.1 equivalents of the hydridosilane and 0.1 mol% of the Rh(I) catalyst.

Treatment of α,β-unsaturated esters with triethylsilane in benzene in the presence of catalytic amounts of $RhCl(PPh_3)_3$ at room temperature yields the corresponding saturated esters. Conjugated diene esters are reduced to the β,γ- or γ,δ-unsaturated esters, depending upon their substitution pattern (Scheme 112)[342].

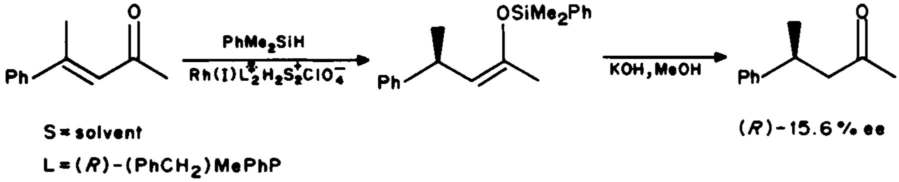


SCHEME 112

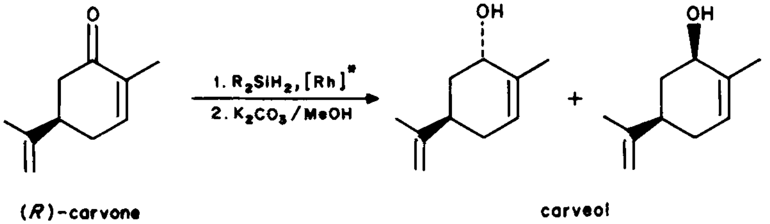
Other Rh catalysts were also employed for hydrosilation of α,β-unsaturated carbonyl compounds and unsaturated nitriles. $Rh(acac)_2$ and a tetrakis(μ-acetato)dirhodium cluster were used as catalysts in the hydrosilation[343] of α,β-unsaturated aldehydes. These reactions, however, are not chemoselective, as acetylenes, conjugated dienes and alkenes are also hydrosilylated, and allylic heterosubstituents are reductively cleaved under reaction conditions.

Optically active, saturated compounds and allylic alcohols were prepared via 1,4- and 1,2-asymmetric hydrosilation of enones using Rh(I) catalysts bearing chiral ligands. For example, 1,4-hydrosilation of α,β-unsaturated ketones afforded the corresponding optically active ketones in 1.4–15.6% enantiomeric excess (Scheme 113)[344]. These reactions were achieved at room temperature with dimethylphenylsilane and either (−)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane ((−)-diop)[344] or $[Rh\{(R)\text{-}(PhCH_2)MePhP\}_2H_2(solvent)_2]^+ClO_4^-$.

Asymmetric 1,2-hydrosilation in benzene of α,β-unsaturated ketones with dihydridosilanes and a chiral Rh(I) catalyst produced allylic alcohols with up to 69% enantiomeric excess. Thus, varying proportions of carveol isomers were obtained from carvone (Scheme 114)[345].



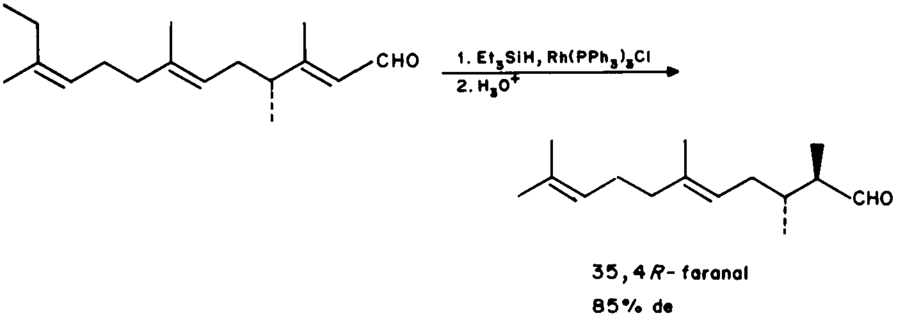
SCHEME 113



Et_2SiH_2/(−)DIOP−Rh(I)	15.5	:	84.5
α-Naph $PhSiH_2$/(+)DIOP−Rh(I)	78.7	:	21.3

SCHEME 114

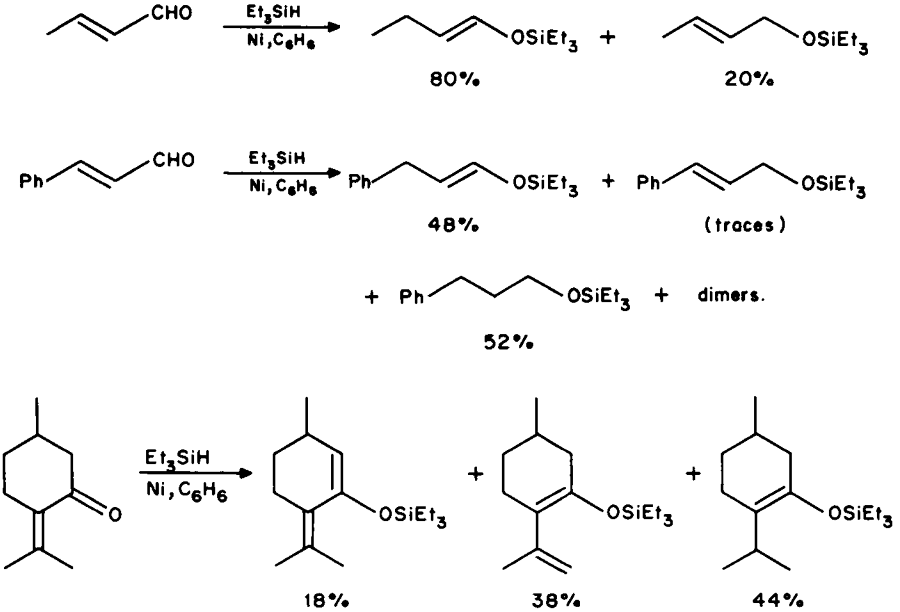
Highly stereoselective 1,2-hydrosilation of an α,β-unsaturated aldehyde was achieved with triethylsilane and nonchiral Wilkinson catalyst[346]. Dehydrofaranal was thus stereoselectivity reduced to the insect pheromone (3*S*,4*R*)-faranal with 85% diastereomeric excess (Scheme 115).



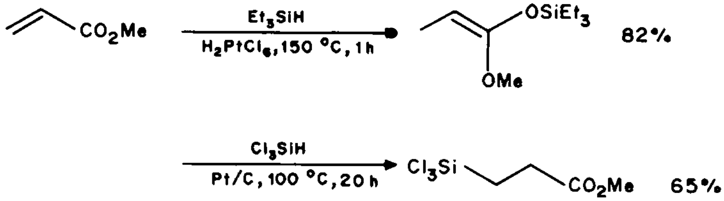
SCHEME 115

The main product in hydrosilation of α,β-unsaturated ketones and aldehydes catalyzed by chloroplatinic acid, platinum on alumina, or metallic nickel is the corresponding silyl enol ether[347]. With nickel catalyst, product distribution is highly dependent on the enone structure, as exemplified in Scheme 116[348].

Hydridosilanes add to α,β-unsaturated esters, producing the corresponding silyl enolate as well as carbon silylated products. The course of addition depends on substrate structure and the hydridosilane utilized. Thus, triethylsilane undergoes 1,4-addition to methyl acrylate in the presence of chloroplatinic acid, while trichlorosilane with either chloroplatinic acid or Pt/C gives the β-silyl ester (Scheme 117)[349].



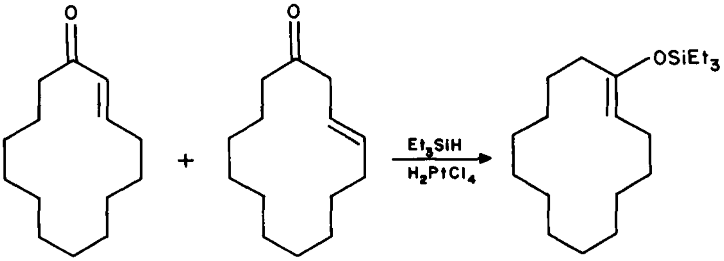
SCHEME 116



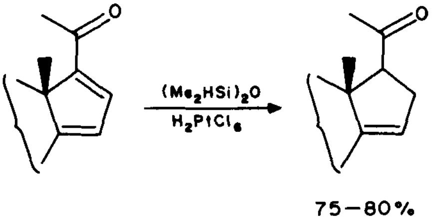
SCHEME 117

This approach was successfully applied to the total synthesis of *d,l*-muscone[350]. Treatment of the α,β- and β,γ-enone mixture (Scheme 118) with triethylsilane in refluxing glyme containing catalytic amounts of chloroplatinic acid afforded 1-triethylsilyloxycyclotetradecene. The two isomeric enones rapidly equilibrate under these conditions.

Selective reduction of pregna-14,16-dien-20-ones to pregn-14-en-20-ones is achieved via hydrosilation with tetramethyldisiloxane and catalytic amounts of chloroplatinic acid (Scheme 119)[351]. α,β-Unsaturated esters are also reduced to the corresponding saturated esters under these conditions[352].



SCHEME 118



SCHEME 119

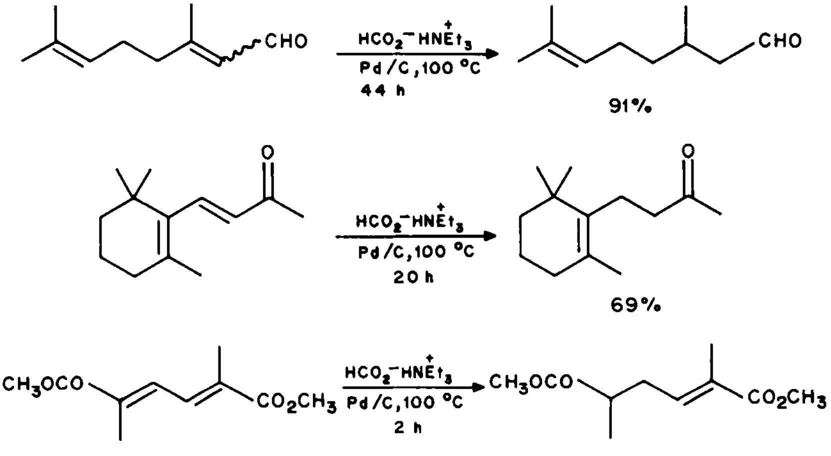
The platinum dimer $(Pt(\mu\text{-}H)(SiR_3)(PR'_3))_2$ also catalyzes the hydrosilation of α, β-unsaturated aldehydes and ketones. Several aldehydes and ketones were hydrosilated in high yield in the presence of this dimer[353] at 60–100 °C and trialkylsilanes, including $MePh_2SiH$, $EtMe_2SiH$ and Et_3SiH. Triethoxysilane, was inert under these reaction conditions. Excellent regioselectivity was generally observed except in cases of highly sterically hindered enones such as tetraphenylcyclopentadienone, where the 1, 2-reduction mode was observed. Saturated aldehydes and ketones were not reduced under these reaction conditions, and unsaturated carboxylic acids and esters were only sluggishly reduced. Unfortunately, terminal olefins and acetylenes were efficiently hydrosilated. A suggested mechanism involves cleavage of the platinum dimer to a platinum hydride species, its coordination to the olefin, and subsequent transfer of the R_3Si group to the carbonyl oxygen, affording a π-allyl platinum complex. Hydride migration from Pt to the allylic ligand produces the corresponding silyl enol ether.

C. Transition Metal-catalyzed Reductions with Other Hydrogen Donors

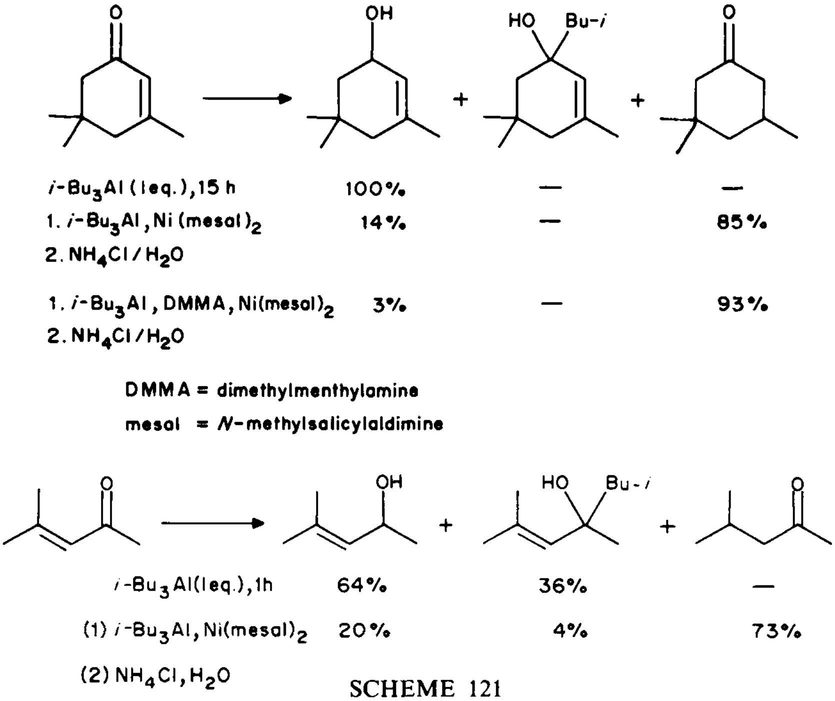
Aldehydes such as α-naphthaldehyde, *p*-tolualdehyde or *p*-chlorobenzaldehyde and DMF can serve as hydrogen donors and transfer their formyl hydrogen to α, β-unsaturated ketones in the presence of $RuCl_2(PPh_3)_3$. However, in some cases, decarbonylation of the aldehyde is so severe that no transfer hydrogenation is observed[354].

A particularly convenient hydrogen donor is formic acid, which not only hydrogenates α, β-unsaturated ketones[355], but also terminal olefins in the presence of a variety of ruthenium complexes under mild conditions[356].

Trialkylammonium formate and catalytic amounts of palladium on carbon form a convenient reducing system for reduction of a number of organic functional groups, including α, β-unsaturated aldehydes, ketones and esters[357]. Conjugated dienes are reduced to monoenes with one equivalent of reagent fairly selectively. Typical reductions are carried out at 100 °C with 10% excess formic acid, 30% excess triethyl- or tributylamine, and 1 mol% of palladium in the form of 10% Pd/C. Progress of the reduction is conveniently monitored by measuring the amount of CO_2 evolved. Some examples are given in Scheme 120[357]. The chemoselectivity of this system is somewhat limited, as it affects many other functionalities, such as halo- and nitroaromatic compounds[358], allylic heterosubstituents[359], and terminal acetylenes and olefins[357].



SCHEME 120



i-Bu_3Al (1eq.), 15 h	100%	—	—
1. *i*-Bu_3Al, Ni (mesal)$_2$ 2. NH_4Cl/H_2O	14%	—	85%
1. *i*-Bu_3Al, DMMA, Ni(mesal)$_2$ 2. NH_4Cl/H_2O	3%	—	93%

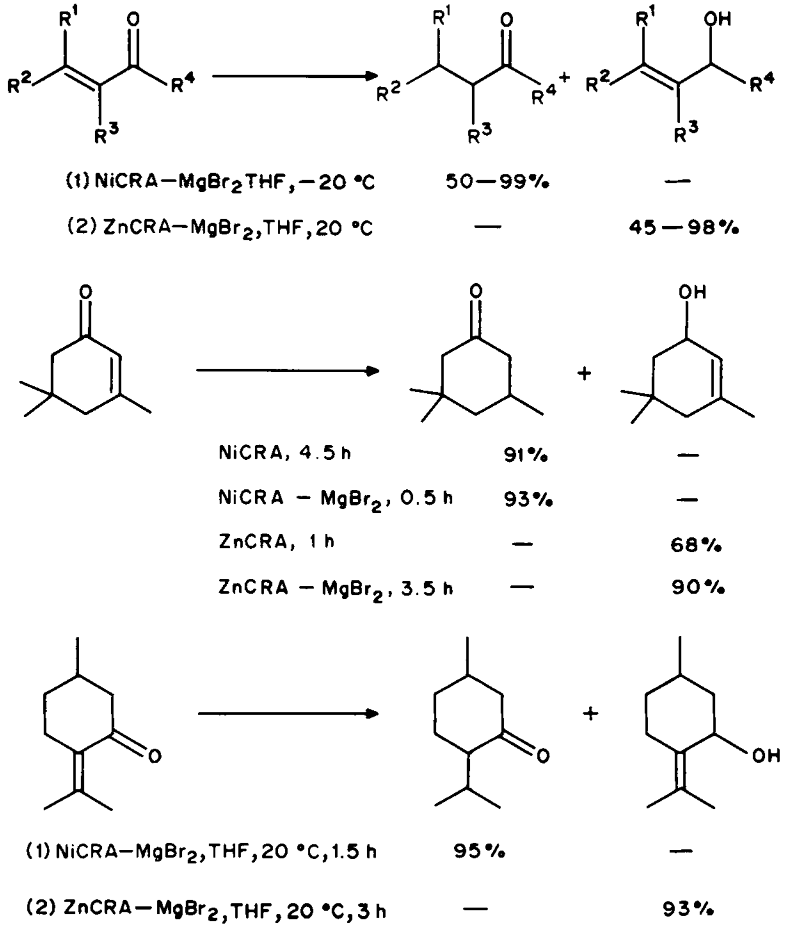
DMMA = dimethylmenthylamine
mesal = *N*-methylsalicylaldimine

i-Bu_3Al(1eq.), 1h	64%	36%	—
(1) *i*-Bu_3Al, Ni(mesal)$_2$ (2) NH_4Cl, H_2O	20%	4%	73%

SCHEME 121

The reaction between triisobutylaluminum and α, β-unsaturated ketones, in pentane at room temperature, leads to products which correspond to a 1, 2-addition processes. The extent of such reactions depends both on the structure of the enone and of the concentration ratio between reagent and substrate. Under these experimental conditions, bis(*N*-methylsalicylaldimine)nickel catalyzes conjugate reduction of α, β-unsaturated ketones by triisobutylaluminum[360]. The cyclic and acyclic saturated ketones are obtained in 40–90% yield, the lower figure corresponding to enones substituted at the α-position (Scheme 121). In all cases, 1, 2-reduction products were also obtained (probably via noncatalyzed reduction) and, in some cases, side-products containing an isobutyl group were also formed. The reaction is interpreted in terms of a catalytic cycle involving a hydridonickel intermediate formed by reaction of *i*-Bu_3Al with the nickel complex. Addition of the hydridonickel to the olefin affords a nickel enolate that undergoes transmetallation, to aluminum enolate. The latter is finally hydrolyzed to the saturated ketone.

A number of composite reducing systems comprised of heterogeneous mixtures of transition metal salts, sodium alkoxides and sodium hydride were developed, which are



SCHEME 122

useful for reduction of various organic functional groups[361]. In organic chemistry, sodium hydride is generally used as a base for proton abstraction. Although some substrates can be reduced by NaH, it is by itself a poor reducing agent.

Typical reducing systems (known as complex reducing agents, CRA)[361] are prepared from a transition-metal chloride or acetate, sodium *tert*-amyloxide and sodium hydride (in 1:1:4 ratio) in either THF or DME. Obviously, neither the exact structure of the actual reducing entity nor their reduction mechanism is fully understood.

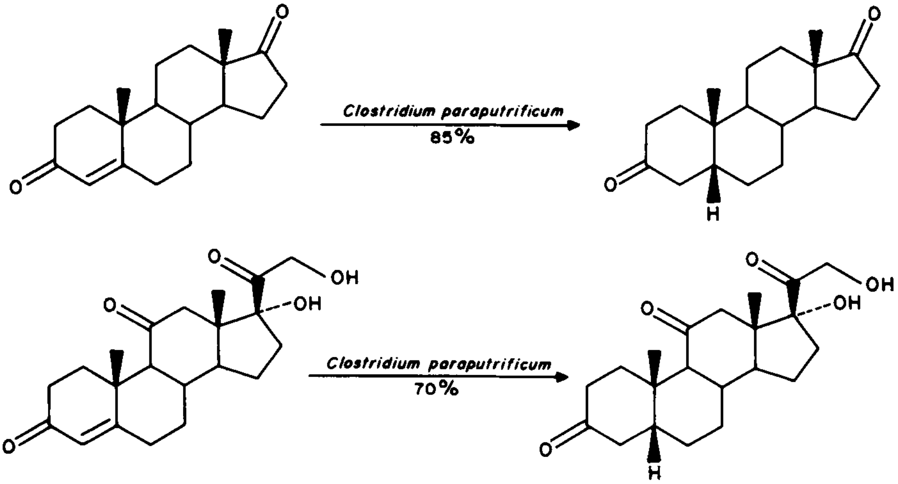
The CRA reagents involving nickel salts exhibit reducing properties that are significantly different from those of the corresponding CRA prepared from zinc or magnesium salts. It was demonstrated that the three-component mixture, NaH/RONa/Ni(OAc)$_2$ (NiCRA), reduces carbon–carbon double bonds[362]. Conversely, the mixture NaH/RONa/ZnCl$_2$ (ZnCRA) reduces olefins poorly but effectively reduces saturated carbonyl functionalities, particularly when mixed with alkaline- or alkaline earth-metal salts[363]. These observations led to the expected complementary regioselectivity when reducing α,β-unsaturated carbonyl compounds with these reagents.

Indeed, NiCRA exhibits very high regioselectivity for 1,4-reduction of a number of α,β-unsaturated ketones, while under the same conditions ZnCRA is an effective reagent mixture for highly regioselective 1,2-reduction of these substrates (Scheme 122)[364]. Addition of magnesium bromide enhances the activity of both reagent mixtures. It is important to remember that the general applicability of CRA reagents is limited, due to their high basicity as well as their tendency to undergo side-reactions via one electron-transfer processes. The heterogeneity of these reagents limits reproducible reduction yields.

VII. BIOCHEMICAL REDUCTIONS

A. Enzymatic Reductions

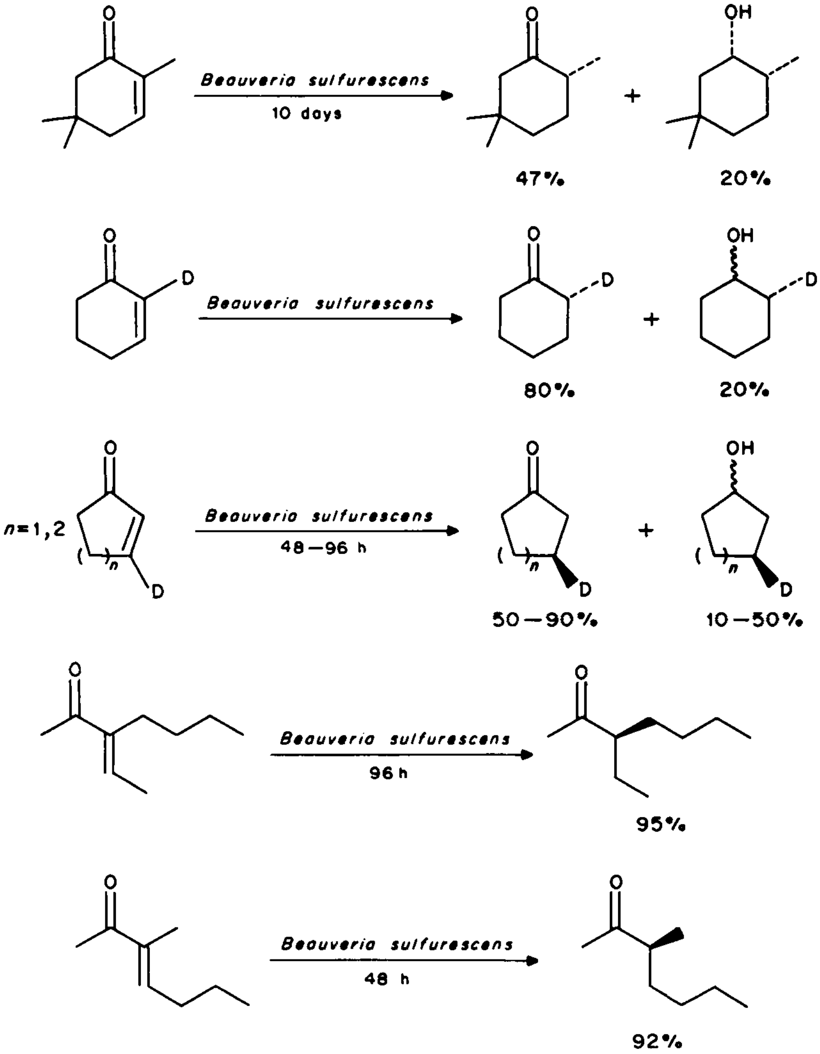
Much work has been published on the microbiological reduction of α,β-unsaturated ketones. Under anaerobic conditions the reduction of Δ^4-3-keto steroids by *Clostridium paraputrificum* led to the 3-keto-5β derivatives[365] (Scheme 123). Similar transformations



SCHEME 123

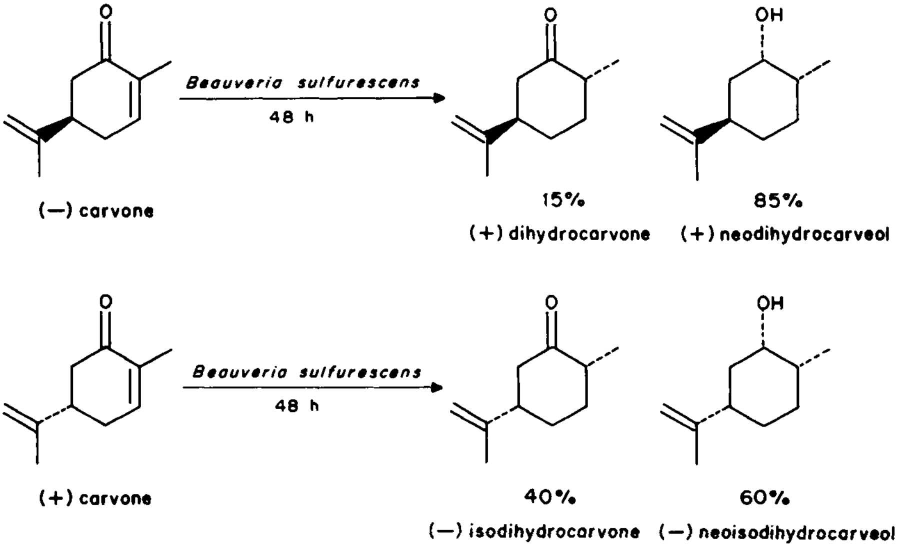
were observed previously with *Bacillus putrificus*[366], *Penicillium decumbens*[367], *Rhizopus nigricans*[368] or *Aspergillus niger*[369]. In most cases further reduction led to the corresponding 3α-hydroxy-5β derivatives.

Highly enantioselective conjugate reductions of substituted cyclopentenones and cyclohexenones were reported by Kergomard using *Beauveria sulfurescens* (ATCC 7159) under anaerobic conditions[370]. The reaction takes place only with substrates containing a small substituent in the α-position and hydrogen in the β-position. The saturated ketones obtained were, in some cases, accompanied by saturated alcohols. A number of useful transformations, including enantioselective reductions of acyclic substrates, are illustrated in Scheme 124.



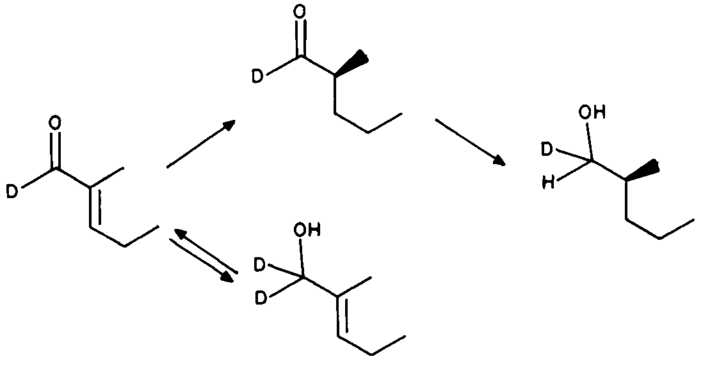
SCHEME 124

Both naturally occurring enantiomers of carvone were selectively reduced by *B. sulfurescens* (Scheme 125). (−)-Carvone was reduced to (+)-dihydrocarvone (*trans*) and further to (−)-neodihydrocarveol, whereas (+)-carvone was reduced to (−)-isodihydrocarvone (*cis*), which was then converted to (−)-neoisodihydrocarveol[371]. Similar reductions with identical stereoselectivities were observed earlier with *Pseudomonas ovalis* (strain 6–1) and with a strain of *Aspergillus niger*[371].



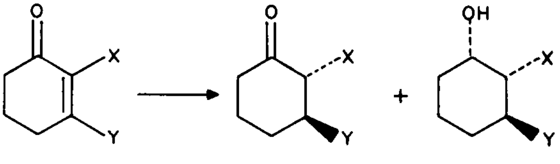
SCHEME 125

The reduction of α,β-unsaturated aldehydes by *Beauveria sulfurescens* proceeds along two mechanistic pathways: (a) reversible formation of the corresponding allylic alcohols and (b) irreversible formation of the saturated alcohol (Scheme 126)[372]. The latter involves initial, slow 1,4-reduction, followed by fast reduction of the resultant saturated aldehyde. A similar sequence was proposed for the reduction of geranial and geraniol to (*R*)-citronellol with *Saccharomyces cerevisiae*.



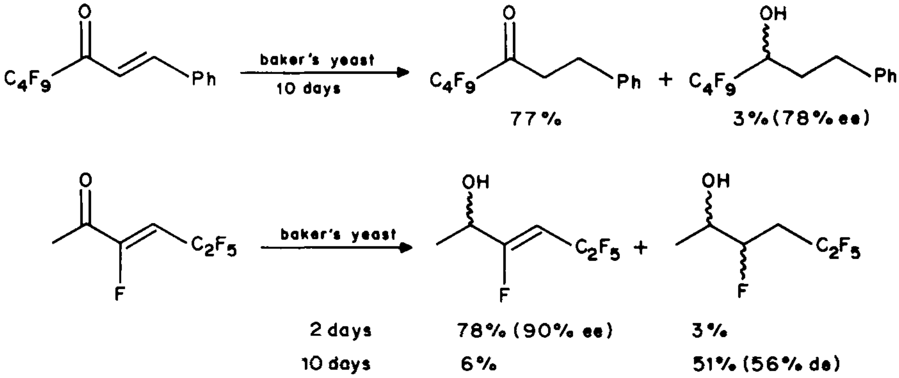
SCHEME 126

The above-described reducing characteristics of *B. sulfurescens* were found to be a general phenomenon exhibited by many types of eukaryotic organisms (six fungi) and prokaryotes (more than 20 Actinomycetes and Clostridium species)[373]. For example, in conjugate reduction of cyclohexenone derivatives the addition of two hydrogen atoms across the olefin occurs with *trans* stereochemistry, as shown in Scheme 127 where X represents a small alkyl group and Y a hydrogen atom. In all cases, the 1,4-reduction mode was completed within 48 hours. As these characteristics are shared by many organisms, it was suggested that they all contain very similar reducing enzymes[373].



SCHEME 127

α,β-Unsaturated ketones bearing perfluoroalkyl groups are reduced by baker's yeast (Scheme 128)[374]. Perfluoroalkyl alkenyl ketones give mainly the saturated ketone, along with a small amount of optically active saturated alcohol. Substrates having a perfluoroalkyl group attached to the alkene moiety give mixtures of optically active allylic as well as saturated alcohols, whose relative concentration is time-dependent.

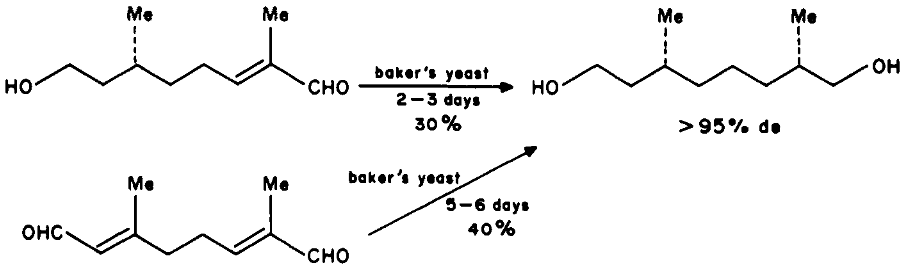


SCHEME 128

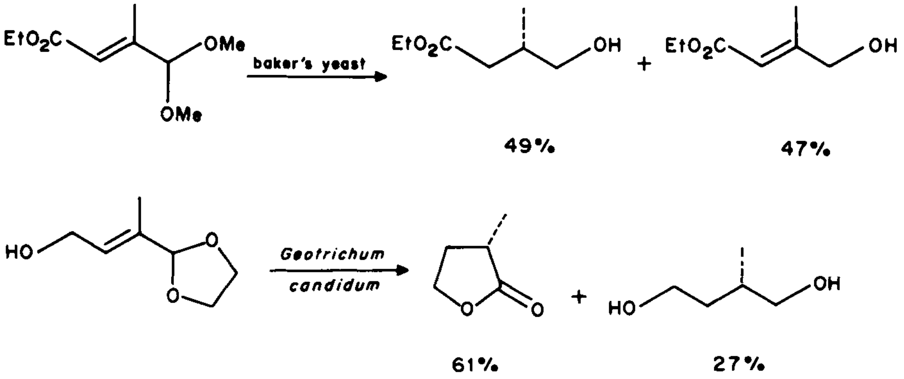
Unsaturated aldehydes derived from citronellol and geraniol are also reduced by baker's yeast to the corresponding saturated primary alcohols with very high enantioselectivity (Scheme 129)[375].

Two key chiral building blocks used in the total synthesis of α-tocopherol were prepared via microbial reduction of unsaturated carbonyl compounds with baker's yeast and with *Geotrichum candidum*, as illustrated in Scheme 130[376].

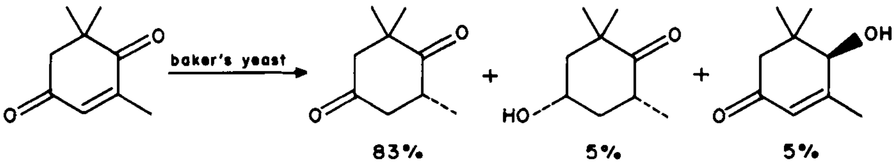
Similarly, a key intermediate in the total synthesis of optically active natural carotenoids was prepared by microbial reduction of oxo-isophorone with baker's yeast (Scheme 131)[377].



SCHEME 129

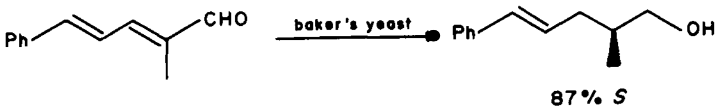


SCHEME 130



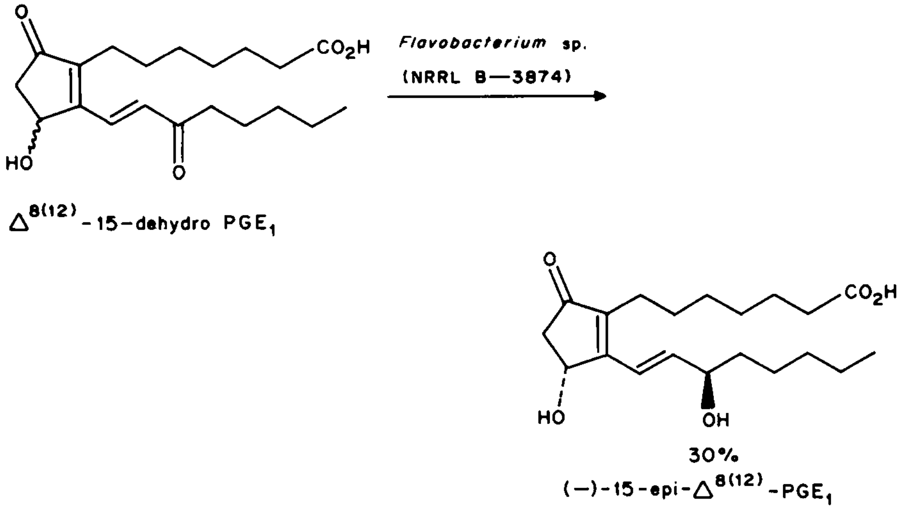
SCHEME 131

An alternative approach to the synthesis of α-tocopherol employs a chiral building block that was obtained by baker's yeast reduction of 2-methyl-5-phenylpentadienal (Scheme 132)[378].



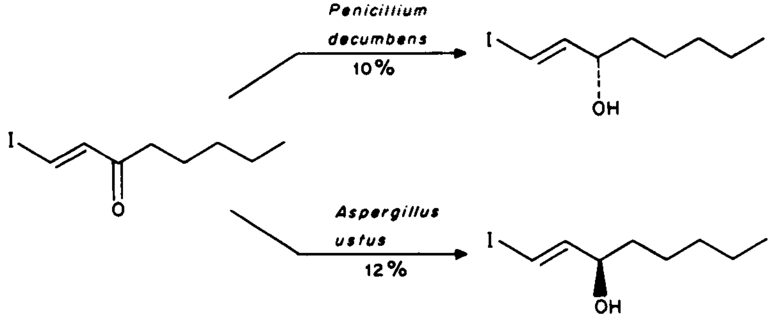
SCHEME 132

Microbial reduction of enones has been applied to prostaglandin synthesis. For example, enantioselective reduction of the enone system in $\Delta^{8(12)}$-15-dehydro-PGE$_1$ with *Flavobacterium* sp. (NRRL B-3874) provided optically pure (−)-15-*epi*-$\Delta^{8(12)}$-PGE$_1$ (Scheme 133)[379].



SCHEME 133

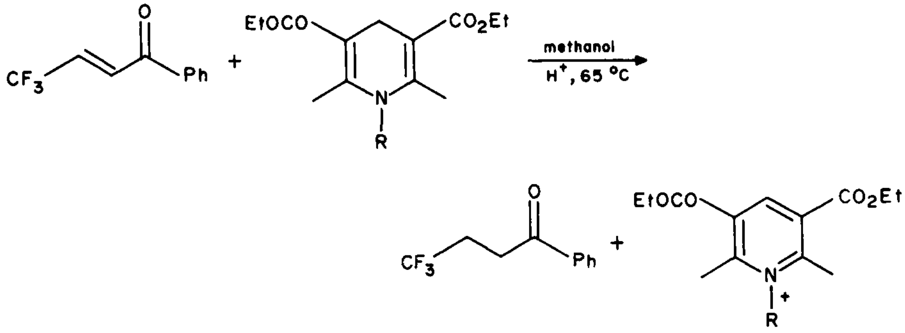
As a general rule of enzymatic reductions, the 1,4-reduction of enones is preferred over the 1,2-reduction mode. However, when an electronegative substituent, such as halogen, is introduced that stabilizes the double bond, enzymatic reduction to allylic alcohols may be achieved[276]. A 1,2-reduction of a β-iodo enone is illustrated in Scheme 134.



SCHEME 134

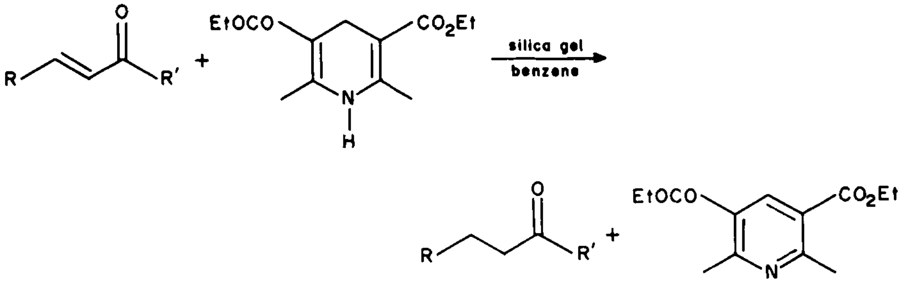
B. Biomimetic Reductions with NAD(P)H Models

A number of pyridine nucleotide-linked dehydrogenases catalyze the reversible hydrogenation–dehydrogenation of the double bond in α,β-unsaturated ketones[380]. Similar biomimetic conjugate reduction of α,β-unsaturated aldehydes and ketones occurs with NAD(P)H models, such as 3,5-dicarboethoxy-2,6-dimethyl-1,4-dihydropyridine (Hantzsch ester). With highly electron-deficient olefins, such as maleic acid, maleic anhydride, diethyl maleate, diethyl fumarate, etc., reductions proceed well[381]. Similarly, the olefinic bond of 1-phenyl-4,4,4-trifluoro-2-buten-1-one is reduced by dihydropyridines under mild condition (Scheme 135)[382]. Tracer experiments showed that hydrogen is transferred directly from the 4-position of the pyridine ring to the β-position of the enone system. The reaction thus parallels the enzymatic reduction of androstenedione[383].



SCHEME 135

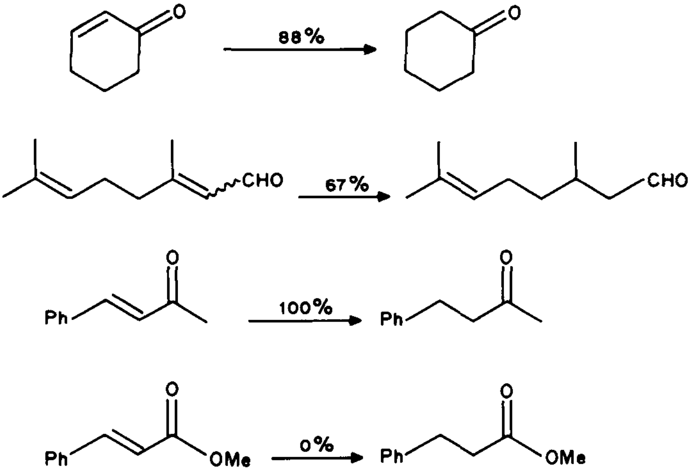
However, these reaction condition (refluxing methanol or photoactivation at room temperature) are useful only for the reduction of highly activated double bonds[384]. Nevertheless, it was found that the reaction is promoted by silica gel[385], broadening the scope of reducible enone substrates (Scheme 136).



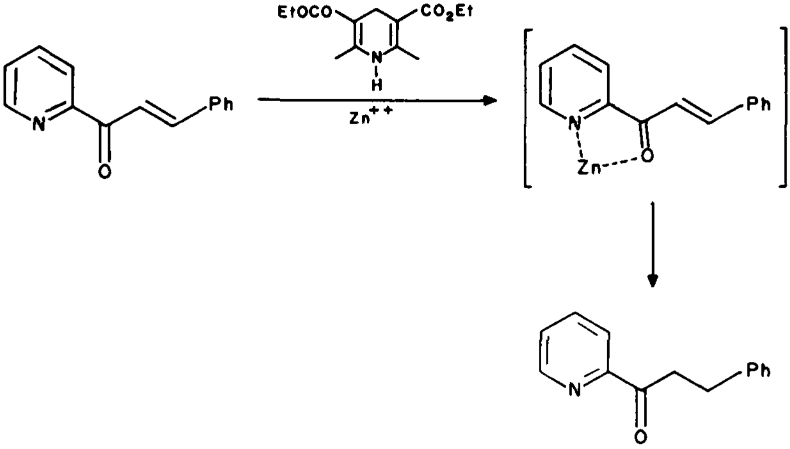
SCHEME 136

The method is highly chemoselective as no alcoholic products are observed, and carbonyl, nitro, cyano, sulfinyl and sulfonyl groups remain intact under the reaction conditions (Scheme 137).

Pandit has provided evidence for the Lewis-acid catalysis postulated to operate in these reductions[386]. The reduction of various cinnamoylpyridines by 1,4-dihydropyridine derivatives to the corresponding saturated ketones is catalyzed by zinc or magnesium cations. The reduction rate was fastest in the case of 2-cinnamoylpyridine, in which the metal ion can complex simultaneously to both the nitrogen and oxygen sites (Scheme 138). This example is regarded as a model of Lewis-acid catalysis of the NADH-dependent enzymatic reduction of δ^4-3-ketosteroids.



SCHEME 137

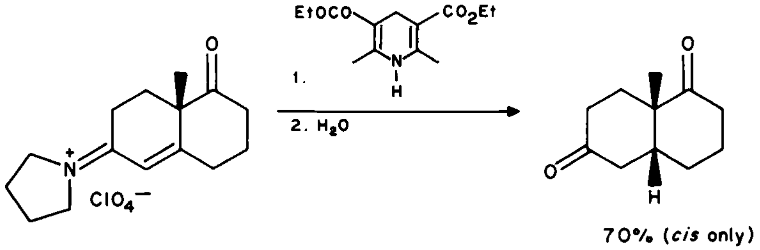


SCHEME 138

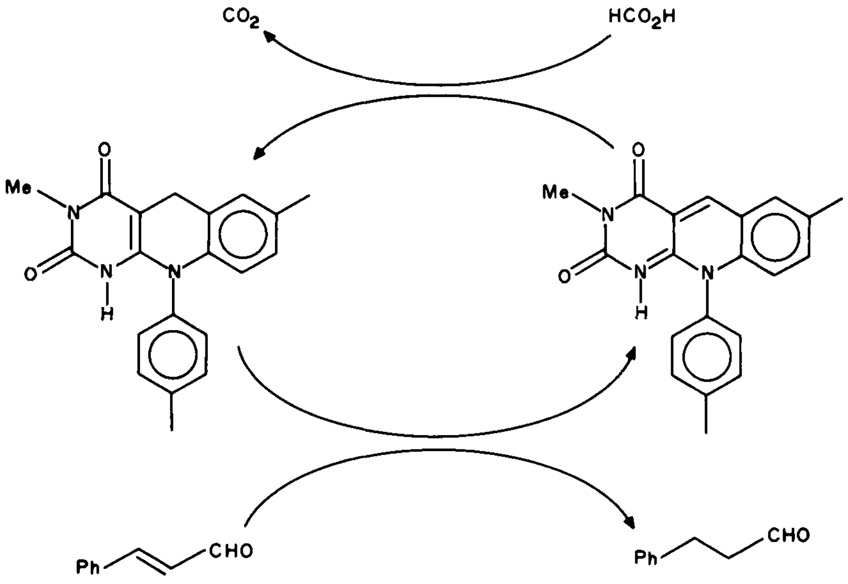
In a similar manner, iminium salts derived from α, β-unsaturated aldehydes and ketones are reduced by Hantzsch ester (Scheme 139)[387]. The ratio between the 1,4- and 1,2-reduction products depends upon the pK_a of the amine component.

An autorecycling system for the specific 1,4-reduction of α, β-unsaturated ketones and aldehydes was based on 1,5-dihydro-5-deazaflavin, which can be regarded as an NADH model[388]. The reaction occurs on heating the substrate with catalytic amounts of 5-deazaflavin in 98% formic acid, typically at 120 °C for 24 h (Scheme 140).

The iminium salts of 3,3,5-trimethylcyclohex-2-en-1-one were reduced with 1,4-dihydronicotinamide sugar pyranosides to give the corresponding optically active



SCHEME 139



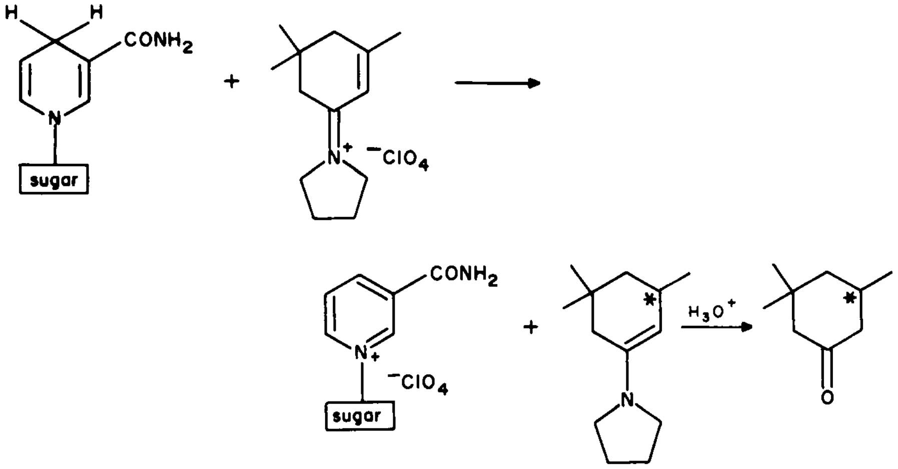
SCHEME 140

saturated ketone in enantiomeric excess ranging over 3–31%. The product stereochemistry changed sensitively with structural variations in the sugar residues (Scheme 141)[389].

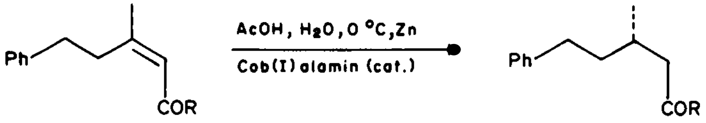
The cob(I)alamin catalyzed reduction of α-methyl-α,β-unsaturated carbonyl compounds produces the corresponding saturated derivatives having an *S* configuration at the α-carbon (Scheme 142)[390]. The highest enantiomeric excess (33%) is exhibited by the *Z*-configurated methyl ketone. The *E*-configurated enone is reduced by this system to the corresponding *R*-product with poor enantiomeric excess.

VIII. MISCELLANEOUS REDUCING AGENTS

Several techniques utilizing miscellaneous reagents, that were not mentioned in the preceding sections, have been reported to effect the 1,4-reduction of α,β-unsaturated aldehydes and ketones.



SCHEME 141



R=OEt, OH, NH_2, NMe_2, CH_3

SCHEME 142

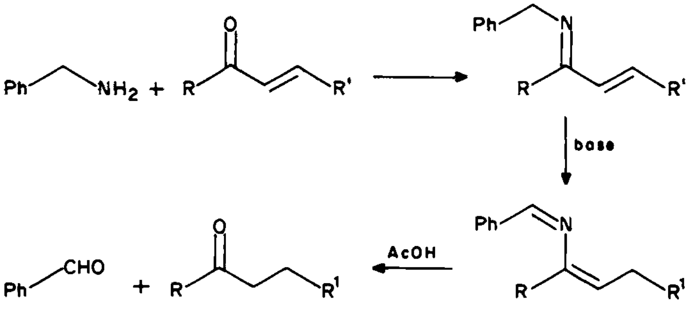
Sodium dithionite under nitrogen atmosphere at 80 °C in a water–benzene mixture and in the presence of a phase-transfer catalyst was shown to be a useful reducing agent. Dienoic carboxylic acids and esters were reduced in a 1,6-mode using this approach[391].

2-Phenylbenzothiazoline reduced α,β-unsaturated carbonyl compounds in a 1,4-fashion in the presence of stoichiometric amounts of aluminum chloride[392]. No 1,2-reduction products or saturated alcohols were detected. The reagent reduces unsaturated esters and aldehydes much less effectively.

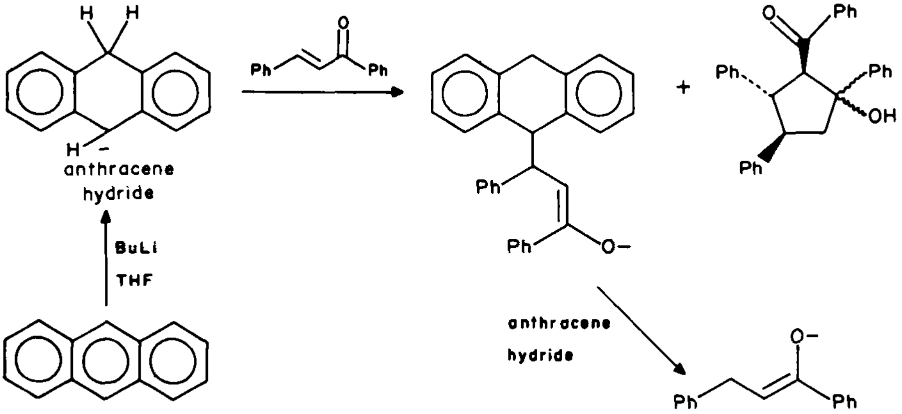
Condensation of an α,β-unsaturated ketone with benzylamine gives the corresponding Schiff base. Treatment with a base, such as potassium *t*-butoxide, affects rearrangement to a benzaldehyde derivative, as shown in Scheme 143[393]. Hydrolysis of the latter with dilute acetic acid furnishes the corresponding saturated ketone with concomitant formation of benzaldehyde.

A reagent prepared from tellurium powder and sodium borohydride in ethanol engenders 1,4-reduction of α,β-unsaturated aldehydes, ketones and esters in high yield and with good regio- and chemoselectivity (no 1,2-reduction and no reduction of isolated double bonds)[394].

Anthracene hydride (the anion derived from 9,10-dihydroanthracene) reacts rapidly with chalcone to form an anionic Michael adduct along with a chalcone dimerization product (Scheme 144)[395]. Prolonged reaction in the presence of anthracene hydride cleaves the Michael adduct into anthracene and the enolate of the saturated ketone. The partial structure RCCCO is essential for this fragmentation, as mesityl oxide, for example, gave only the Michael adduct.



SCHEME 143



SCHEME 144

Photolysis of 4a-methyl-4,4a,9,10-tetrahydro-2-(3*H*)-phenanthrone in isopropanol gave rearranged and 1,4-reduction products, along with traces of 1,2-reduction and small amounts of coupling products[396].

2-Propanol doped on dehydrated alumina reduces at room temperature various aldehydes and ketones to the corresponding alcohols[397]. α,β-Unsaturated aldehydes are selectively reduced under these conditions to the corresponding allylic alcohols. For example, citral is converted to geraniol in 88% yield.

α,β-Unsaturated nitriles are reduced to saturated nitriles with triethylamineformic acid azeotrope in DMF[398].

α,β-Unsaturated ketones are reduced to allylic alcohols with β-branched trialkylaluminum compounds, such as $(i\text{-Bu})_3Al$ and tris-((*S*)-2-methylbutyl)aluminum. The latter reagent reduces prochiral enones to optically active allylic alcohols with 7–15% enantiomeric excess[399].

IX. REFERENCES

1. H. C. Brown and S. Krishnamurthy, *Tetrahedron*, **35**, 567 (1979).
2. (a) A. J. Birch and H. Smith, *Quart. Rev.*, **12**, 17 (1958).
   (b) A. J. Birch and G. Subba-Rao, in *Advances in Organic Chemistry* (Ed. E. C. Taylor), Vol. 8, Wiley, New York, 1972, p. 1.
3. C. Djerassi, *Steroid Reactions*, Holden-Day, Inc., San Francisco, 1963, pp. 299–325.
4. H. L. Dryden, Jr., in *Organic Reactions in Steroid Chemistry* (Eds. J. Fried and J. A. Edwards), Vol. I, Van Nostrand Reinhold Co., New York, 1972, p. 1.
5. H. O. House, *Modern Synthetic Reactions*, 2nd ed., Benjamin, Menlo Park, California, 1972.
6. F. Johnson, *Chem. Rev.*, **68**, 375 (1968).
7. F. J. McQuillin, in *Techniques of Organic Chemistry* (Ed. A. Weissberger), Vol. XI, Part I, Interscience, New York, 1963, Chap. 9.
8. H. Smith, *Organic Reactions in Liquid Ammonia*, Wiley, New York, 1963.
9. M. Smith, in *Reduction* (Ed. R. L. Augustine), Marcel Dekker, New York, 1968, Chap. 2.
10. D. Caine, *Org. React.*, **23**, 1 (1976).
11. (a) M. C. R. Symons. *Quart. Rev.*, **13**, 99 (1959).
    (b) U. Schindewolf, *Angew. Chem., Int. Ed. Engl.*, **7**, 190 (1968).
    (c) J. L. Dye, *Acc. Chem. Res.*, **1**, 306 (1968).
12. (a) H. Normant, *Angew, Chem., Int. Ed. Engl.*, **6**, 1046 (1967).
    (b) H. Normant, *Bull. Soc. Chim. Fr.*, 791 (1968).
    (c) K. W. Bowers, R. W. Giese, J. Grimshaw, H. O. House, N. H. Kolodny, K. Kronberger and D. K. Roe, *J. Am. Chem. Soc.*, **92**, 2783 (1970).
    (d) M. Larcheveque, *Ann. Chim. (Paris)*, **5**, 129 (1970).
13. (a) J. L. Down, J. Lewis, B. Moore and G. Wilkinson, *J. Chem. Soc.*, 3767 (1959).
    (b) C. Agami, *Bull. Soc. Chim. Fr.*, 1205 (1968).
    (c) J. L. Dye, M. G. DeBacker and V. A. Nicely, *J. Am. Chem. Soc.*, **92**, 5226 (1970).
    (d) C. D. Pedersen, *J. Am. Chem. Soc.*, **89**, 7017 (1967); **92**, 386, 391 (1970).
14. D. H. R. Barton and C. H. Robinson, *J. Chem. Soc.*, 3054 (1954).
15. G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **82**, 1512 (1960); **86**, 1761 (1964).
16. M. J. T. Robinson, *Tetrahedron*, **21**, 2475 (1965).
17. (a) R. Howe and F. J. McQuillin, *J. Chem. Soc.*, 2670 (1956).
    (b) G. L. Chetty, G. S. Krishna Rao, S. Dev and D. K. Banerjee, *Tetrahedron*, **22**, 2311 (1966).
18. F. J. McQuillin, *J. Chem. Soc.*, 528 (1955).
19. A. J. Birch, H. Smith and R. E. Thornton, *J. Chem. Soc.*, 1339 (1957).
20. H. E. Zimmerman, *J. Am. Chem. Soc.*, **78**, 1168 (1956).
21. O. Wallach, *Ann. Chem.*, **279**, 377 (1894).
22. O. Wallach, *Ann. Chem.*, **275**, 111 (1893).
23. O. Diels and E. Abderhalden, *Chem. Ber.*, **39**, 884 (1906).
24. L. H. Knox, E. Blossy, H. Carpio, L. Cervantes, P. Crabbe, E. Velarde and J. A. Edwards, *J. Org. Chem.*, **30**, 2198 (1965).
25. J. A. Barltrop and A. C. Day, *Tetrahedron*, **22**, 3181 (1966).
26. T. A. Spencer, R. A. J. Smith, D. L. Storm and R. M. Villarica, *J. Am. Chem. Soc.*, **93**, 4856 (1971).
27. L. E. Hightower, L. R. Glasgow, K. M. Stone, D. A. Albertson and H. A. Smith, *J. Org. Chem.*, **35**, 1881 (1970).
28. H. A. Smith, B. J. L. Huff, W. J. Powers and D. Caine, *J. Org. Chem.*, **32**, 2851 (1967).
29. J. F. Eastham and D. R. Larkin, *J. Am. Chem. Soc.*, **81**, 3652 (1959).
30. H. O. House, *Rec. Chem. Prog.*, **28**, 98 (1967).
31. W. L. Jolly and L. Prizant, *Chem. Commun.*, 1345 (1968).
32. A. P. Krapcho and A. A. Bothner-By, *J. Am. Chem. Soc.*, **81**, 3658 (1959).
33. D. C. Burke, J. H. Turnbull and W. Wilson, *J. Chem. Soc.*, 3237 (1953).
34. I. N. Nazarov and I. A. Gurvich, *J. Gen. Chem. USSR*, **25**, 921 (1955).
35. A. J. Birch, E. Pride and H. Smith, *J. Chem. Soc.*, 4688 (1958).
36. G. Buchi, S. J. Gould and F. Naf, *J. Am. Chem. Soc.*, **93**, 2492 (1971).
37. M. E. Kuehne, *J. Am. Chem. Soc.*, **83**, 1492 (1961).
38. G. Stork, P. Rosen and N. L. Goldman, *J. Am. Chem. Soc.*, **83**, 2965 (1961).
39. G. Stork, P. Rosen, N. L. Goldman, R. V. Coombs and J. Tsuji, *J. Am. Chem. Soc.*, **87**, 275 (1965).

40. M. J. Weiss, R. E. Schaub, G. R. Allen, Jr., J. F. Poletta, C. Pidacks, R. B. Conrow and C. J. Coscia, *Tetrahedron*, **20**, 367 (1964); *Chem. Ind.* (*London*), 118 (1963).
41. A. Coulombeau, *Bull. Soc. Chim. Fr.*, 4407 (1970).
42. R. Deghenghi, C. Revesz and R. Gaudry, *J. Med. Chem.*, **6**, 301 (1963).
43. R. M. Coates and R. L. Sowerby, *J. Am. Chem. Soc.*, **93**, 1027 (1971).
44. (a) R. Deghenghi and R. Gaudry, *Tetrahedron Lett.*, 489 (1962).
    (b) R. E. Schaub and M. J. Weiss, *Chem. Ind.* (*London*), 2003 (1961).
45. G. Stork and J. E. McMurry, *J. Am. Chem. Soc.*, **89**, 5464 (1967).
46. G. Stork, S. Uyeo, T. Wakamatsu, P. Grieco and J. Labovitz, *J. Am. Chem. Soc.*, **93**, 4945 (1971).
47. T. A. Spencer, T. D. Weaver, R. M. Villarica, R. J. Friary, J. Posler and M. A. Schwartz, *J. Org. Chem.*, **33**, 712 (1968).
48. K. W. Bowers, R. W. Giese, J. Grimshaw, H. O. House, N. H. Kolodny, K. Kronberger and D. K. Roe, *J. Am. Chem. Soc.*, **92**, 2783 (1970).
49. C. L. Perrin, *Prog. Phys. Org. Chem.*, **3**, 165 (1965).
50. M. M. Baizer and J. P. Petrovich, *Adv. Phys. Org. Chem.*, **7**, 189 (1970).
51. D. Miller, L. Mandell and R. A. Day, Jr., *J. Org. Chem.*, **36**, 1683 (1971).
52. J. Weimann, S. Risse and P. -F. Casals, *Bull. Soc. Chim. Fr.*, 381 (1966).
53. B. J. L. Huff, Ph.D. Dissertation, Georgia Institute of Technology, 1969, *Diss. Abstr. B*, **29** (12), 4589 (1969).
54. G. Stork, M. Nussim and B. August, *Tetrahedron, Suppl.*, **8**, 105 (1966).
55. P. Angibeaund, H. Riviere and B. Tchoubar, *Bull. Soc. Chim. Fr.*, 2937 (1968).
56. T. A. Spencer, R. J. Friary, W. W. Schmiegel, J. F. Simeone and D. S. Watt, *J. Org. Chem.*, **33**, 719 (1968).
57. R. E. Ireland and G. Pfister, *Tetrahedron Lett.*, 2145 (1969).
58. G. Stork and J. Tsuji, *J. Am. Chem. Soc.*, **83**, 2783 (1961).
59. P. S. Venkataramani, J. E. Karoglan and W. Reusch, *J. Am. Chem. Soc.*, **93**, 269 (1971).
60. T. A. Spencer, K. K. Schmiegel and W. W. Schmiegel, *J. Org. Chem.*, **30**, 1626 (1965).
61. R. G. Carlson and R. G. Blecke, *J. Chem. Soc., Chem. Commun.*, 93 (1969).
62. M. Tanabe, J. W. Chamberlin and P. Y. Nishiura, *Tetrahedron Lett.*, 601 (1961).
63. B. M. Trost, Abstracts of Papers, Joint Conference CIC–ACS, Toronto, Canada, May 24–29, 1970, Organic Section, Paper No. 42.
64. C. Amendolla, G. Rosenkranz and F. Sondheimer, *J. Chem. Soc.*, 1226 (1954).
65. T. Anthonsen, P. H. McCabe, R. McGrindle and R. D. H. Murray, *Tetrahedron*, **25**, 2233 (1969).
66. T. Masamune, A. Murai, K. Orito, H. Ono, S. Numata and H. Suginome, *Tetrahedron*, **25**, 4853 (1969).
67. H. Bruderer, D. Arigoni and O. Jeger, *Helv. Chim. Acta*, **39**, 858 (1956).
68. R. Howe, F. J. McQuillin and R. W. Temple, *J. Chem. Soc.*, 363 (1959).
69. K. S. Kulkarni and A. S. Rao, *Tetrahedron*, **21**, 1167 (1965).
70. K. Irmscher, W. Beerstecher, H. Metz, R. Watzel and K. -H. Bork, *Chem. Ber.*, **97**, 3363 (1964).
71. A. Spassky-Pasteur, *Bull. Soc. Chim. Fr.*, 2900 (1969).
72. R. M. Coates and J. E. Shaw, *Tetrahedron Lett.*, 5405 (1968); *J. Org. Chem.*, **35**, 2597 (1970).
73. R. M. Coates and J. E. Shaw, *J. Org. Chem.*, **35**, 2601 (1970).
74. R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1615 (1962).
75. M. Vandewalle and F. Compernolle, *Bull. Soc., Chim. Belg.*, **75**, 349 (1966).
76. M. Vandewalle and F. Compernolle, *Bull. Soc. Chim. Belg.*, **76**, 43 (1967).
77. D. S. Watt, J. M. McKenna and T. A. Spencer, *J. Org. Chem.*, **32**, 2674 (1967).
78. J. E. Shaw and K. K. Knutson, *J. Org. Chem.*, **36**, 1151 (1971).
79. J. A. Campbell and J. C. Babcock, *J. Am. Chem. Soc.*, **81**, 4069 (1959).
80. A. F. Daglish, J. Green and V. D. Poole, *J. Chem. Soc.*, 2627 (1954).
81. F. Johnson, G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 1302 (1954).
82. J. A. Marshall and H. Roebke, *J. Org. Chem.*, **33**, 840 (1968).
83. M. Nussim, Y. Mazur and F. Sondheimer, *J. Org. Chem.*, **29**, 1120 (1964).
84. H. Van Kamp, P. Westerhof and H. Niewind, *Rec. Trav. Chim. Pays-Bas*, **83**, 509 (1964).
85. E. Wenkert, A. Afonso, J. B. Bredenberg, C. Kaneko and A. Tahara, *J. Am. Chem. Soc.*, **86**, 2038 (1964).
86. P. Westerhof and E. H. Reerink, *Rec. Trav. Chim. Pays-Bas*, **79**, 771 (1960).
87. K. P. Dastur, *Tetrahedron Lett.*, 4333 (1973).
88. A. Zurcher, H. Heusser, O. Jeger and P. Geistlich, *Helv. Chim. Acta*, **37**, 1562 (1954).

89. G. Bach. J. Capitaine and Ch. R. Engel, *Can. J. Chem.*, **46**, 733 (1968).
90. H. Heusser, M. Roth, O. Rohr and R. Anliker, *Helv. Chim. Acta*, **38**, 1178 (1955).
91. W. F. Johns, *J. Org. Chem.*, **36**, 711 (1971).
92. E. Shapiro, T. Legatt, L. Weber, M. Steinberg and E. P. Oliveto, *Chem. Ind. (London)*, 300 (1962).
93. W. Cocker, B. Donnelly, H. Gobinsingh, T. B. H. McMurry and N. A. Nisbet, *J. Chem. Soc.*, 1262 (1963).
94. B. R. Ortiz de Montellano, B. A. Loving, T. C. Shields and P. D. Gardner, *J. Am. Chem. Soc.*, **89**, 3365 (1967).
95. D. J. Marshall and R. Deghenghi, *Can. J. Chem.*, **47**, 3127 (1969).
96. T. G. Halsall, D. W. Theobald and K. B. Walshaw, *J. Chem. Soc.*, 1029 (1964).
97. A. J. Birch, *Quart. Rev.*, **4**, 69 (1950).
98. R. G. Harvey, *Synthesis*, 161 (1970).
99. W. Nagata, T. Terasawa, S. Hirai and K. Takeda, *Tetrahedron Lett.*, 27 (1960); *Chem. Pharm. Bull. (Tokyo)*, **9**, 769 (1961).
100. W. S. Johnson, E. R. Rogier, J. Szmuszkovicz, H. I. Hadler, J. Ackerman, B. K. Bhattacharyya, B. M. Bloom, L. Stalmann, R. A. Clement, B. Bannister and H. Wynberg, *J. Am. Chem. Soc.*, **78**, 6289 (1956).
101. W. F. Johns, *J. Org. Chem.*, **28**, 1856 (1963).
102. W. S. Johnson, J. M. Cox, D. W. Graham and H. W. Whitlock, Jr., *J. Am. Chem. Soc.*, **89**, 4524 (1967).
103. M. V. R. Koteswara Rao, G. S. Krishna Rao and S. Dev., *Tetrahedron*, **22**, 1977 (1966).
104. F. B. Colton, L. N. Nysted, B. Riegel and A. L. Raymond, *J. Am. Chem. Soc.*, **79**, 1123 (1957).
105. A. Bowers, H. J. Ringold and E. Denot, *J. Am. Chem. Soc.*, **80**, 6115 (1958).
106. I. A. Gurvich, V. F. Kucherov and T. V. Ilyakhina, *J. Gen. Chem. USSR*, **31**, 738 (1961).
107. P. S. Venkataramani, J. P. John, V. T. Ramakrishnan and S. Swaminathan, *Tetrahedron*, **22**, 2021 (1966).
108. P. T. Lansbury, P. C. Briggs, T. R. Demmin and G. E. DuBois, *J. Am. Chem. Soc.*, **93**, 1311 (1971).
109. H. Kaneko, K. Nakamura, Y. Yamoto and M. Kurokawa, *Chem. Pharm. Bull. (Tokyo)*, **17**, 11 (1969).
110. R. E. Schaub and M. J. Weiss, *J. Org. Chem.*, **26**, 3915 (1961).
111. P. Beak and T. L. Chaffin, *J. Org. Chem.*, **35**, 2275 (1970).
112. E. Wenkert and B. G. Jackson, *J. Am. Chem. Soc.*, **80**, 217 (1958).
113. G. Stork and F. H. Clarke, *J. Am. Chem. Soc.*, **77**, 1072 (1955); **83**, 3114 (1961).
114. S. Dube and P. Deslongchamps, *Tetrahedron Lett.*, 101 (1970).
115. W. G. Dauben, W. W. Epstein, M. Tanabe and B. Weinstein, *J. Org. Chem.*, **28**, 293 (1963).
116. J. R. Hanson, *Synthesis*, 1 (1974).
117. J. E. McMurry, *Acc. Chem. Res.*, **7**, 281 (1974).
118. T.-L. Ho, *Synthesis*, 1 (1979).
119. (a) C. E. Castro, R. D. Stephens and S. Moje, *J. Am. Chem. Soc.*, **88**, 4964 (1966).
    (b) A. Zurqiyah and C. E. Castro, *Org. Synth. Coll. Vol.*, **5**, 993 (1973).
120. (a) E. Knecht, *Ber. Dtsch. Chem. Ges.*, **36**, 166 (1903).
    (b) P. Karrer, Y. Yen and I. Reichstein, *Helv. Chim. Acta*, **13**, 1308 (1930).
    (c) L. C. Blaszczak and J. E. McMurry, *J. Org. Chem.*, **39**, 258 (1974).
121. (a) J. R. Hanson and E. Premuzic, *J. Chem. Soc. (C)*, 1201 (1969).
    (b) J. R. Hanson and E. Premuzic, *Angew. Chem., Int. Ed. Engl.*, **7**, 247 (1968).
122. H. O. House and E. F. Kinloch, *J. Org. Chem.*, **39**, 1173 (1974).
123. J. B. Conant and H. B. Cutter, *J. Am. Chem. Soc.*, **48**, 1016 (1926).
124. E. J. Corey, R. L. Danheiser and S. Chandrasekaran, *J. Org. Chem.*, **41**, 260 (1976).
125. S. C. Welch and M. E. Walters, *J. Org. Chem.* **43**, 2715 (1978).
126. (a) A. Berndt, *Angew. Chem., Int. Ed. Engl.*, **6**, 251 (1967).
    (b) A. Berndt, *Tetrahedron Lett.*, 177 (1970).
127. (a) P. Bladon, J. W. Cornforth and R. H. Jaeger, *J. Chem. Soc.*, 863 (1958).
    (b) H. Lund, *Acta Chim. Scand.*, **11**, 283 (1957).
128. R. C. Fuson, *Rec. Chem. Prog.*, **12**, 1 (1951).
129. (a) C. G. Overberger and A. M. Schiller, *J. Org. Chem.*, **26**, 4230 (1961).
    (b) E. L. Totton, N. C. Camp III, G. M. Cooper, B. D. Haywood and D. P. Lewis, *J. Org. Chem.*, **32**, 2033 (1967).

(c) H. Rosen, Y. Arad, M. Levy and D. Vofsi, *J. Am. Chem. Soc.*, **91**, 1425 (1969).
(d) P. Matsuda, *Tetrahedron Lett.*, 6193 (1966).
(e) A. Zysman, G. Dana and J. Wiemann, *Bull. Soc. Chim. Fr.*, 1019 (1967).
(f) J. Wiemann, M. R. Monot, G. Dana and J. Chuche, *Bull. Soc. Chim. Fr.*, 3293 (1967).
(g) E. Touboul, F. Weisbuch and J. Wiemann, *Bull. Soc. Chim. Fr.*, 4291 (1967).
(h) C. Glacet, *Compt. Rend.*, **227**, 480 (1948).
(i) J. Wiemann and R. Nahum, *Compt. Rend.*, **238**, 2091 (1954).

130. (a) R. N. Gourley, J. Grimshaw and P. G. Miller, *J. Chem. Soc. (C)*, 2318 (1970).
(b) L. Horner and D. H. Skaletz, *Tetrahedron Lett.*, 3679 (1970).
(c) A. Spassky-Pasteur, *Bull. Soc. Chim. Fr.*, 2900 (1969).

131. (a) M. M. Baizer, *J. Org. Chem.*, **29**, 1670 (1964); **31**, 3847 (1966).
(b) M. M. Baizer and J. D. Anderson, *J. Org. Chem.*, **30**, 1348, 1351, 1357, 3138 (1965).
(c) J. D. Anderson, M. M. Baizer and E. J. Prill, *J. Org. Chem.*, **30**, 1645 (1965).
(d) J. D. Anderson, M. M. Baizer and J. P. Petrovich, *J. Org. Chem.*, **31**, 3890, 3897 (1966).
(e) J. H. Wagenknecht and M. M Baizer, *J. Org. Chem.*, **31**, 3885 (1966).
(f) M. R. Ort and M. M Baizer, *J. Org. Chem.*, **31**, 1646 (1966).
(g) M. M. Baizer and J. D. Anderson, *J. Electrochem. Soc.*, **111**, 223, 226 (1964); M. M. Baizer, *J. Electrochem.*, **111**, 215 (1964).
(h) For reviews, see: M. M. Baizer, J. D. Anderson, J. H. Wagenknecht, M. R. Ort and J. P. Petrovich, *Prog. Electrochem. Acta*, **12**, 1377 (1967); J. D. Anderson, J. P. Petrovich and M. M. Baizer, *Adv. Org. Chem.*, **6**, 257 (1969); M. M. Baizer and J. P. Petrovich, *Prog. Phys. Org. Chem.*, **7**, 189 (1970).

132. D. A. Jaeger, D. Bolikal and B. Nath, *J. Org. Chem.*, **52**, 276 (1987).
133. B. R. James, *Homogeneous Hydrogenation*, Wiley–Interscience, New York, 1973.
134. (a) P. S. Rylander, *Hydrogenation Methods*, Academic Press, London, 1985.
(b) P. S. Rylander, *Catalytic Hydrogenation in Organic Syntheses*, Academic Press, London, 1979.
135. M. Freifelder, *Catalytic Hydrogenation in Organic Synthesis*, Willey–Interscience, New York, 1978.
136. G. R. Ames and W. Davey, *J. Chem. Soc.*, 3001 (1956).
137. J. J. Brunet, P. Gallois and P. Caubere, *J. Org. Chem.*, **45**, 1937, 1946 (1980).
138. H. Adkins and R. Connor, *J. Am. Chem. Soc.*, **53**, 1091 (1931).
139. N. F. Hayes, *Synthesis*, 702 (1975).
140. E. Breitner, E. Roginski and P. N. Rylander, *J. Org. Chem.*, **24**, 1855 (1959).
141. A. Skita, *Chem. Ber.*, **48**, 1486 (1915).
142. C. Weygand and W. Meusel, *Chem. Ber.*, **76**, 498 (1943).
143. R. Adams, J. W. Kern and R. L. Shriner, *Org. Synth. Coll. Vol.*, **1**, 101 (1932).
144. R. L. Augustine, *J. Org. Chem.*, **23**, 1853 (1958).
145. R. E. Harmon, J. L. Parsons, D. W. Cooke, S. K. Gupta and J. Schoolenberg, *J. Org. Chem.*, **34** 3684 (1969).
146. (a) C. Djerassi and J. Gutzwiller, *J. Am. Chem. Soc.*, **88**, 4537 (1966).
(b) A. J. Birch and K. A. M. Walker, *J. Chem. Soc. (C)* 1894 (1966).
147. P. L. Cook, *J. Org. Chem.*, **27**, 3873 (1962).
148. K. Sakai and K. Watanabe, *Bull. Chem. Soc. Jpn.*, **40**, 1548 (1967).
149. Y. Watanabe, Y. Matsumura, Y. Izumi and Y. Mizutani, *Bull. Chem. Soc. Jpn.*, **47**, 2922 (1974).
150. R. L. Augustine, *Adv. Catal.*, **25**, 63 (1976) and references cited therein.
151. R. L. Augustine, *Ann. N.Y. Acad. Sci.*, **145**, 19 (1967).
152. F. J. McQuillin, W. O. Ord and P. L. Simpson, *J. Chem. Soc.*, 5996 (1963).
153. (a) R. L. Augustine, *J. Org. Chem.*, **23**, 1853 (1958).
(b) R. L. Augustine and A. D. Broom, *J. Org. Chem.*, **25**, 802 (1960).
(c) R. L. Augustine, D. C. Migliorini, R. E. Foscante, C. S. Sodano and M. J. Sisbarro, *J. Org. Chem.*, **34**, 1075 (1969).
(d) S. Nishimura, M. Shimahara and M. Shiota, *J. Org. Chem.*, **31**, 2394 (1966).
(e) M. G. Combe, H. B. Henbest and W. R. Jackson, *J. Chem. Soc. (C)*, 2467 (1967).
(f) H. B. Henbest, W. R. Jackson and I. Malunowicz, *J. Chem. Soc. (C)*, 2469 (1967).
(g) I. Gardine, R. W. Howsam and F. J. McQuillin, *J. Chem. Soc. (C)*, 260 (1969).
(h) H. J. E. Loewenthal, *Tetrahedron*, **6**, 269 (1959).
(i) L. Velluz, J. Valls and G. Nomine, *Angew. Chem., Int. Ed. Engl.*, **4**, 181 (1965).

154. T. C. McKenzie, *J. Org. Chem.*, **39**, 629 (1974).
155. Z. J. Hajos and D. R. Parrish *J. Org. Chem.*, **38**, 3239 (1973).
156. (a) T. Kametani, M. Tsubuki, H. Furuyama and T. Honda, *J. Chem. Soc., Perkin Trans. 1*, 557 (1985).
     (b) T. Kametani, M. Tsubuki, K. Higurashi and T. Honda, *J. Org. Chem.*, **51**, 2932 (1986).
157. (a) N. V. Borunova, L. K. Friedlin, L. I. Gvinter, T. Atabekov, V. A. Zamureenko and I. M. Kustanovich, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **6**, 1299 (1972); *Chem. Abstr.*, **77**, 87461 (1972).
     (b) L. K. Friedlin, L. I. Gvinter, N. V. Borunova, S. F. Dymova and I. M. Kustanovich, *Katal Reakts. Zhidk. Faze*, 309 (1972); *Chem. Abstr.*, **79**, 115066z (1973).
158. P. C. Traas, H. Boelens and H. J. Takken, *Synth. Commun.*, **6**, 489 (1976).
159. (a) S. Nishimura and K. Tsuneda, *Bull. Chem. Soc. Jpn.*, **42**, 852 (1969).
     (b) S. Nishimura, T. Ichino, A. Akimoto and K. Tsuneda, *Bull. Chem. Soc. Jpn.*, **46**, 279 (1973).
     (c) S. Nishimura, T. Ichino, A. Akimoto, K. Tsuneda and H. Mori, *Bull. Chem. Soc. Jpn.*, **48**, 2852 (1975).
160. J. Azran, O. Buchman, I. Amer and J. Blum, *J. Mol. Catal.*, **34**, 229 (1986).
161. D. L. Reger, M. M. Habib and D. J. Fauth, *J. Org. Chem.*, **45**, 3860 (1980).
162. J. H. Schauble, G. J. Walter and J. G. Morin, *J. Org. Chem.*, **39**, 755 (1974).
163. A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 1350 (1964).
164. E. Schenker, in *Newer Methods of Preparative Organic Chemistry* (Ed. W. Forest), Vol. IV, Academic Press, New York, 1968, p. 196.
165. J. Bottin, O. Eisenstein, C. Minot and N. T. Anh, *Tetrahedron Lett.*, 3015 (1972).
166. M. K. Johnson and B. Rickborn, *J. Org. Chem.*, **35**, 1041 (1970).
167. S. Geribaldi, M. Decouzon, B. Boyer and C. Moreau, *J. Chem. Soc., Perkin Trans. 2*, 1327 (1986).
168. W. R. Jackson and Z. Zurquiyah, *J. Chem. Soc., Chem. Commun.*, 5280 (1965).
169. S. Kim, C. H. Oh, J. S. Ko, K. H. Ahn and Y. J. Kim, *J. Org. Chem.*, **50**, 1927 (1985) and references cited therein.
170. S. B. Kadin, *J. Org. Chem.*, **31**, 620 (1966).
171. B. Ganem and J. M. Fortunato, *J. Org. Chem.*, **41**, 2194 (1976).
172. S. Krishnamurthy and H. C. Brown, *J. Org. Chem.*, **40**, 1864 (1975).
173. Z. J. Duri and J. R. Hanson, *J. Chem. Soc., Perkin Trans. 2*, 363 (1984).
174. J. MacMillan and C. L. Willis, *J. Chem. Soc., Perkin Trans. 2*, 357 (1984).
175. (a) M. H. Beale, *J. Chem. Soc., Perkin Trans. 1*, 1151 (1985).
     (b) M. H. Beale, J. MacMillan, C. R. Spray, D. A. Taylor and B. O. Phinney, *J. Chem. Soc., Perkin Trans. 1*, 541 (1984).
176. B. Voigt and G. Adam, *Tetrahedron*, **39**, 449 (1983).
177. E. J. Corey, K. B. Becker and R. K. Varma, *J. Am. Chem. Soc.*, **94**, 8616 (1972).
178. P. Joseph-Nathan, M. E. Garibay and R. L. Santillan, *J. Org. Chem.*, **52**, 759 (1987).
179. A. R. Chamberlin and S. H. Reich, *J. Am. Chem. Soc.*, **107**, 1440 (1985).
180. R. O. Hutchins and D. Kandasamy, *J. Org. Chem.*, **40**, 2530 (1975).
181. S. Kim, Y. C. Moon and K. H. Ahn, *J. Org. Chem.*, **47**, 3311 (1982).
182. (a) J. -L. Luche, *J. Am. Chem. Soc.*, **100**, 2226 (1978).
     (b) J. -L. Luche and A. L. Gemal, *J. Am. Chem. Soc.*, **101**, 5848 (1979).
     (c) A. L. Gemal and J. -L. Luche, *J. Am. Chem. Soc.*, **103**, 5454 (1981).
183. C. W. Jefford, T. W. Wallace, N. T. H. Can and C. G. Rimbault, *J. Org. Chem.*, **44**, 689 (1979).
184. (a) C. Kashima and Y. Yamamoto, *Chem. Lett.*, 1285 (1978).
     (b) C. Kashima, Y. Yamamoto and Y. Tsuda, *J. Org. Chem.*, **40**, 526 (1975).
185. (a) T. Nishio and Y. Omote, *Chem. Lett.*, 1223 (1979).
     (b) T. Nishio and Y. Omote, *J. Chem. Soc., Perkin Trans. 1*, 934 (1981).
186. J. Malek, *Org. React.*, **34**, 1 (1985).
187. H. C. Brown and P. M. Weissman, *J. Am. Chem. Soc.*, **87**, 5614 (1965).
188. (a) H. C. Brown, S. C. Kim and S. Krishnamurthy, *J. Org. Chem.*, **45**, 1 (1980).
     (b) H. C. Brown, P. K. Jadhav and A. K. Mandal, *Tetrahedron*, **37**, 3547 (1981).
     (c) M. Fieser and L. F. Fieser, *Reagents for Organic Synthesis*, Vols. I–XIII, Wiley–Interscience, New York, 1967–1988.
     (d) S. I. Yamada and K. Koga, in *Selective Organic Transformations*, Vol. I (Ed. B. S. Thyagarajan), Wiley–Interscience, New York, 1970.
     (e) B. D. James, *Rec. Chem. Prog.*, **31**, 199 (1970).
     (f) J. Vit, *Eastman Org. Chem. Bull.*, **42**, 1 (1970); *Chem. Abstr.*, 74, 99073p (1971).

(g) D. M. S. Wheeler and M. M. Wheeler, in *Organic Reactions in Steroid Chemistry* (Eds. J. Fried and J. A. Edwards), Vol. I, Van Nostrand Reinhold, New York, 1972, Chap. 2.
(h) J. Malek and M. Cerny, *Synthesis*, 217 (1972).
(i) A. S. Kushner and T. Vaccariello, *J. Chem. Educ.*, **50**, 154, 157 (1973).
(j) H. Mishima, *Yuki Gosei Kagaku Kyokai Shi*, **32**, 1014 (1974); *Chem. Abstr.*, **82**, 138613b (1975).
(k) C. F. Lane, *Chem. Rev.*, **76**, 773 (1976).
(l) C. F. Lane, in *Aspects of Mechanistic Organometallic Chemistry* (Proceedings of Symposium) (Ed. J. H. Brewster), Plenum Press, New York, 1978, pp. 181–198.
(m) J. R. Boone and E. C. Ashby, *Top. Stereochem.*, **11**, 53 (1979).
(n) P. A. Bartlett, *Tetrahedron*, **36**, 2 (1980).
(o) S. O. Kim, *Hwakhak Kwa Kongop Ui Chinbo*, **20**, 293 (1980); *Chem. Abstr.*, **94**, 102222g (1981).

189. Reference 5, Chap. 2.
190. E. R. H. Walker, *Chem. Soc. Rev.*, **5**, 23 (1976).
191. (a) A. Hajos, *Komplexe Hydride*, VEB Deutscher Verlag der Wissenschaften, East Berlin, 1966.
    (b) A. Hajos, *Complex Hydrides and Related Reducing Agents in Organic Synthesis*, Elsevier Scientific Publ. Co., Amsterdam, 1979.
192. H. C. Brown, *Boranes in Organic Chemistry*, Cornell University Press, Ithaca, New York, 1972, Chaps. 12–13.
193. (a) D. R. Boyd and M. A. McKervey, *Quart. Rev.*, **22**, 95 (1968).
    (b) J. Mathieu and J. Weill-Raynal, *Bull. Soc. Chim. Fr.*, 1211 (1968).
    (c) T. D. Inch, *Synthesis*, 466 (1970).
    (d) J. D. Morrison and H. S. Mosher, *Asymmetric Organic Reactions*, Prentice Hall, Englewood Cliffs, N. J., 1971, pp. 116–132, 202–215, 386–389; Reprint ed., American Chemical Society, Washington, D.C., 1976.
    (e) H. J. Schneider and R. Haller, *Pharmazie*, **28**, 417 (1973).
    (f) J. W. Scott and D. Valentine, Jr., *Science*, **184**, 943 (1974).
    (g) D. Valentine, Jr. and J. W. Scott, *Synthesis*, 329 (1978).
    (h) J. W. ApSimon and R. P. Seguin, *Tetrahedron*, **35**, 2797 (1979).
194. O. Eisenstein, J. M. Lefour, C. Minot, N. T. Anh and G. Soussan, *C.R. Acad. Sci. Paris, Ser.* C, **274**, 1310 (1972).
195. J. Durand, N. T. Anh and J. Huet, *Tetrahedron Lett.*, 2397 (1974).
196. J. Bottin, O. Eisenstein, C. Minot and N. T. Anh, *Tetrahedron Lett.*, 3015 (1972).
197. R. G. Pearson, *J. Chem. Educ.*, **45**, 581 (1968).
198. J. Seyden-Penne, *Bull. Soc. Chim. Fr.*, 3871 (1968).
199. H. C. Brown and H. M. Hess, *J. Org. Chem.*, **34**, 2206 (1969).
200. A. Loupy and J. Seyden-Penne, *Tetrahedron*, **36**, 1937 (1980).
201. (a) J. C. Richer and A. Rossi, *Can. J. Chem.*, **50**, 438 (1972).
    (b) J. A. Marshall and J. A. Ruth, *J. Org. Chem.*, **39**, 1971 (1974).
202. M. E. Cain, *J. Chem. Soc.*, 3532 (1964).
203. M. F. Semmelhack, R. D. Stauffer and A. Yamashita, *J. Org. Chem.*, **42**, 3180 (1977).
204. J. E. Baldwin, R. C. Thomas, L. I. Kruse and L. Silberman, *J. Org. Chem.*, **42**, 3846 (1977).
205. (a) P. L. Southwick, N. Latif, B. M. Fitzgerald and N. M. Zaczek, *J. Org. Chem.*, **31**, 1 (1966).
    (b) J. Durand and J. Huet, *Bull. Soc. Chim. Fr.*, Pt. 2, 428 (1978).
206. P. A. Bartlett and W. S. Johnson, *J. Am. Chem. Soc.*, **95**, 7501 (1973).
207. G. D. Prestwich, F. B. Whitfield and G. Stanley, *Tetrahedron*, **32**, 2945 (1976).
208. (a) R. L. Markezich, W. E. Willy, B. E. McCarry and W. S. Johnson, *J. Am. Chem. Soc.*, **95**, 4414 (1973).
    (b) W. S. Johnson, B. E. McCarry, R. L. Markezich and S. G. Boots, *J. Am. Chem. Soc.*, **102**, 352 (1980).
209. P. C. Traas, H. Boellens and H. J. Takken, *Recl. Trav. Chim. Pays-Bas*, **95**, 57 (1976).
210. K. E. Wilson, R. T. Seidner and S. Masamune, *J. Chem. Soc., Chem. Commun.*, 213 (1970).
211. D. V. Banthorpe, A. J. Curtis and W. D. Fordham, *Tetrahedron Lett.*, 3865 (1972).
212. N. Lander and R. Mechoulam, *J. Chem. Soc., Perkin Trans. 1*, 484 (1976).
213. R. A. Finnegan and P. L. Bachman, *J. Org. Chem.*, **30**, 4145 (1965).
214. D. Caine, P. C. Chen, A. S. Frobese and J. T. Gupton, *J. Org. Chem.*, **44**, 4981 (1979).
215. R. E. Ireland, M. I. Dawson, S. C. Welch, A. Hagenbach, J. Bordner and B. Trus, *J. Am. Chem. Soc.*, **95**, 7829 (1973).

216. E. Winterfeldt, *Synthesis*, 617 (1975).
217. E. C. Ashby and J. J. Lin, *Tetrahedron Lett.*, 3865 (1976).
218. H. C. Brown, U. S. NTIS, AD Rep. AD-A026132 (1976); *Chem. Abstr.* **85**, 176353m (1976).
219. H. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1852 (1973).
220. W. L. Dilling and R. A. Plepys, *J. Chem. Soc., Chem. Commun.*, 417 (1969).
221. W. L. Dilling and R. A. Plepys, *J. Org. Chem.*, **35**, 1971 (1970).
222. J. P. Bugel, P. Ducos, O. Gringore and F. Rouessac, *Bull. Soc. Chim. Fr.*, 4371 (1972).
223. P. R. Story and S. R. Fahrenholtz, *J. Am. Chem. Soc.*, **87**, 1623 (1965).
224. J. B. Wiel and F. Rouessac, *J. Chem. Soc., Chem. Commun.*, 446 (1976).
225. J. B. Wiel and F. Rouessac, *Bull. Soc. Chim. Fr.*, Pt. 2, 273 (1979).
226. E. J. Corey and J. Gorzynski Smith, *J. Am. Chem. Soc.*, **101**, 1038 (1979).
227. M. F. Semmelhack and R. D. Stauffer, *J. Org. Chem.*, **40**, 3619 (1975).
228. M. Vandewalle and E. Madeleyn, *Tetrahedron*, **26**, 3551 (1970).
229. C. J. Sih, R. G. Salomon, P. Price, R. Sood and G. Peruzzotti, *J. Am. Chem. Soc.*, **97**, 857 (1975).
230. M. Suzuki, T. Kawagishi, T. Suzuki and R. Noyori, *Tetrahedron Lett.*, **23**, 4057 (1982).
231. P. A. Grieco, N. Fukamiya and M. Miyashita, *J. Chem. Soc., Chem. Commun.*, 573 (1976).
232. (a) Z. G. Hajos, D. R. Parrish and E. P. Oliveto, *Tetrahedron Lett.*, 6495 (1966).
(b) Z. G. Hajos, D. R. Parrish and E. P. Oliveto, *Tetrahedron*, **24**, 2039 (1968).
233. G. Saucy, R. Borer and A. Furst, *Helv. Chim. Acta*, **54**, 2034 (1971).
234. G. Saucy and R. Borer, *Helv. Chim. Acta*, **54**, 2121 (1971).
235. E. Fujita, T. Fujita and Y. Nagao, *Tetrahedron*, **25**, 3717 (1969).
236. R. E. Ireland and D. M. Walba, *Tetrahedron Lett.*, 1071 (1976).
237. K. F. Cohen, R. Kazlauskas and J. T. Pinhey, *J. Chem. Soc., Perkin Trans. 1*, 2076 (1973).
238. G. Stork, G. A. Kraus and G. A. Garcia, *J. Org. Chem.*, **39**, 3459 (1974).
239. G. Stork and G. A. Kraus, *J. Am. Chem. Soc.*, **98**, 2351 (1976).
240. (a) R. Pappo and P. W. Collins, *Tetrahedron Lett.*, 2627 (1972).
(b) R. Pappo and C. J. Jung, Ger. Offen. 2,321,984 (1973); *Chem. Abstr.* **80**, 26827b (1974).
(c) M. M. S. Bruhn and R. Pappo, Ger. Offen 2,415,765 (1974); *Chem. Abstr.*, **82**, 86119y (1975).
(d) R. Pappo and C. J. Jung, U. S. Pat. 3,969,391 (1976); *Chem. Abstr.*, **86**, 55057e (1977).
(e) C. J. Sih, J. B. Heather, G. P. Peruzzotti, P. Price, R. Sood and L. F. Hsu Lee, *J. Am. Chem. Soc.*, **95**, 1676 (1973).
(f) C. J. Sih, J. B. Heather, R. Sood, P. Price, G. P. Peruzzotti, L. F. Hsu Lee and S. S. Lee, *J. Am. Chem. Soc.*, **97**, 865 (1975).
(g) C. J. Sih and J. B. Heather, U. S. Pat. 3, 968, 141 (1976); *Chem. Abstr.*, **86**, 29416b (1977).
241. (a) C. J. Sih, J. B. Heather, G. P. Peruzzotti, P. Price, R. Sood and L. F. Hsu Lee, *J. Am. Chem. Soc.*, **95**, 1676 (1973).
(b) C. J. Sih, J. B. Heather, R. Sood, P. Price, G. P. Peruzzotti, L. F. Hsu Lee and S. S. Lee, *J. Am. Chem. Soc.*, **97**, 867 (1975).
242. Y. Asaka, T. Kamikawa and T. Kubota, *Tetrahedron Lett.*, 1597 (1972).
243. V. Bazant, M. Capka, M. Cerny, V. Chvalovsky, K. Kochloefl, M. Kraus and J. Malek, *Tetrahedron Lett.*, 3303 (1968).
244. M. Capka, V. Chvalovsky, K. Kochloefl and M. Kraus, *Collect. Czech. Chem. Commun.*, **34**, 118 (1969).
245. H. C. Brown and N. M. Yoon, *J. Am. Chem. Soc.*, **88**, 1464, (1966).
246. H. C. Brown, U. S. Clearinghouse, *Fed. Sci. Tech. Inform.*, AD 645581 (1966); *Chem. Abstr.*, **67**, 99306x (1967).
247. H. C. Brown and P. M. Weissman, *Isr. J. Chem.*, **1**, 430 (1963).
248. O. Kriz, J. Machacek and O. Strouf, *Collect. Czech. Chem. Commun.*, **38**, 2072 (1973).
249. J. V. Forsch, I. T. Harrison, B. Lythgoe and A. K. Saksena, *J. Chem. Soc., Perkin Trans. 1*, 2005 (1974).
250. W. Sucrow, *Tetrahedron Lett.*, 4725 (1970).
251. G. Buchi, B. Gubler, R. S. Schneider and J. Wild, *J. Am. Chem. Soc.*, **89**, 2776 (1967).
252. S. Antus, A. Gottsegen and M. Nogradi, *Synthesis*, 574 (1981).
253. S. Kim and K. H. Ahn, *J. Org. Chem.*, **49**, 1749 (1984).
254. B. M. Trost and L. N. Jungheim, *J. Am. Chem. Soc.*, **102**, 7910 (1980).
255. H. J. Williams, *Tetrahedron Lett.*, 1271 (1975).
256. (a) M. M. Bokadia, B. R. Brown, D. Cobern, A. Roberts and G. A. Somerfield, *J. Chem. Soc.*, 1658 (1962).

(b) J. Broome, B. R. Brown, A. Roberts and A. M. S. White, *J. Chem. Soc.*, 1406 (1960).

257. (a) E. C. Ashby and J. J. Lin, *Tetrahedron Lett.*, 4453 (1975).
    (b) E. C. Ashby J. J. Lin and R. Kovar, *J. Org. Chem.*, **41**, 1941 (1976).
258. (a) O. Cervinka, O. Kriz and J. Cervenka, *Z. Chem.*, **11**, 109 (1971).
    (b) O. Cervinka and O. Kriz, *Collect. Czech. Chem. Commun.*, **38**, 294 (1973).
259. R. Noyori, I. Tomino and M. Nishizawa, *J. Am. Chem. Soc.*, **101**, 5843 (1979).
260. S. Terashima, N. Tanno and K. Koga, *J. Chem. Soc., Chem. Commun.*, 1026 (1980).
261. (a) S.Terashima, N. Tanno and K. Koga, *Tetrahedron Lett.*, **21**, 2753 (1980).
    (b) S. Terashima, N. Tanno and K. Koga, *Chem. Lett.*, 981 (1980).
262. J. Huton, M. Senior and N. C. A. Wright, *Synth. Commun.*, **9**, 799 (1979).
263. N. Cohen, R. J. Lopresti, C. Neukom and G. Saucy, *J. Org. Chem.*, **45**, 582 (1980).
264. R. S. Brinkmeyer and V. M. Kapoor, *J. Am. Chem. Soc.*, **99**, 8339 (1977).
265. W. S. Johnson, R. S. Brinkmeyer, V. M. Kapoor and T. M. Yarnell, *J. Am. Chem. Soc.*, **99**, 8341 (1977).
266. J. P. Vigneron and V. Bloy, *Tetrahedron Lett.*, 2683 (1979).
267. J. P. Vigneron and V. Bloy, *Tetrahedron Lett.*, **21**, 1735 (1980).
268. J. P. Vigneron and J. M. Blanchard, *Tetrahedron Lett.*, **21**, 1739 (1980).
269. M. Nishizawa, M. Yamada and R. Noyori, *Tetrahedron Lett.*, **22**, 247 (1981).
270. S. R. Landor, B. J. Miller and A. R. Tatchell, *J. Chem. Soc. (C)*, 1822 (1966).
271. S. R. Landor, B. J. Miller and A. R. Tatchell, *Proc. Chem. Soc.*, 227 (1964).
272. S. R. Landor, B. J. Miller and A. R. Tatchell, *J. Chem. Soc. (C)*, 2339 (1971).
273. M. Nishizawa and R. Noyori, *Tetrahedron Lett.*, **21**, 2821 (1980).
274. T. Sato, Y. Gotoh, Y. Wakabayashi and T. Fujisawa, *Tetrahedron Lett.*, **24**, 4123 (1983).
275. R. Noyori, I. Tomino and M. Nishizawa, *J. Am. Chem. Soc.*, **101**, 3843 (1979).
276. C. J. Sih, J. B. Heather, R. Sood, P. Price, G. Peruzzotti, L. F. Hsu Lee and S. S. Lee, *J. Am. Chem. Soc.*, **97**, 865 (1975).
277. Y. Nagai, *Intra-Sci. Chem. Rep.*, **4**, 115 (1970).
278. D. N. Kursanov, Z. N. Parnes and N. M. Loim, *Synthesis*, 633 (1974).
279. (a) Z. N. Parnes, N. M. Loim, V. A. Baranova and D. N. Kursanov, *Zh. Org. Khim.*, **7**, 2066 (1977); *Chem. Abstr.*, **76**, 13495 (1972).
    (b) D. N. Kursanov *et al.*, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 843 (1974).
280. D. N. Kursanov, N. M. Loim, V. A. Baranova, L. V. Moiseeva, L. P. Zalukaev and Z. N. Parnes, *Synthesis*, 420 (1973).
281. E. Yoshii, T. Koizumi, I. Hayashi and Y. Hiroi, *Chem. Pharm. Bull.*, **25**, 1468 (1977).
282. G. G. Furin, O. A. Vyazankina, B. A. Gostevsky and N. S. Vyazankin, *Tetrahedron*, **44**, 2675 (1988).
283. R. J. P. Corriu, R. Perz and C. Reye, *Tetrahedron*, **39**, 999 (1983).
284. M. P. Doyle, C. T. West, S. J. Donnelly and C. C. McOsker, *J. Organomet. Chem.*, **117**, 129 (1976).
285. M. Kira, K. Sato and H. Sakurai, *J. Org. Chem.*, **52**, 948 (1987).
286. R. A. Benkeser, *Acc. Chem. Res.*, **4**, 94 (1971).
287. (a) H. G. Kuivila, *Synthesis*, 499 (1970).
    (b) A. Hajos, *Complex Hydrides and Related Reducing Agents in Organic Synthesis*, Amsterdam, Elsevier, 1979.
    (c) Y. I. Baukov and I. F. Lutsenko, *Organomet. Chem. Rev., A*, **6**, 355 (1970).
288. (a) H. G. Kuivila and O. F. Beumel, *J. Am. Chem. Soc.*, **83**, 1246 (1961).
    (b) H. G. Kuivila and O. F. Beumel, *J. Am. Chem. Soc.*, **80**, 3798 (1958).
    (c) G. J. M. Van Der Kerk, J. G. A. Luijten and J. G. Noltes, *Chem. Ind.*, 352 (1956).
    (d) G. J. M. Van Der Kerk, J. G. Noltes and J. G. A. Luijten, *J. Appl. Chem.*, **7**, 356 (1957).
    (e) G. J. M. Van Der Kerk and J. G. Noltes, *J. Appl. Chem.*, **9**, 106 (1959).
    (f) J. G. Noltes and G. J. M. Van Der Kerk, *Chem. Ind.*, 294 (1959).
    (g) I. F. Lutsenko, S. V. Ponomarev and O. P. Petri, *Obshch. Khim.*, **32**, 896 (1962).
    (h) M. Pereyre and J. Valade, *C.R. Acad. Sci. Paris*, **258**, 4785 (1964).
    (i) M. Pereyre and J. Valade, *C.R. Acad. Sci. Paris*, **260**, 581 (1965).
    (j) M. Pereyre and J. Valade, *Bull. Soc. Chim. Fr.*, 1928 (1967).
    (k) M. Pereyre, G. Colin and J. Valade, *Tetrahedron Lett.*, 4805 (1967).
    (l) A. J. Leusink and J. G. Noltes, *Tetrahedron Lett.*, 2221 (1966).

289. M. Pereyre and J. Valade, *Tetrahedron Lett.*, 489 (1969).
290. H. Laurent, P. Esperling and G. Baude, *Ann. Chem.*, 1996 (1983).
291. (a) B. R. Laliberte, W. Davidson and M. C. Henry, *J. Organomet. Chem.*, **5**, 526 (1966).
(b) A. J. Leusink and J. G. Noltes, *J. Organomet. Chem.*, **16**, 91 (1969).
(c) W. P. Neumann, H. Niermann and R. Sommer, *Ann. Chim.*, **659**, 27 (1962).
(d) M. Pereyre, G. Colin and J. Valade, *Bull. Soc. Chim. Fr.*, 3358 (1968).
(e) S. Matsuda, Sh. Kikkava and I. Omae, *J. Organomet. Chem.*, **18**, 95 (1969).
292. (a) A. J. Leusink and J. G. Noltes, *Tetrahedron Lett.*, 335 (1966).
(b) W. P. Neumann and R. Sommer, *Ann. Chim.*, **675**, 10 (1964).
293. G. A. Posner, *Org. React.*, **19**, 1 (1972).
294. (a) M. F. Semmelhack and R. D. Stauffer, *J. Org. Chem.*, **40**, 3619 (1975).
(b) M. F. Semmelhack, R. D. Stauffer and A. Yamashita, *J. Org. Chem.*, **42**, 3180 (1977).
295. M. E. Osborn, J. F. Pegues and L. A. Paquette, *J. Org. Chem.*, **45**, 167 (1980).
296. T. Saegusa, K. Kawasaki, T. Fujii and T. Tsuda, *J. Chem. Soc., Chem. Commun.*, 1013 (1980).
297. T. Tsuda, T. Hayashi, H. Suton, T. Kamamoto and T. Saegusa, *J. Org. Chem.*, **51**, 537 (1986).
298. R. K. Boeckman, Jr. and R. Michalak, *J. Am. Chem. Soc.*, **96**, 1623 (1974).
299. S. Masamune, G. S. Bates and P. E. Georghiou, *J. Am. Chem. Soc.*, **96**, 3686 (1974).
300. E. C. Ashby, J. J. Lin and A. B. Goel, *J. Org. Chem.*, **43**, 183 (1978).
301. T. H. Lemmen, K. Folting, J. C. Huffman and K. G. Caulton, *J. Am. Chem. Soc.*, **107**, 7774 (1985).
302. W. S. Mahoney, D. M. Brestensky and J. M. Stryker, *J. Am. Chem. Soc.*, **110**, 291 (1988).
303. (a) G. F. Cainelli, M. Panunzio and A. Umani-Ronchi, *J. Chem. Soc., Perkin Trans 1*, 1273 (1975).
(b) G. F. Cainelli, M. Panunzio and A. Umani-Ronchi, *Tetrahedron Lett.*, 2491 (1973).
304. M. Yamashita, K. Miyoshi, Y. Okada and R. Suemitsu, *Bull. Chem. Soc. Jpn.*, **55**, 1329 (1982).
305. G. P. Boldrini and A. Umani-Ronchi, *J. Organomet. Chem.*, **171**, 85 (1979).
306. (a) J. P. Collman, R. G. Finke, P. L. Matlock, R. Wahren and J. I. Brauman, *J. Am. Chem. Soc.*, **98**, 4685 (1976).
(b) J. P. Collman, R. G. Finke, P. L. Matlock, R. Wahren, R. G. Komoto and J. I. Brauman, *J. Am. Chem. Soc.*, **100**, 1119 (1978).
307. T. Imamoto, T. Mita and M. Yokomoto, *J. Chem. Soc., Chem. Commun.*, 163 (1984).
308. G. P. Boldrini and A. Umani-Ronchi, *Synthesis*, 596 (1976).
309. R. W. Goetz and M. Orchin, *J. Am. Chem. Soc.*, **85**, 2782 (1963).
310. P. H. Gibson and Y. S. El-Omrani, *Organometallics*, **4**, 1473 (1985).
311. (a) A. W. Johnstone, A. H. Wilby and I. D. Entwistle, *Chem. Rev.*, **85**, 129 (1985).
(b) G. Brieger and T. J. Nestrick, *Chem. Rev.*, **74**, 567 (1974).
(c) G. W. Parshall, *Catal. Rev.*, **23**, 107 (1981).
312. Y. Sasson and J. Blum, *J. Org. Chem.*, **40**, 1887 (1975).
313. Y. Sasson and J. Blum, *Tetrahedron Lett.*, 2167 (1971).
314. V. Z. Sharf, L. K. Freidlin, I. S. Shekoyan and V. N. Krutii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 575 (1976); 834 (1977) [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **25**, 557 (1976); **26**, 758 (1977)].
315. Y. Sasson, M. Cohen and J. Blum, *Synthesis*, 359 (1973).
316. G. Descotes and J. Sabadie, *Bull. Soc. Chim. Fr.*, Pt-2, 158 (1978).
317. G. Speier and L. Marko, *J. Organomet. Chem.*, **210**, 253 (1981).
318. S. L. Regen and G. M. Whitesides, *J. Org. Chem.*, **37**, 1832 (1972).
319. Y. Sasson, J. Blum and E. Dunkelblum, *Tetrahedron Lett.*, 3199 (1973).
320. Y. Sasson and G. L. Rempel, *Can. J. Chem.*, **52**, 3825 (1974).
321. T. Nishiguchi, H. Imai, Y. Hirose and K. Fukuzumi, *J. Catal.*, **41**, 249 (1976).
322. A. Dobson, D. S. Moore and S. D. Robinson, *J. Organomet. Chem.*, **177**, C8 (1979).
323. M. Bianchi, U. Matteoli, G. Menchi, P. Frediani, F. Piacenti and C. Botteghi, *J. Organomet. Chem.*, **195**, 337 (1980).
324. K. Ohkubo, I. Terada and K. Yoshinaga, *Inorg. Nucl. Chem. Lett.*, **15**, 421 (1979).
325. (a) K. Ohkubo, K. Hirata, K. Yoshinaga and M. Okada, *Chem. Lett.*, 183 (1976).
(b) K. Ohkubo, K. Hirata and K. Yoshinaga, *Chem. Lett.*, 577 (1976).
(c) K. Ohkubo, T. Shoji, I. Terada and K. Yoshinaga, *Inorg. Nucl. Chem. Lett.*, **13**, 443 (1977).
326. G. Descotes and D. Sinou, *Tetrahedron Lett.*, 4083 (1976).
327. G. Descotes, J. P. Praly and D. Sinou, *J. Mol. Catal.*, **6**, 421 (1979).
328. (a) D. Beaupere, P. Bauer and R. Uzan, *Can. J. Chem.*, **57**, 218 (1979).

(b) D. Beaupere, L. Nadjo, R. Uzan and P. Bauer, *J. Mol. Catal.*, **14**, 129 (1982).
(c) D. Beaupere, P. Bauer, L. Nadjo and R. Uzan, *J. Organomet. Chem.*, **231**, C49 (1982).
(d) D. Beaupere, P. Bauer, L. Nadjo and R. Uzan, *J. Mol. Catal.*, **18**, 73 (1983).
329. D. Beaupere, L. Nadjo, R. Uzan and P. Bauer, *J. Mol. Catal.*, **20**, 185, 195 (1983).
330. A Camus, G. Mestroni and G. Zassinovich, *J. Organomet. Chem.*, **184**, C10 (1980).
331. E. Keinan and P. A. Gleize, *Tetrahedron Lett.*, **23**, 477 (1982).
332. (a) P. Four and F. Guibe, *Tetrahedron Lett.*, **23**, 1825 (1982).
(b) Y. T. Xian, P. Four, F. Guibe and G. Balavoine, *Nouv. J. Chim.*, **8**, 611 (1984).
333. E. Keinan and N. Greenspoon, *Tetrahedron Lett.*, **23**, 241 (1982).
334. (a) E. Keinan and N. Greenspoon, *J. Org. Chem.*, **48**, 3545 (1983).
(b) E. Keinan and N. Greenspoon, *Isr. J. Chem.*, **24**, 82 (1984).
(c) N. Greenspoon and E. Keinan, *J. Org. Chem.*, **53**, 3723 (1988).
335. (a) E. Keinan and N. Greenspoon, *J. Am. Chem. Soc.*, **108**, 7314 (1986).
(b) E. Keinan and N. Greenspoon, *Tetrahedron Lett.*, **26**, 1353 (1985).
336. E. Keinan, N. Godinger and N. Greenspoon, unpublished results.
337. (a) T. Tatsumi, M. Shibagaki and H. Tominaga, *J. Mol. Catal.*, **13**, 331 (1981).
(b) T. Tatsumi, K. Hashimoto, H. Tominaga, Y. Mizuta, K. Hata, M. Hidai and Y. Uchida, *J. Organomet. Chem.*, **252**, 105 (1983).
(c) Y. Lin and X. Lu, *J. Organomet. Chem.*, **251**, 321 (1983).
338. (a) L. Marko and Z. Nagy-Magos, *J. Organomet. Chem.*, **285**, 193 (1985).
(b) E. N. Frankel, *J. Org. Chem.*, **37**, 1549 (1972).
(c) M. Sodeoka and M. J. Shibasaki, *J. Org. Chem.*, **50**, 1147 (1985).
339. E. Keinan and D. Perez, *J. Org. Chem.*, **52**, 2576 (1987).
340. D. Perez, N. Greenspoon and E. Keinan, *J. Org. Chem.*, **52**, 5570 (1987).
341. (a) I. Ojima, T. Kogure and Y. Nagai, *Tetrahedron Lett.*, 5035 (1972).
(b) I. Ojima and T. Kogure, *Organometallics*, **1**, 1390 (1982).
(c) I. Ojima, M. Nihonyanagi, T. Kogure, M. Kumagai, S. Horiuchi and K. Nakatsugawa, *J. Organomet. Chem.*, **94**, 449 (1975).
342. H. J. Liu and B. Ramani, *Synth. Commun.*, **15**, 965 (1985).
343. A. J. Cornish, M. F. Lappert, G. L. Filatvos and T. A. Nile, *J. Organomet. Chem.*, **172**, 153 (1979).
344. T. Hayashi, K. Yamamoto and M. Kumada, *Tetrahedron Lett.*, 3 (1975).
345. (a) T. Kogure and I. Ojima, *J. Organomet. Chem.*, **234**, 249 (1982).
(b) I. Ojima and T. Kogure, *Chem. Lett.*, 985 (1975).
346. M. Kobayashi, T. Koyama, K. Ogura, S. Seto, F. J. Ritter and I. E. M. Bruggemann-Rotgans, *J. Am. Chem. Soc.*, **102**, 6602 (1980).
347. (a) D. L. Bailey, U. S. Patent 2,917,530 (1959), *Chem. Abstr.*, **54**, 6549 (1960); U. S. Patent 2,970,150 (1961), *Chem. Abstr.*, **55**, 16423 (1961).
(b) E. Y. Lukevits, *Izv. Akad. Nauk Latv. SSSR*, 111 (1963).
(c) A. D. Petrov and S. I. Sadykh-Zade, *Dokl. Akad. Nauk SSSR*, **121**, 119 (1959).
(d) A. D. Petrov, V. F. Mironov, V. A. Ponomarenko, S. I. Sadykh-Zade and E. A. Chernyshov, *Izv. Akad. Nauk SSSR*, 954 (1968).
(e) S. I. Sadykh-Zade and A. D. Petrov, *Zh. Obshch. Khim.*, **29**, 3194 (1959).
348. (a) E. Frainnet, *Pure Appl. Chem.*, **19**, 489 (1969).
(b) E. Frainnet and R. Bourhis, *Bull. Soc. Chim. Fr.*, 2134 (1966).
(c) R. Bourhis, E. Frainnet and F. Moulines, *J. Organomet. Chem.*, **141**, 157 (1977).
349. (a) A. D. Petrov and S. I. Sadykh-Zade, *Bull. Soc. Chim. Fr.*, 1932 (1959).
(b) A. D. Petrov, S. I. Sadykh-Zade and E. I. Filatova, *Zh. Obshch. Khim.*, **29**, 2936 (1959).
350. G. Stork and T. L. Macdonald, *J. Am. Chem. Soc.*, **97**, 1264 (1975).
351. E. Yoshii, H. Ikeshima and K. Ozaki, *Chem. Pharm. Bull.*, **20**, 1827 (1972).
352. E. Yoshii, Y. Kobayashi, T. Koizumi and T. Oribe, *Chem. Pharm. Bull.*, **22**, 2767 (1974).
353. A. P. Barlow, N. M. Boag and F. G. A. Stone, *J. Organomet. Chem.*, **191**, 39 (1980).
354. J. Blum, Y. Sasson and S. Iflah, *Tetrahedron Lett.*, 1015 (1972).
355. H. Imai, T. Nishiguchu and K. Fukuzumi, *Chem. Lett.*, 655 (1976).
356. (a) M. E. Vol'pin, V. P. Kukolev, V. O. Chernyshev and I. S. Kolomnikov, *Tetrahedron Lett.*, 4435 (1971).
(b) I. S. Kolomnikov, Y. D. Koreshov, V. P. Kukolev, V. A. Mosin and M. E. Vol'pin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 175 (1973) [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **22**, 180 (1973)].
357. N. A. Cortese and R. F. Heck, *J. Org. Chem.*, **43**, 3985 (1978).

358. N. A. Cortese and R. F. Heck, *J. Org. Chem.*, **42**, 3491 (1977).
359. J. Tsuji and T. Yamakawa, *Tetrahedron Lett.*, 613 (1979).
360. A. M. Caporusso, G. Giacomelli and L. Lardicci, *J. Org. Chem.*, **47**, 4640 (1982).
361. P. Caubere, *Angew. Chem., Int. Ed. Engl.*, **22**, 599 (1983).
362. J. J. Brunet, L. Mordenti, B. Loubinoux and P. Caubere, *Tetrahedron Lett.*, 1069 (1978).
363. J. J. Brunet, L. Mordenti and P. Caubere, *J. Org. Chem.*, **43**, 4804 (1978).
364. L. Mordenti, J. J. Brunet and P. Caubere, *J. Org. Chem.*, **44**, 2203 (1979).
365. A. Fauve and A. Kergomard, *Tetrahedron*, **37**, 899 (1981).
366. L. Mamoli, R. Roch and H. Teschen, *Z. Physiol. Chem.*, **261**, 287 (1939).
367. T. L. Miller and E. J. Hessler, *Biochem. Biophys. Acta*, **202**, 354 (1970).
368. H. C. Murray and D. H. Peterson, US Patent 2659743 (1953); *Chem. Abstr.*, **48**, 13737c (1954).
369. H. C. Murray and D. H. Peterson, US Patent 2649402 (1953).
370. (a) A. Kergomard, M. F. Renard and H. Veschambre, *J. Org. Chem.*, **47**, 792 (1982).
(b) A. Kergomard, M. F. Renard and H. Veschambre, *Tetrahedron Lett.*, 5197 (1978).
(c) G. Dauphin, J. C. Gramain, A. Kergomard, M. F. Renard and H. Veschambre, *Tetrahedron Lett.*, **21**, 4275 (1980).
(d) G. Dauphin, J. C. Gramain, A. Kergomard, M. F. Renard and H. Veschambre, *J. Chem. Soc. Chem. Commun.*, 318 (1980).
371. (a) Y. Noma, S. Nonomura, H. Ueda and C. Tatsumi, *Agric. Biol. Chem.*, **38**, 735 (1974).
(b) Y. Noma and S. Nonomura, *Agric. Biol. Chem.*, **38**, 741 (1974).
372. (a) M. Bostmembrun-Desrutt, G. Dauphin A. Kergomard, M. F. Renard and H. Veschambre, *Tetrahedron*, **41**, 3679 (1985).
(b) M. Desrut, A. Kergomard, M. F. Renard and H. Veschambre, *Tetrahedron*, **37**, 3825 (1981).
373. (a) A. Kergomard, M. F. Renard and H. Veschambre, *Agric. Biol. Chem.*, **49**, 1497 (1985).
(b) M. Desrut, A. Kergomard, M. F. Renard and H. Veschambre, *Biochem. Biophys. Res. Commun.*, **110**, 908 (1983).
(c) A. Kergomard, M. F., Renard and H. Veschambre, *Agric. Biol. Chem.*, **46**, 97 (1982).
(d) A. Kergomard, M. F., Renard, H. Veschambre, C. A. Groliere and J. Dupy-Blanc, *Agric. Biol. Chem.*, **50**, 487 (1986).
374. T. Kitazume and N. Ishikawa, *Chem. Lett.*, 587 (1984).
375. (a) P. Gramatica, P. Manitto and L. Poli, *J. Org. Chem.*, **50**, 4625 (1985).
(b) P. Gramatica, P. Manitto, B. M. Ranzi, A. Delbianco and M. Francavilla, *Experientia*, **38**, 775 (1982).
376. H. G. W. Leuenberger, W. Boguth, R. Barner, M. Schmid and R. Zell, *Helv. Chim. Acta*, **62**, 455 (1979).
377. H. G. W. Leuenberger, W. Boguth, E. Widmer and R. Zell, *Helv. Chim. Acta*, **59**, 1832 (1976).
378. C. Fuganti and P. Grasselli, *J. Chem. Soc., Chem. Commun.*, 995 (1979).
379. M. Miyano, C. R. Dorn, F. B. Colton and W. J. Marsheck, *J. Chem. Soc., Chem. Commun.*, 425 (1971).
380. (a) B. Eckstein and A. Nimrod, *Biochim. Biophys. Acta*, **1**, 499 (1977).
(b) I. A. Watkinson, D. C. Wilton, A. D. Rahimtula and M. M. Akhtar, *Eur. J. Biochem.*, **1**, 23 (1971).
381. E. A. Braude, J. Hannah and R. Linstead, *J. Chem. Soc.*, 3257 (1960).
382. B. E. Norcross, P. E. Klinedinst, Jr. and F. H. Westheimer, *J. Am. Chem. Soc.*, **84**, 797 (1962).
383. J. S. McGuire and G. M. Tompkins, *Fed. Proc.*, **19**, A29 (1960).
384. (a) Y. Ohnishi, M. Kagami and A. Ohno, *Chem. Lett.*, 125 (1975).
(b) Y. Ohnishi, M. Kagami, T. Numakunai and A. Ohno, *Chem. Lett.*, 915 (1976).
385. K. Nakamura, M. Fujii, A. Ohno and S. Oka, *Tetrahedron Lett.*, **25**, 3983 (1984).
386. R. A. Gase and U. K. Pandit, *J. Am. Chem. Soc.*, **101**, 7059 (1979).
387. (a) M. J. de Nie-Sarink and U. K. Pandit, *Tetrahedron Lett.*, 2449 (1979).
(b) U. K. Pandit, F. R. Mas Cabre, R. A. Gase and M. J. de Nie-Sarink, *J. Chem. Soc., Chem. Commun.*, 627 (1974).
388. F. Yoneda, K. Kuroda and K. Tanaka, *J. Chem. Soc., Chem. Commun.*, 1194 (1984).
389. N. Baba, T. Makino, J. Oda and Y. Inouye, *Can. J. Chem.*, **58**, 387 (1980).
390. A. Fischli and D. Suss, *Helv. Chim. Acta*, **62**, 2361 (1979).
391. (a) F. Camps, J. Coli, A. Guerrero, J. Guitart and M. Riba, *Chem. Lett.*, 715 (1982).
(b) O. Louis-Andre and G. Gelbard, *Tetrahedron Lett.*, **26**, 831 (1985).
392. H. Chikashita, M. Miyazaki and K. Itoh, *Synthesis*, 308 (1984).

393. S. K. Malhotra, D. F. Moakley and F. Johnson, *J. Am. Chem. Soc.*, **89**, 2794 (1967).
394. M. Yamashita, Y. Kato and R. Suemitsu, *Chem. Lett.*, 847 (1980).
395. H. Stamm, A. Sommer, A. Onistschenko and A. Woderer, *J. Org. Chem.*, **51**, 4979 (1986).
396. A. C. Chan and D. I. Schuster, *J. Am. Chem. Soc.*, **108**, 4561 (1986).
397. G. H. Posner and A. W. Runquist, *Tetrahedron Lett.*, 3601 (1975).
398. K. Nanjo, K. Suzuki and M. Sekiya, *Chem. Pharm. Bull.*, **25**, 2396 (1977).
399. G. Giacomelli, A. M. Caporusso and L. Lardicci, *Tetrahedron Lett.*, **22**, 3663 (1981).