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Synthesis of allylic alcohols from alkenes and their derivatives

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Abstract. The reagents used to transform epoxides, alkenes and α,β-unsaturated carbonyl compounds into allylic alcohols are considered. The bibliography includes 127 references.

I. Introduction

The presence of an allyl alcohol fragment in the molecules of organic compounds offers extensive opportunities for further modification for obtaining diverse natural and synthetic physiologically active compounds. Among the numerous existing methods for the synthesis of allyl alcohols, cleavage of α-epoxides, allylic hydroxylation and reduction of α,β-unsaturated carbonyl compounds are used most frequently. This review is devoted to these methods; the information is classified according to the type of reagent used for the transformations. Attention is concentrated on the studies published during the last 10 – 15 years.

II. Reagents for epoxide cleavage

Epoxides are important intermediates in the synthesis of various organic compounds. This is due not only to the ease of their preparation but also to the polarity and strain of the oxirane ring, which makes epoxides highly reactive towards electrophiles, nucleophiles, acids, bases, various reducing agents and some oxidants.

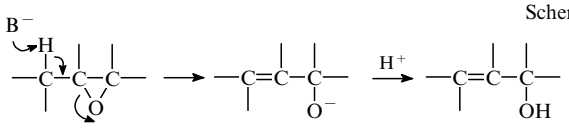
1. Isohypsic cleavage of epoxides to allylic alcohols

This Section covers the reactions of epoxide cleavage that are not accompanied by redox transformations (isohypsic reactions).

One of the most popular methods for the synthesis of allylic alcohols is treatment of epoxides with strong bases, for example, alkali metal amides. The role of the base is to eliminate the proton from the α-position with respect to the oxirane ring (Scheme 1).[1 – 3]

Unfortunately, these reagents are of little utility for the cleavage of epoxides containing additional labile functional groups. A number of reagents found in recent years have markedly extended the scope of application of this strategy.

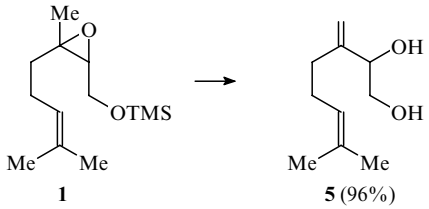
Scheme 1



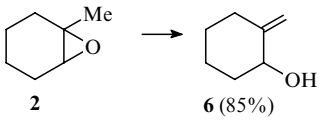
a. Methylmagnesium-*N*-cyclohexyl-*N*-isopropylamide

Falck and co-workers have shown[4] that methylmagnesium-*N*-cyclohexyl-*N*-isopropylamide [MeMgN(cyclo-C_6H_{11})Pr^i, NMA] induces efficient isomerisation of epoxides into allylic alcohols. This reagent is prepared by mixing toluene solutions of methylmagnesium bromide and lithium *N*-cyclohexyl-*N*-isopropylamide.

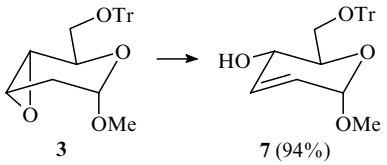
Examples of effective cleavage of epoxides **1** – **4** on treatment with MeMgN(cyclo-C_6H_{11})Pr^i to give allylic alcohols **5** – **8** are presented below.[4,5]



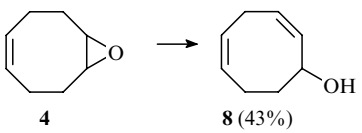
1 **5** (96%)



2 **6** (85%)



3 **7** (94%)



4 **8** (43%)

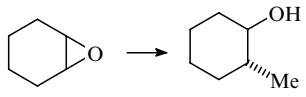
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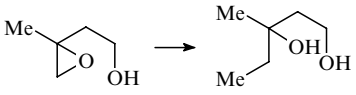
Presumably, the formation of allylic alcohols from epoxides follows a β-elimination mechanism.[1–3]

Ethylmagnesium- and isopropylmagnesium-*N*-cyclohexyl-*N*-isopropylamides behave in a similar way, whereas the use of phenylmagnesium-*N*-cyclohexyl-*N*-isopropylamide results in low yields of allylic alcohols.

On treatment with NMA, cyclohexene oxide (**9**) and 2-(2-hydroxyethyl)-2-methyloxirane (**10**) are converted into saturated alcohols **11** and **12**.[4] In this case, oxirane is attacked by the methyl anion formed from the reagent.



9 **11** (42%)

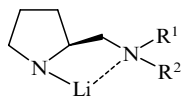


10 **12** (50%)

Smooth opening of the oxirane ring in labile epoxides of the oxylipin series containing carboxy and ester groups has also been effected using NMA.

b. Chiral lithium amides

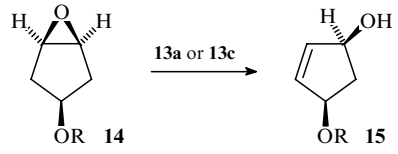
It has been shown [6,7] that oxides of cyclic and acyclic alkenes can be cleaved under the action of chiral lithium amides **13a**–**h** to give the corresponding optically active alcohols.



13a–**h**

R^1–R^2 = $(CH_2)_4$ (**a**), $(CH_2)_5$ (**b**), $(CH_2)_2O(CH_2)_2$ (**c**), $(CH_2)_2NMe(CH_2)_2$ (**d**), $R^1 = R^2$ = Et (**e**), Pr^i (**f**), R^1 = Et, $R^2 = Pr^i$ (**g**), R^1 = Bn, $R^2 = (CH_2)_2NBn_2$ (**h**).

For example, protected 3,4-epoxycyclopentanol (**14**) reacts with chiral lithium amides **13a** and **13c** to yield allylic alcohols **15** with a high enantiomeric excess (*ee* 89%–90%).[6]



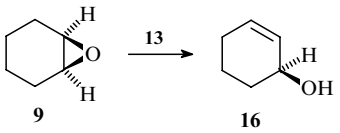
13a or **13c**

OR **14** OR **15**

R = THP (*ee* 90%) (THP is tetrahydropyran-2-yl), Bu^tMe_2Si (*ee* 89%).

Benzene, ether, toluene or THP can be used as solvents in this reaction (THF is the solvent of choice). This method has been used [8] in the synthesis of (−)-untenone A isolated from a sea sponge.

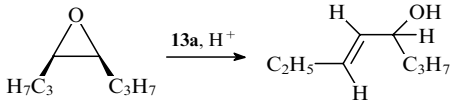
The transformation of epoxycyclohexane (**9**) on treatment with chiral lithium amides (**13a**,**b**,**d**–**h**) has been studied.[7,9] The enantiomeric excess of cyclohex-2-enol (**16**) varied from medium to high (40%–90%). The transformation of epoxycyclohexane was carried out in THF, ether, 1,2-dimethoxyethane (DME) and benzene; the best results were attained in THF.



9 **16**

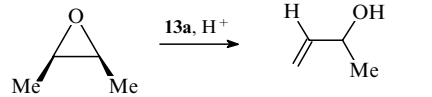
Amide **13**	Yield of **16** (%)	*ee* (%)
a	75–78	82–90
b	71	81
d	67	68
e	69	83
f	75	40
g	75	70
h	75	82

This reaction has also been carried out with symmetrical (*Z*)-4,5-epoxyoctane (**17**), which reacts with chiral lithium amide **13a** being converted into (*E*)-oct-5-en-4-ol (**18**) in 52% yield.[7] The yield of alcohol **18** can be increased to 60% by using additives, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

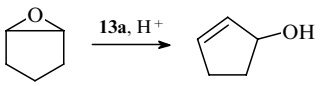


17 **18** (66%, *ee* 60%)

(*Z*)-2,3-Epoxybutane (**19**) and epoxycyclopentane (**20**) behave in a similar way being converted into compounds **21** and **22**.

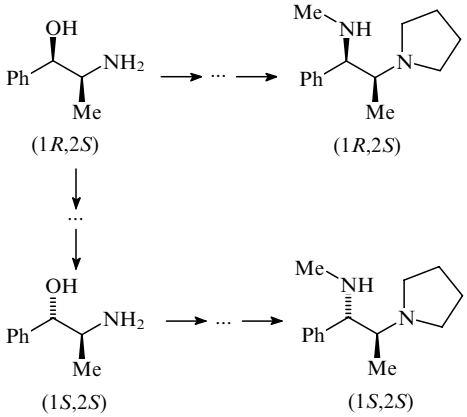


19 **21** (60%, *ee* 72%)



20 **22** (53%, *ee* 41%)

Colman *et al.*[10] used chiral diamines prepared on the basis of (1*R*,2*S*)- and (1*S*,2*S*)-norephedrine for opening of the oxirane ring.



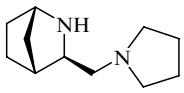
(1*R*,2*S*) (1*R*,2*S*)

(1*S*,2*S*) (1*S*,2*S*)

Opening of the oxirane ring in 4-amino-1,2-epoxycyclopentane under the action of chiral lithium amide obtained from (2*S*,3*aS*,7*aS*)-2-pyrrolidinomethyloctahydroindole has been reported.[11] A (1*S*,4*R*)-4-aminocyclopent-2-enol derivative has been synthesised with an enantiomeric excess of ~90%. O'Brien *et al.*[12] have used (*R*)-*N*-methyl-l-phenyl-2-pyrrolidinoethylamine to cleave the oxirane ring in the substituted epoxycyclopentane

(the enantiomeric excess of the alcohol was 60%). Several more examples of using chiral lithium amides for the synthesis of optically active compounds from prochiral epoxides have been reported.[13]

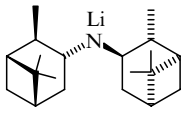
Using a large number of examples, Andersson and co-workers[14–16] have demonstrated efficient use of catalytic amounts of chiral diamines **23** and their derivatives for enantioselective transformation of *meso*-epoxides of cyclic and alicyclic olefins into optically active allylic alcohols.



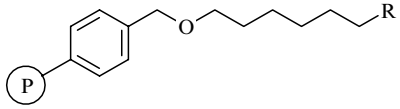
23

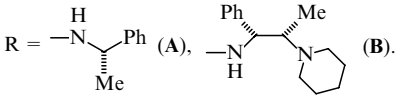
The reaction should be carried out in the presence of stoichiometric amounts of lithium diisopropylamide and up to 5 equiv. of DBU. Subsequently, it has been shown that this system of reagents is suitable for kinetic resolution of racemic epoxides (only one enantiomer reacts and, hence, the racemate is resolved).[17]

A recent study[18] describes the synthesis of chiral cyclohex-2-enol (**16**) from *meso*-epoxycyclohexane (**9**) with the use of chiral lithium amide.



Johansson *et al.*[19] performed cleavage of the oxirane ring in epoxycyclohexane on treatment with chiral lithium amides formed from amines attached to a polymeric support.





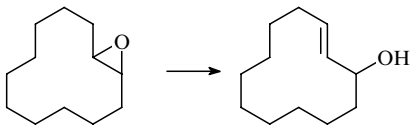
It was shown that immobilisation of ligand **A** on a support results in a markedly higher reaction enantioselectivity: the enantiomeric excess of (*S*)-**16** increases from 19% to 81%. Meanwhile, immobilisation of ligand **B** did not result in a desired increase in the enantioselectivity; conversely, the *ee* value decreased from 93% to 70%.

Thus, the above results demonstrate that chiral lithium amides are valuable reagents for the synthesis of chiral allylic alcohols from *meso*-epoxides of various structures.

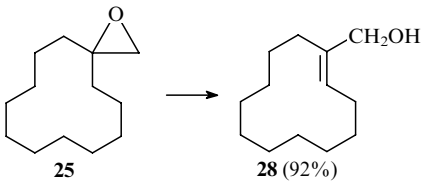
c. Organoaluminium amides

The behaviour of organoaluminium amides in the transformation of epoxides into allylic alcohols differs somewhat from the behaviour of lithium dialkylamides. Aluminium derivatives have a relatively low basicity and a higher Lewis acidity; therefore, they are mainly coordinated to the oxygen atom of the epoxide ring. The subsequent proton elimination from the α-position takes place within this complex.[20]

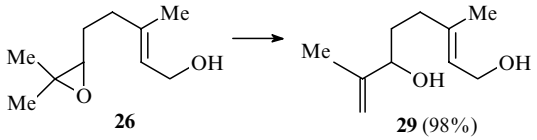
Diethylaluminium 2,2,6,6-tetramethylpiperidide (DATMP) is the most promising reagent. Using this compound, oxiranes **24**–**26** were converted into allylic alcohols **27**–**29** in very high yields.



24 **27** (99%)



25 **28** (92%)

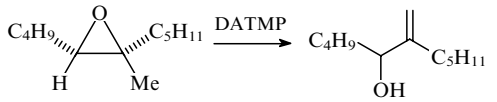


26 **29** (98%)

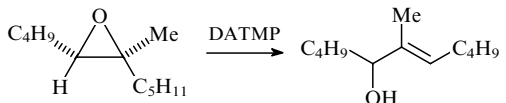
Benzene and hexane are the solvents of choice for the transformations of oxiranes into allylic alcohols on treatment with organoaluminium amides, because these solvents do not solvate aluminium amides. In ether, these reactions proceed in lower yields, while in THF, they barely take place. Other diethylaluminium amides Et_2AlNR_2 (R = Et, Pr^i, cyclo-C_6H_{11}) can also be used for converting oxiranes into allylic alcohols, but the reaction rates are markedly lower than that in the case of DATMP.

cis-Cyclododecene oxide reacts very slowly with DATMP, the corresponding allylic alcohol being formed in a low yield (~8%). Cycloalkene oxides with 5 to 8 carbon atoms in the ring do not react with DATMP.[20]

The structures of the allylic alcohols formed from oxiranes under the action of DATMP depend on the oxirane stereochemistry. For example, the transformation of *Z*-oxirane **30** gave methylene-type allylic alcohol **31** in 96% yield, while *E*-oxirane **32** was converted into allylic alcohol **33** with an internal double bond (yield 83%).[20]



30 **31** (96%)

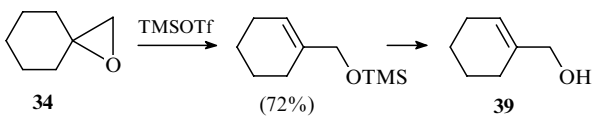


32 **33** (83%)

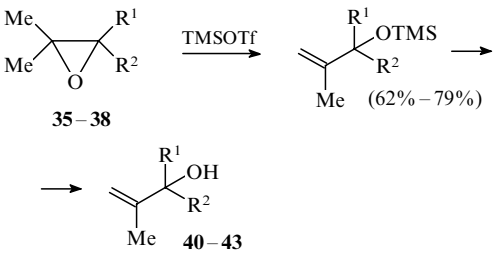
This reaction pattern is due to the fact that aluminium amides preferentially abstract the α-proton from the alkyl group that is located on the same side of the oxirane molecule as the hydrogen atom, because the aluminium-containing reagent attacks the substrate from the sterically less hindered side of the ring. This gives preferentially the allylic alcohol with the *E*-configured double bond.

d. Trimethylsilyl trifluoromethanesulfonate

Noyori and co-workers[21] have proposed the trimethylsilyl triflate (TMSOTf)–amine (DBU or lutidine) system for transformation of oxiranes into allylic alcohols. Trimethylsilyl triflate, which is a weak Lewis acid, activates the epoxide fragment; as a result, the amine basicity becomes sufficient for eliminating the hydrogen atom from the α-position relative to the oxirane ring. The reaction is carried out in benzene or toluene. The target allylic alcohols are formed initially as trimethylsilyl ethers. The trimethylsilyl group is removed by treatment with dilute hydrochloric acid or potassium fluoride in methanol. For example, oxiranes **34**–**38** were converted into allylic alcohols **39**–**43**.



34 (72%) **39**



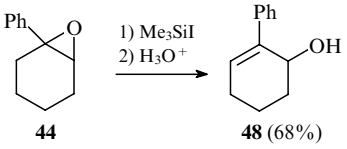
35 – 38 **40 – 43** (62% – 79%)

$R^1 = R^2 = H$ (**35**, **40**), Me (**36**, **41**); $R^1 = H$: $R^2 = CH(Me)CH_2C(O)Me$ (**37**, **42**), $(CH_2)_2CH(Me)CH_2CO_2Me$ (**38**, **43**).

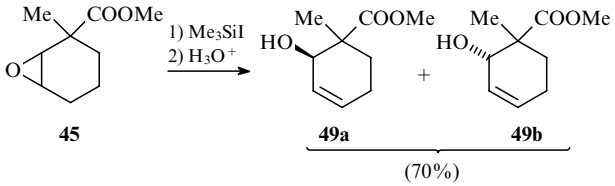
The method has some limitations, in particular, it is inapplicable to the synthesis of allylic alcohols from mono- and 2,3-dialkyl-substituted oxiranes.

e. Trialkylsilyl iodides

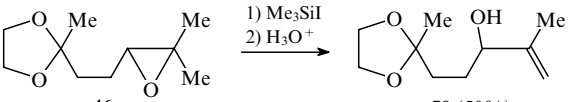
The transformation of epoxides **44** – **47** into allylic alcohols **48** – **51** under the action of iodotrimethylsilane and 1,5-diazabicyclo[4.3.0]non-5-ene has been reported.[22]



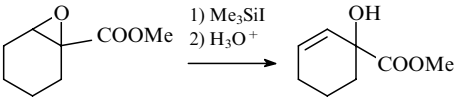
44 **48** (68%)



45 **49a** **49b** (70%)

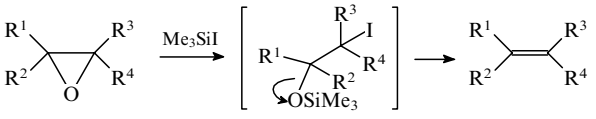


46 **50** (50%)

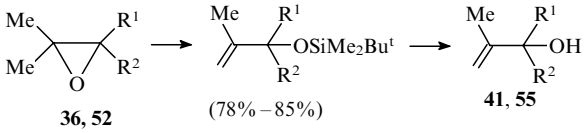


47 **51**

Allylic alcohols **48** – **50** were prepared in satisfactory yields (alcohol **51**, in a low yield). Triethylamine and diisopropylethylamine proved to be much less effective dehydrohalogenating agents than DBN. The reactions were carried out in acetonitrile. The initial ring opening in the epoxide rapidly occurs at room temperature, but dehydrohalogenation of the intermediate iodohydrin is completed only after heating the reaction mixture to the boiling point of the solvent. It is noteworthy that the ester and the ketal functional groups remain intact during the reaction, although they are known [23] to be reactive towards iodotrimethylsilane. In view of the mild reaction conditions, the ready accessibility of the reagents and the simple workup procedure for the reaction mixture, this method can make a good alternative to the Noyori method described above,[21] although the product yields are somewhat lower in this case, due to the formation of side deoxygenation products.

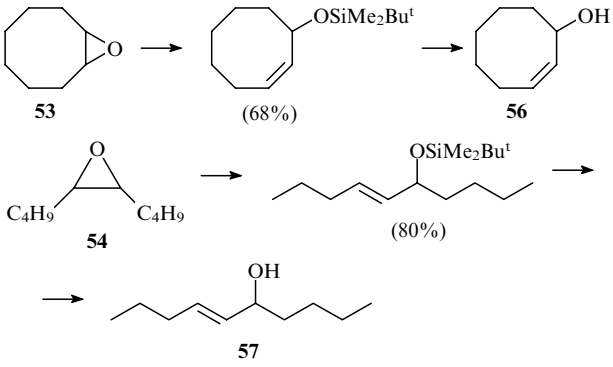


In the case of substituted oxiranes, the formation of deoxygenation products can be avoided by using Bu^tMe_2SiI in place of Me_3SiI;[24] however, this complicates somewhat the cleavage of the silyl ethers. This strategy was used to transform oxiranes **36** and **52** – **54** into the corresponding *tert*-butyl dimethylsilyl ethers in good yields. The protective group was removed by treatment of the ethers with tetraalkylammonium fluoride in moist DMSO or THF, or with potassium fluoride in the presence of catalytic amounts of 18-crown-6 ether; unsaturated alcohols **41** and **55** – **57** were thus liberated.



36, 52 (78% – 85%) **41**, **55**

$R^1 = R^2 = Me$ (**36**, **41**); $R^1 = H$, $R^2 = Et$ (**52**, **55**).



53 (68%) **56**

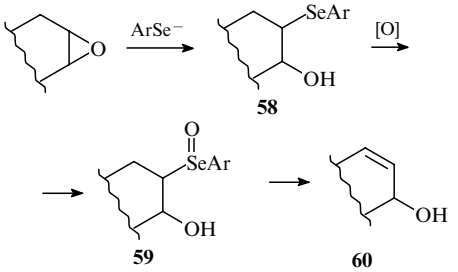
54 (80%)

57

The mechanism of the reaction of silyl iodides with oxiranes is not entirely clear.[25 – 27] The reaction furnishes a mixture of products of deoxygenation and ring opening (both silylated and non-silylated ones).

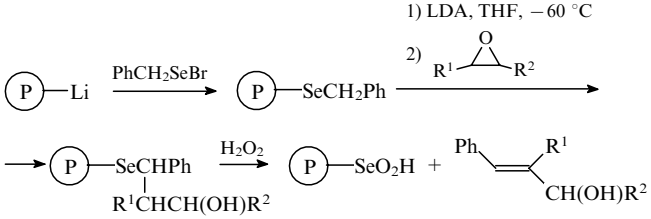
f. Selenols

The salts of selenols (usually, areneselenols) generated by various procedures easily cleave the epoxide ring giving rise to β-hydroxy selenides **58**.[28] Treatment of these products with mild oxidants gives selenium oxides **59**, which spontaneously split off ArSeOH with elimination of only the hydrogen atom located on the opposite side of the chain with respect to the oxygen function. This affords allylic alcohols **60**.[28] Most often, the products are formed in good yields.



58 **59** **60**

The use of polystyrene-immobilised selenides for opening of the oxirane ring has been documented.[29]

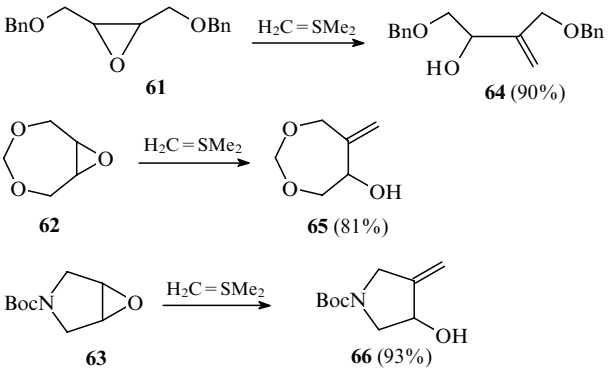


$R^1 = H$: $R^2 = Me$ (85%), Ph (86%), $PhOCH_2$ (84%);
$R^1 – R^2 = (CH_2)_4$ (77%).

g. Dimethylsulfonium methylide

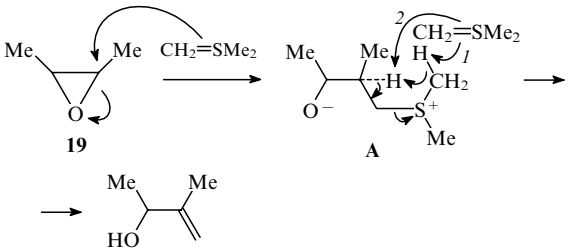
Dimethylsulfonium methylide (DMSM, Corey's reagent) represents a special case among the reagents considered in this Section. This compound reacts with epoxides C_n to give homological allylic alcohols C_{n+1}. Evidently, DMSM serves as the source of an additional carbon atom.[30,31] Since the oxidation state of the starting compound does not change upon the reaction, this reaction should be classified as isohypsic.

Treatment of *cis*-epoxides **61**–**63** with excess DMSM gave allylic alcohols **64**–**66** in very high yields.[32]



Noteworthy is the high chemoselectivity of this reaction: only the *cis*-isomers are cleaved, whereas the *trans*-isomers remain intact. Thus, the *cis*- and *trans*-isomers of the epoxides can be easily separated in this way. This method is widely used in the synthesis of natural products containing a fragment of 1,2-disubstituted allylic alcohol.

The reaction mechanism has been considered in relation to the cleavage of (*Z*)-2,3-epoxybutane (**19**). The nucleophilic addition of DMSM to epoxide **19** yields betaine intermediate **A**, which undergoes β-elimination of dimethyl sulfide. The elimination may follow either pathway *1* or pathway *2*. Both lead to the same allylic alcohol.



2. Reduction of epoxides, resulting in allylic alcohol

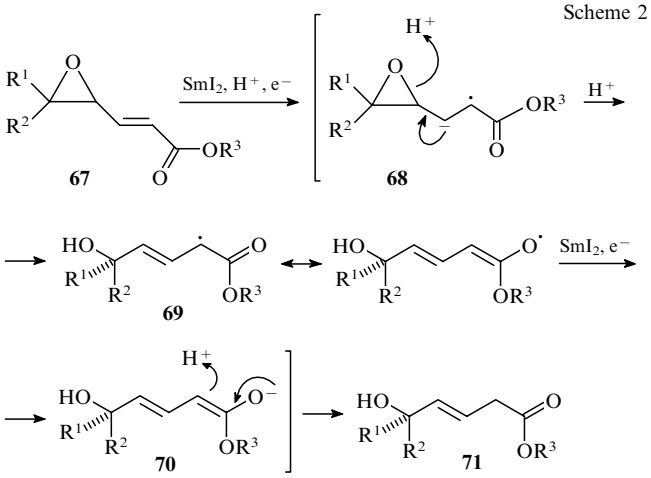
As noted above, oxiranes and allylic alcohols occur in the same oxidation state. Therefore, the reduction reactions considered in this Section are applied to epoxides that contain additional functional groups. The reducing reagents can be subdivided into two groups, *i.e.*, proper reductants and carbanionic synthons.

a. Samarium diiodide

It has been found[33] that treatment of functionalised vinyl-substituted oxiranes **67** with samarium diiodide in THF in the presence of a proton donor induces reductive opening of the oxirane ring, while functional groups such as keto, ester and nitrile groups remain intact. The reaction proceeds at a high rate at −90 °C and is complete, most often, over a period of five minutes.

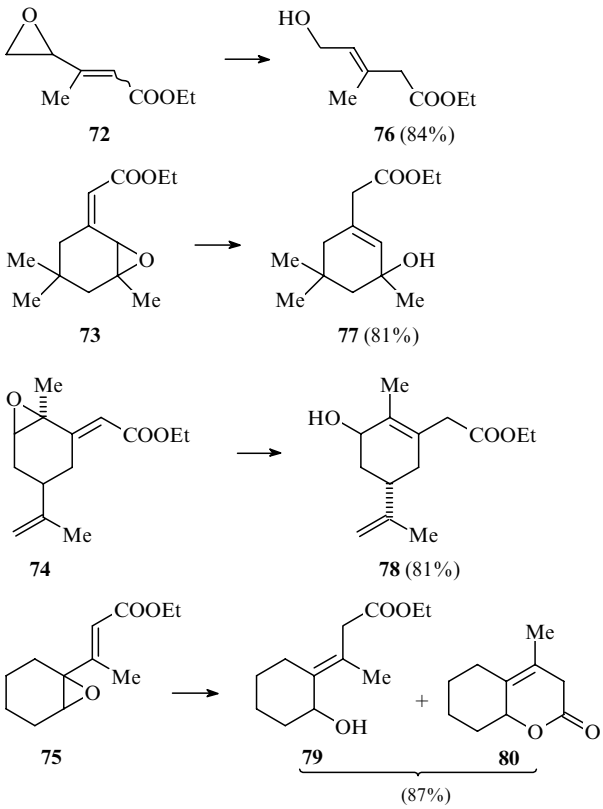
The reaction mechanism (Scheme 2) includes the formation of radical anion **68**, which adds a proton, being converted into radical **69** containing an ester group. This compound isomerises to a conjugated radical, which produces conjugated dienolate **70** upon the addition of an electron. Regioselective protonation of dienolate **70** furnishes β,γ-unsaturated carbonyl compound **71**.

Scheme 2

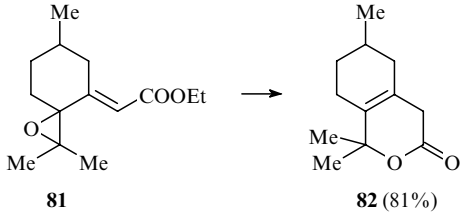


Since the reaction occurs in a nearly neutral medium, no shift of the equilibrium towards the conjugated isomer **70** is observed.

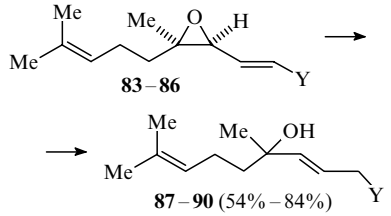
The reactions of epoxides **72**–**75** with samarium diiodide gave allylic alcohols **76**–**79** in very high yields.



In addition to allylic alcohol **79**, cleavage of epoxide **75** yields lactone **80** (the ratio **79** : **80** = 1 : 1). In the case of epoxide **81**, the formation of 'allylic' lactone **82** becomes the predominant reaction route.

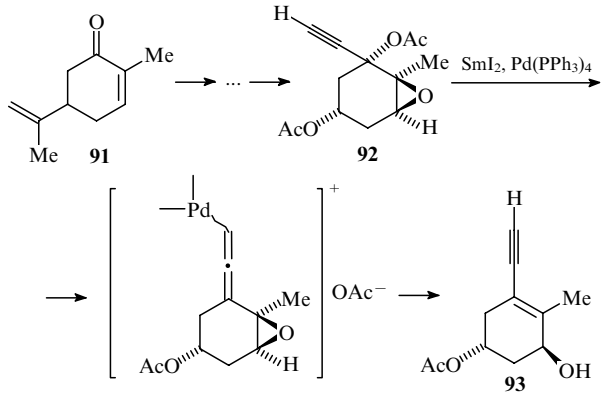


Apart from epoxides with ester groups, unsaturated epoxides with other electron-withdrawing groups can also participate in these reactions. Thus epoxides **83**–**86** were converted into allylic alcohols **87**–**90**.[33]



Y = COSEt (**83**, **87**), SO_2Ph (**84**, **88**), SPh (**85**, **89**), $PO(OEt)_2$ (**86**, **90**).

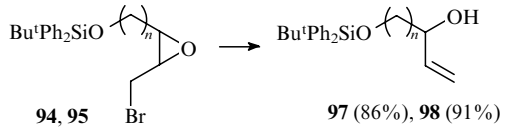
Okamura *et al.*[34] reported the synthesis of allylic alcohols from carvone (**91**) using samarium diiodide. Treatment of epoxy diacetate **92** with two equivalents of samarium diiodide and $Pd(PPh_3)_4$ in the absence of a proton donor yielded allylic alcohol **93**.



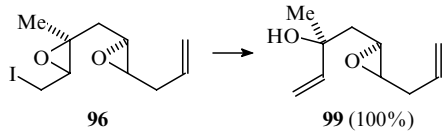
Thus, the reactions of samarium diiodide with epoxides constitute a promising method for the synthesis of diverse functionally substituted allylic alcohols. The use of chiral unsaturated epoxides in this reaction opens up the way to the synthesis of optically active compounds.

b. The reduction of α-haloepoxides catalysed by metal compounds

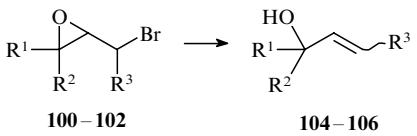
Epoxy halides **94**–**96** containing halogen atoms in the α-position to the oxirane ring react with sodium iodide and zinc dust in boiling methanol to give allylic alcohols **97**–**99** in high yields.[35] This strategy is used to prepare pure enantiomers by Sharpless asymmetric epoxidation of olefinic precursors.[36]



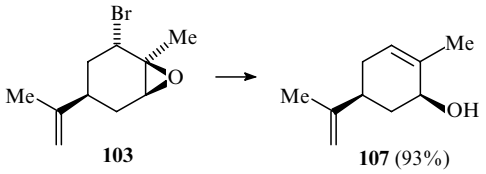
n = 1 (**94**, **97**), 2 (**95**, **98**)



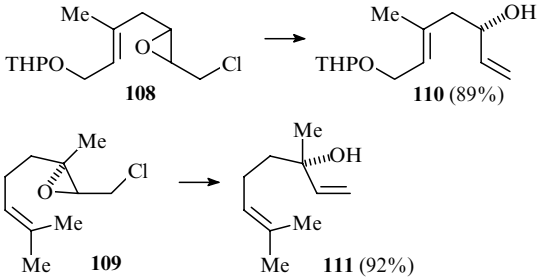
The same results were obtained upon the reduction of α-bromoepoxides **100**–**103** with a zinc/copper couple under sonochemical conditions.[37] The yields of allylic alcohols **104**–**107** were satisfactory. This method is applicable to oxirane ring opening not only in primary but also in secondary epoxy bromides.



Compound	R^1	R^2	R^3	Yield of alcohol (%)
100, **104**	Alk	Me	H	94
101, **105**	H	Ph	H	95
102, **106**	H	Ph	Me	93



n-Butyllithium can also be used for the reductive cleavage of the oxirane ring in α-haloepoxides. By treatment of α-haloepoxides **103**, **108** and **109** with this reagent, allylic alcohols **107**, **110** and **111**, respectively, have been prepared.[35]

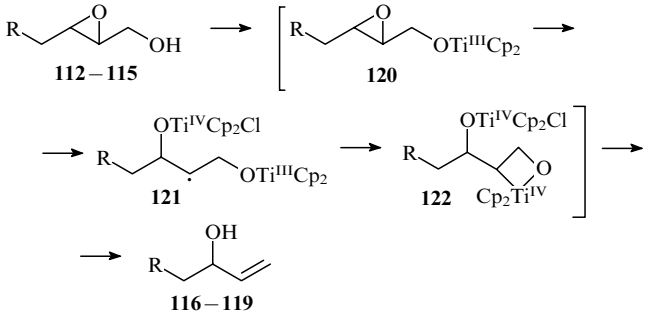


The reactions were carried out at −23 °C. In this case, the organolithium compound functions as a reducing agent rather than a C-nucleophile.

c. Bis(cyclopentadienyl)titanium chloride

It has been found[38] that α-hydroxyepoxides **112**–**115** react with Cp_2TiCl to give allylic alcohols **116**–**119** in good yields. Presumably, the reaction involves the intermediate formation of species **120**–**122** (Scheme 3).

Scheme 3



Compound	R	Yield of alcohol (%)
112, **116**	Bu	82
113, **117**	EtCH=CH	85
114, **118**	$CH_2=CH(CH_2)_2$	85
115, **119**	OBn	91

It is significant that the chirality of the starting epoxides at the 3-position is fully retained in allylic alcohols.

The starting optically active 2,3-epoxy alcohols are usually prepared by Sharpless asymmetric epoxidation[36] of isomeric allylic alcohols. Thus, the epoxidation–Cp_2TiCl reduction sequence represents a convenient protocol of an asymmetric

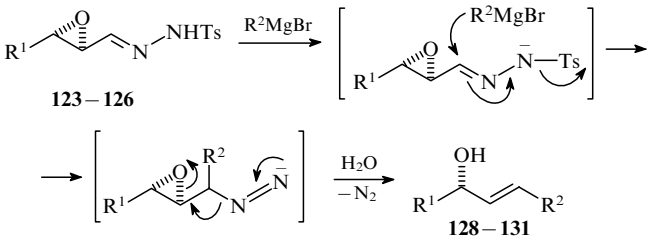
allylic rearrangement, which may yield multipurpose chiral synthons.[39]

The reagent Cp_2TiCl has also been used[40] to reduce vinylic epoxides to allylic alcohols.

d. Alkylmagnesium bromides

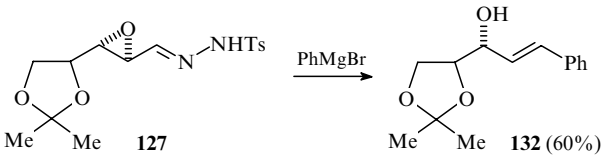
The Section deals with epoxide ring opening under the action of reagents serving as sources of additional carbon atoms.

As a further development of the research into alkylation of tosylhydrazones accompanied by elimination,[41] it has been shown[42] that α-epoxyaldehyde tosylhydrazones **123**–**127** can be converted into allylic alcohols **128**–**132** *via* the reaction with alkylmagnesium bromides.



123–**126** **128**–**131**

Epoxide	R^1	R^2	Alcohol	Yield (%)
123	n-C_7H_{15}	Et	**128a**	66
		Bu	**128b**	68
		Ph	**128c**	58
124	OBn	Et	**129a**	64
		Bu	**129b**	65
		Ph	**129c**	70
125	Ph	Et	**130a**	62
		Bu	**130b**	65
126	$CH_2=CH(CH_2)_8$	Et	**131a**	71

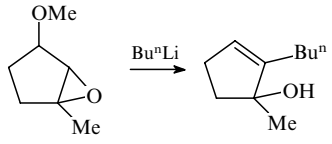


127 **132** (60%)

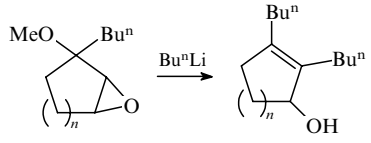
This reaction is also suitable for the preparation of optically active substances; for this purpose, the starting epoxy aldehydes are prepared by Sharpless asymmetric epoxidation.[43]

e. Organolithium compounds

Treatment of bicyclic α-methoxyepoxides **133**–**136** with various organolithium reagents leads to allylic alcohols **137**–**140**.[44]

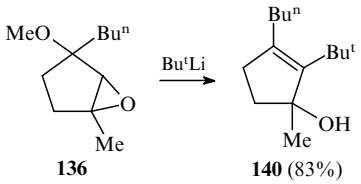


133 **137** (88%)



134, **135** **138** (85%), **139** (76%)

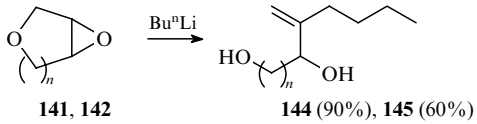
n = 1 (**134**, **138**), 2 (**135**, **139**).



136 **140** (83%)

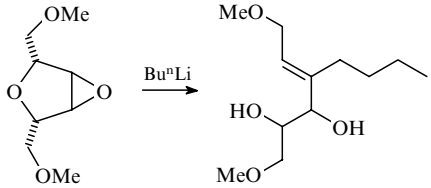
The reaction includes the formation of a carbene-like intermediate from the metallated oxirane followed by the insertion of alkyllithium and elimination of MeOLi.

Similar reactions involving 3,4-epoxydihydrofurans (**141**) and -pyrans (**142**) and derivative **143** result in diols **144**–**146**, containing an allylic alcohol fragment.[45]



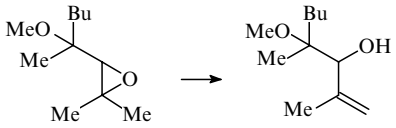
141, **142** **144** (90%), **145** (60%)

n = 1 (**141**, **144**), 2 (**142**, **145**).



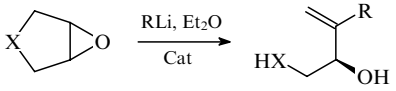
143 **146** (90%)

It is noteworthy that acyclic substrate **147** does not react to give the carbenoid, but is converted instead into the classical β-elimination product **148**.

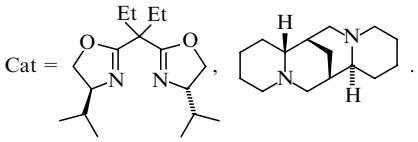


147 **148** (89%)

Hodgson *et al.*[46] reported the synthesis of unsaturated diols and amino alcohols containing an allylic alcohol fragment by cleavage of five- and three-membered heterocycles in the corresponding 3,4-epoxydihydrofurans and -pyrroles upon the reaction with alkyllithium in the presence of chiral diamines (Cat).

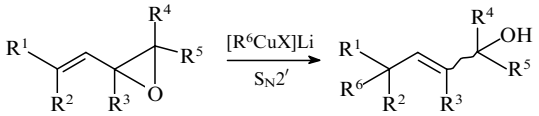


X = O, NSO_2Bu^t; R = Bu^n, Pr^i;

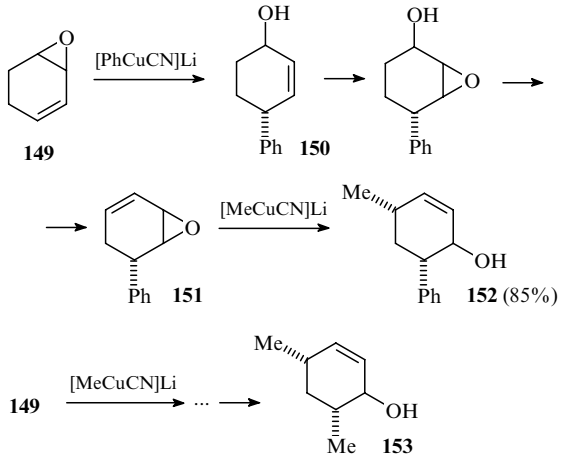


f. Lithium alkylcyanocuprates

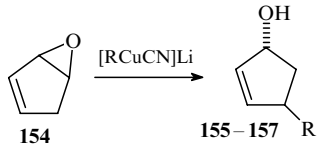
Yet another method for the preparation of allylic alcohols is based on the reaction of vinylic epoxides with lithium organocuprates. A review by Marshall[47] contains numerous examples of opening of the oxirane ring in vinyloxiranes by means of these reagents.



Thus the reaction of epoxycyclohexene **149** with lithium phenylcyanocuprate gives allylic alcohol **150** in a high yield. Alcohol **150** can be converted into the vinylic epoxide **151**, which is made to react with lithium methylcyanocuprate. This sequence of reactions can give allylic alcohol **152**.[48] If lithium methylcyanocuprate is used in the first step instead of phenylcyanocuprate, allylic alcohol **153** containing two methyl groups is formed.

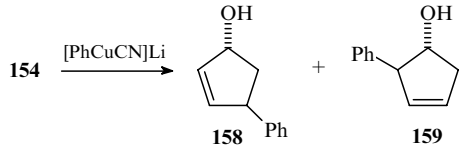


The readily available epoxycyclopentene **154** can also be involved in this reaction; allylic alcohols **155**–**157** were prepared by treatment of **154** with various alkylcyanocuprates.[49]



R = Bu^n (**155**, 95%), Bu^t (**156**, 88%), Me (**157**, 78%).

A similar reaction of lithium phenylcyanocuprate with epoxide **154** is non-regioselective and yields a mixture of isomeric phenylcyclopentenols **158** and **159** in 2 : 1 ratio and in an overall yield of 50%.

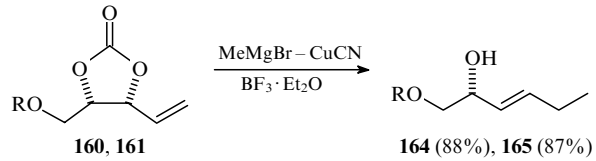


It was found that alkylcyanocuprates obtained from stabilised carbanions react with epoxycyclopentene **154** to give desired allylic alcohols in a low yield (17%). For example, with the use of cyanocuprate [Bu_3SnCH_2CuCN]Li, the yield of the alcohol does not exceed 5%.[48]

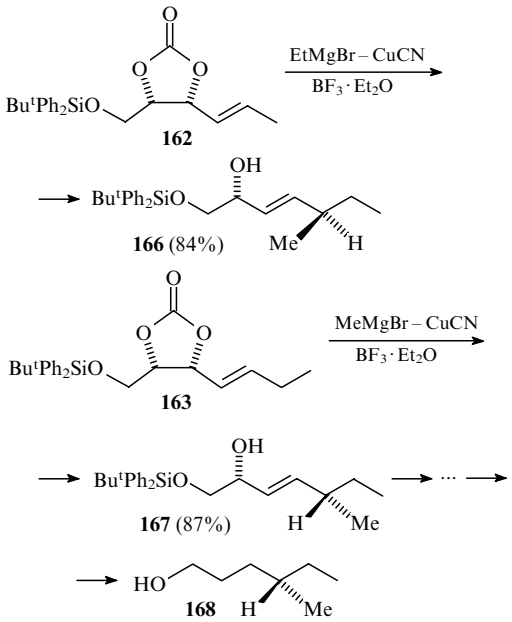
g. Synthesis of allylic alcohols from cyclic vinyl carbonates

This route is similar to the above-described method of synthesis of allylic alcohols from vinylic epoxides. Both reactions include a nucleophilic attack by the reagent on the double bond rather than on the centre bearing the leaving group (S_N2' mechanism).[50–52]

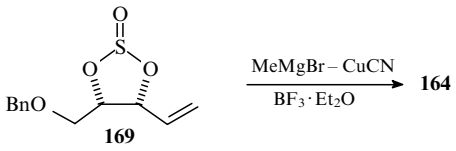
It was found[53] that many cyclic carbonates **160**–**163** react with organic cuprates [RCuCN]Li, [RCuCN]MgBr, RMgBr–CuI (Cat) (R = Me, Et, Bu^n) in the presence of $BF_3 \cdot Et_2O$ giving rise to alkylated (*E*)-allylic alcohols **164**–**167** with very high diastereoselectivities.



R = Bn (**160**, **164**), Bu^{t}Ph$_2$Si (**161**, **165**).



The configuration of the new stereocentre in molecule **167** was confirmed by transforming it into the known (*S*)-(+)-4-methylhexan-1-ol (**168**).[54] Cyclic sulfite **169** reacts with the MeMgBr–CuCN system in the presence of $BF_3 \cdot Et_2O$ in a similar way; the yield of the (*E*)-allylic alcohol **164** is 66%.



3. Miscellaneous methods for the synthesis of allylic alcohols from epoxides

To complete the Section, it is pertinent to mention some other methods used to prepare allylic alcohols from epoxides. Feringa and co-workers[55] have used the dialkylzinc–copper(II) triflate–chiral phosphoramidite system for oxirane ring opening in epoxides; this gave chiral alcohols. This procedure provided kinetic resolution of vinyloxirane isomers containing six- or seven-membered rings with *ee* values above 90%.[56] More detailed information on this topic is available from a review.[57] A recent publication[58] reports the reaction of phenylsulfonyl-substituted vinyl epoxides with various aromatic molecules (benzene, anisole, pyrrole, thiophene) in the presence of boron trifluoride etherate to give sulfonyl-containing allylic alcohols (Friedel–Crafts reaction).

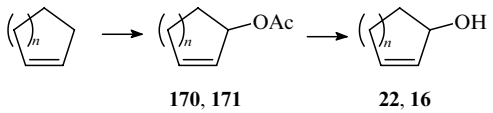
III. Reagents for allylic oxidation

α-Oxidation of alkenes represents yet another strategy for the preparation of allylic alcohols. Below we consider the reagents used for this purpose.

1. Manganese(III) acetate in acetic acid

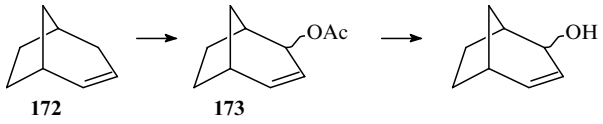
Alkenes are oxidised with manganese(III) acetate in acetic acid in the presence of metal halides to give allylic acetates,[59] which are readily transformed into allylic alcohols. For example, cyclopentene and cyclohexene can be converted into cyclopent- and cyclohex-2-enyl 3-acetates (**170**, **171**) in very good yields; hydrolysis of the acetates affords the corresponding alcohols **22** and **16**. Bicyclo[3.2.l]oct-2-ene (**172**) reacts with manganese acetate in a similar way to give acetate **173** in a good yield. Dihydronaphthalenes **174** and **175** were converted into acetates **176** and **177** but

the product yields were low.† Norbornene does not react with Mn(III) acetate. Manganese(III) acetate can be replaced by palladium,[60] thallium(III)[61] and lead[32] acetates.

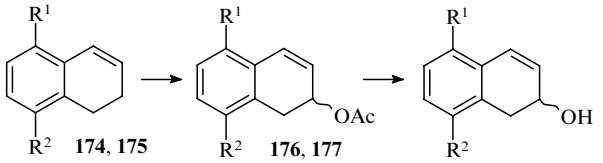


170, **171** **22**, **16**

n = 1 (**170**, **22**), 2 (**171**, **16**).



172 **173**



174, **175** **176**, **177**

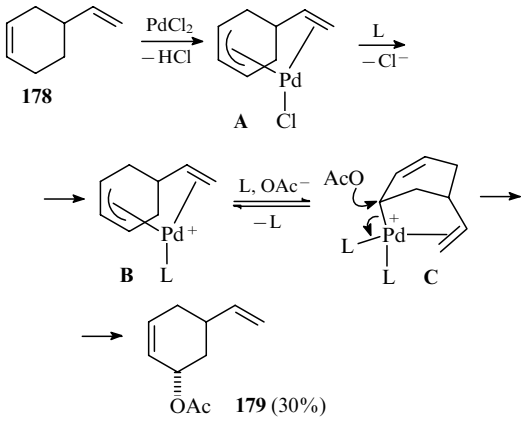
R^1 = R^2 = Me (**174**, **176**), R^1 = H, R^2 = OMe (**175**, **177**).

It has been suggested that alkene oxidation involves the initial abstraction of a hydrogen atom to give a radical, which is rapidly oxidised to give allylic acetate. It is worth noting that this reaction gives good product yields for simple alkenes, whereas in the case of bicyclic alkenes, the yields of allylic acetates are not satisfactory.

2. Acetoxylation of vinylcycloalkenes in the presence of $PdCl_2$

Wagell and co-workers[62] reported the transformation of 4-vinylcyclohexene (**178**) into allylic acetate **179** upon the reaction with $CuCl_2$ or the $CuCl_2$ – LiCl – O_2 system in the NaOAc – AcOH medium in the presence of palladium chloride as a catalyst and an excess of triphenylphosphine (or bisphosphine $Ph_2PCH_2.CH_2PPh_2$) (Scheme 4). Despite variation of the reaction conditions, the yield of allylic acetate was low.

Scheme 4



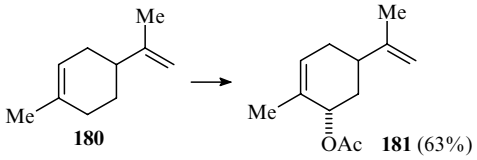
178 **A** **B** **C** **179** (30%)

The formation of compound **179** as the *trans*-isomer and high regioselectivity of the reaction can be explained in terms of the homogeneous catalysis mechanism. The reaction proceeds *via* intermediates **A** – **C**.

A model study has shown that the reaction route is determined by steric and stereoelectronic effects. The reasons for the formation of particularly the *trans*-isomer of compound **179** are related to the fact that triphenylphosphine (L), present in excess, blocks the metal atom in intermediate **C** and, hence, the weaker acetate ligand can approach the substrate only from the 'outside'.[63, 64]

In conformity with the proposed mechanism, the reaction stereochemistry is dictated by the vinyl group in compound **178**, and the phosphine ligand seems to be necessary for stabilisation of intermediate species **B** and **C**.

This reagent was also used to convert limonene (**180**) into allylic acetate **181**.[62]

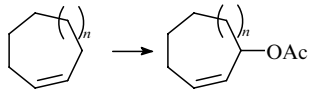


180 **181** (63%)

In this case, in view of the enhanced nucleophilicity of the vinyl group in limonene, acetoxylation can be carried out without a phosphine ligand.

3. Acetoxylation with palladium acetate-containing systems

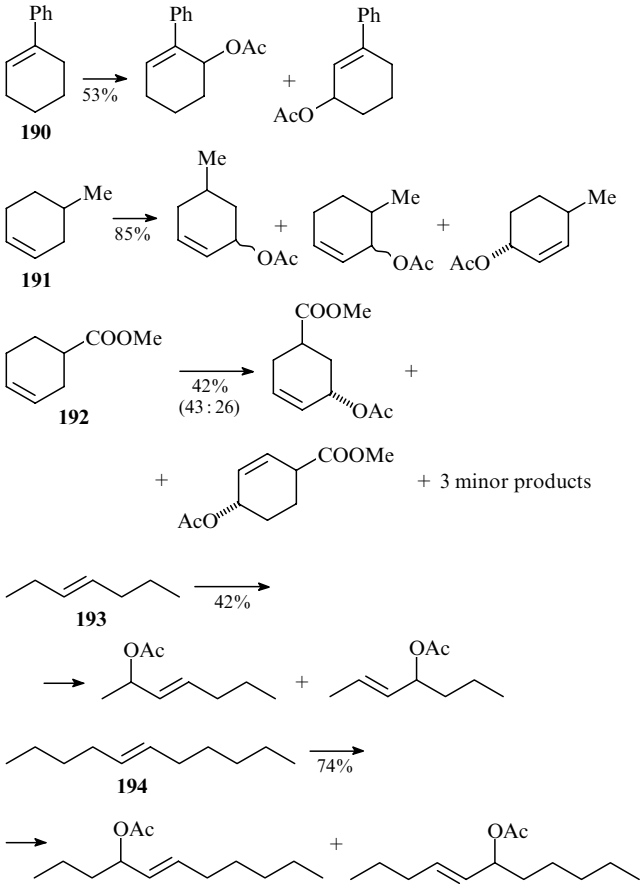
Allylic acetoxylation of alkenes and cycloalkenes by treatment with palladium acetate in the presence of magnesium dioxide (oxidant) and benzoquinone (co-oxidant) in acetic acid has been reported.[65] This procedure was used to transform cycloalkenes **182** – **185** into the corresponding acetates **186** – **189** (in the case of cyclooctene **183**, the yield of allylic acetate **187** is moderate).



182 – **185** **186** – **189**

n = 1 (**182, 186**, 73%), 2 (**183**, **187**, 35%), 4 (**184**, **188**, 78%), 6 (**185**, **189**, 72%).

Asymmetrical alkenes, for example **190** – **194**, are also converted into the corresponding allylic acetates; the total yields of products are quite high but they are formed as isomer mixtures.



190 **191** **192** **193** **194**

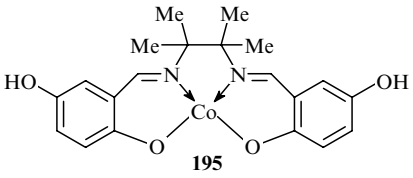
Study of the reaction mechanism has shown that allylic acetoxylation either follows the 1,2-acetoxypalladation mecha-

† A K Banerjee, W J Vera, J A Azocar, unpublished data.

nism with subsequent β-elimination of palladium hydride or involves the formation of an alkene-η^3-allylic complex, which is subjected to a nucleophilic attack by the acetate. The contributions of both mechanisms depend on the alkene structure. For simple alkenes, the η^3-allylic mechanism is relatively unlikely.

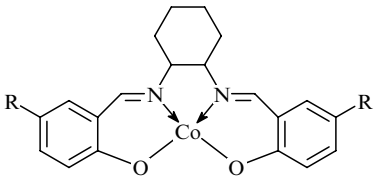
Bystroem *et al.*[66] has performed allylic acetoxylation of alkenes by a procedure similar to that described in another study,[65] but using oxygen instead of MnO_2 and hydroquinone instead of benzoquinone. The reaction was carried in the presence of copper(II) acetate. Copper acetate can be replaced by manganese(III) or cobalt(II) acetate, although these are less efficient. Palladium acetate is an obligatory component; otherwise, the target product is not formed. The reaction rate increases with an increase in the amount of hydroquinone and does not change upon the replacement of hydroquinone by benzoquinone (in the latter case, the induction period almost disappears).

Instead of the hydroquinone (or benzoquinone)–copper acetate system, the reaction can be carried out with complex **195**, which contains a hydroquinone fragment.



195

Acetoxylation of cyclohexene in the presence of complex **195** furnishes cyclohexenyl acetate **171** in 90% yield. The reaction occurs somewhat more slowly than with the copper acetate–hydroquinone system. The use of complexes **196** and **197** with similar structures affords acetate **171** in 68 and 19% yields, respectively. If the reaction is carried out in the presence of a mixture of compound **197** (5 mol %) and hydroquinone (10 mol %), the yield of product **171** increases to 80%.



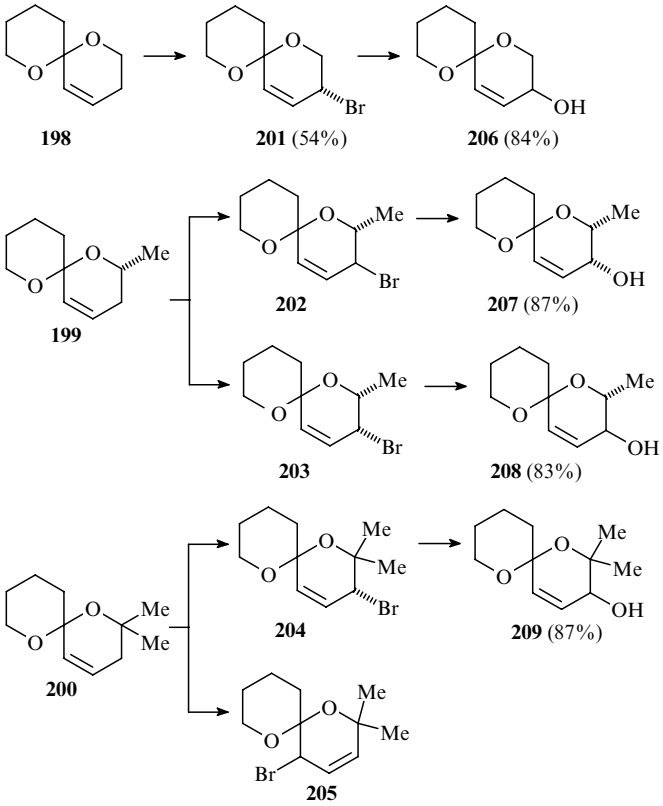
R = OH (**196**), H (**197**).

It is noteworthy that the acetoxylation of cycloalkenes we discuss has not been adequately studied (it has not been tested for all types of alkenes).

The acetoxylation of cyclohexene in the presence of system comprising 5 mol % of palladium acetate, 5 mol % of iron(III) nitrate and acetic acid under an oxygen atmosphere has been reported.[67] Cyclohexenyl acetate was obtained in a high yield (under an argon atmosphere, the acetate is formed in a low yield).[67] The addition of transition metal chlorides or acetates decreases the yield. The introduction of acetic anhydride results in a higher reaction rate. Non-symmetric 1-, 3 and 4-methylcyclohexenes are oxidised by palladium acetate or iron(III) nitrate giving rise to a mixture of isomeric products.

4. *N*-Bromosuccinimide

Brimple *et al.*[68] have developed an efficient method for the introduction of a hydroxyl group into the allylic position of unsaturated spiroketals using *N*-bromosuccinimide. Allylic bromination of unsaturated spiroketals with *N*-bromosuccinimide in tetrachloromethane furnishes bromo-derivatives containing an axial bromine atom. On treatment of these products with KO_2 and 18-crown-6 ether in a THF/DMSO mixture (10 : 1), the Br atom is replaced by an OH group by the S_N2 mechanism to give the alcohol with an equatorial hydroxyl group. This method was used to convert spiroketals **198**–**200** into bromo-derivatives **201**–**205**, which were then transformed into allylic alcohols **206**–**209**. It was found that allylic bromination of spiroketals **199** and **200** gives mixtures of isomeric products and bromide **205** does not enter into the substitution reaction to give the alcohol.



198 **201** (54%) **206** (84%)

199 **202** **207** (87%)

203 **208** (83%)

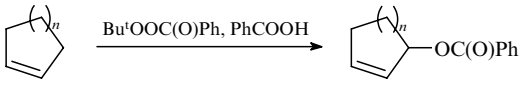
200 **204** **209** (87%)

205

Bernet *et al.*[69] have oxidised a bicyclic spiroketal at the allylic position by selenium dioxide.

5. *tert*-Butyl peroxybenzoate

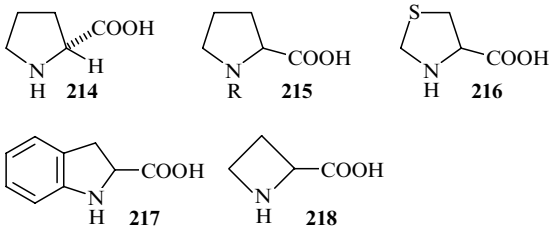
Acyloxylation of alkenes with $Bu^tOOC(O)Ph$ or Bu^tOOH and carboxylic acids RCOOH (R = CF_3, CCl_3, Me, Bu^t, *etc.*) in the presence of catalytic amounts of copper compounds and chiral promoters, (*S*)- and (*R*)-prolines, has been reported.[70] This reaction yields optically active esters. For instance, allylic benzoates **210** and **211** have been prepared from cyclopentene and cyclohexene. Cycloalkenes with larger rings have also been introduced in this reaction.



210–**213**

n = 1 (**210**, 39%, *ee* 56%), 2 (**211**, 59%, *ee* 37%), 3 (**212**, 27%, *ee* 23%), 4 (**213**, 32%, *ee* 4%).

Apart from proline (**214**) and its derivatives **215**, amino acids **216**–**218** were also used as chiral promoters, while acetonitrile or benzene were used as solvents.

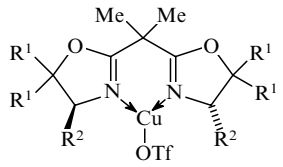


214 **215** **216**

217 **218**

The process enantioselectivity is dictated by the natures of the alkene and the auxiliary chiral reagent and depends little on the nature of the carboxylic acid.

Andrus *et al.*[71] have described allylic acyloxylation of alkenes with *tert*-butyl peroxybenzoate in the presence of catalytic amounts of copper compounds in boiling benzene. Thus cyclic alkenes and oct-1-ene react with $Bu^tOOC(O)Ph$ in the presence of chiral bisoxazoline complexes of copper(I) triflate **219**–**221**

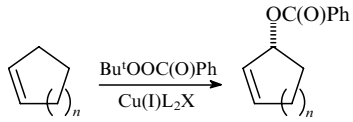


219: $R^1 = H$, $R^2 = Bu^t$;
220: $R^1 = Me$, $R^2 = Bu^t$;
221: $R^1 = Me$, $R^2 = Ph$.

219–**221**

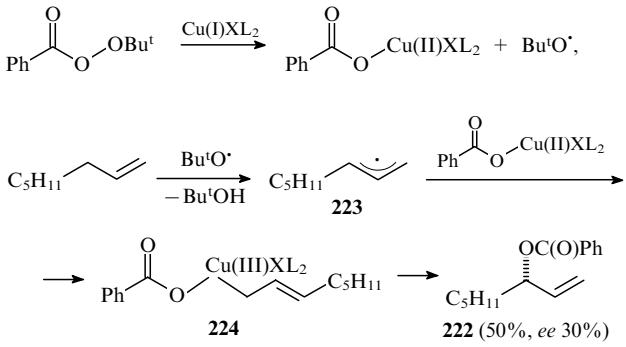
to yield non-racemic allylic benzoates **210**, **211**, **213** and **222**.

In most experiments, acetonitrile served as the solvent, but in some cases (for example, in the synthesis of compound **222**), benzene was used. The reaction mechanism was considered taking oxidation of oct-1-ene as an example.



210, **211**, **213**

Benzoate	*n*	Yield (%)	*ee* (%)
210	1	44	70
211	2	62	67
213	4	62	67



223

224

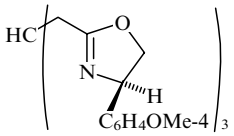
222 (50%, *ee* 30%)

X = OTf.

The reductive homolysis of the peroxide bond under the action of a copper(I) atom affords copper(II) benzoate and a *tert*-butoxyl radical. The latter splits off the allylic hydrogen atom from the olefin, which is converted into allylic radical **223**. This radical rapidly adds to copper(II) benzoate to give a copper(III) complex with the allylic ligand (**224**). The reaction ends in the rearrangement of complex **224** to give allylic ester **222** and to recover the copper(I)-containing catalyst.

Pfaltz *et al.*[72] have also utilised *tert*-butyl peroxybenzoate and copper(I) complexes obtained *in situ* from chiral bisoxazolines and Cu(I)OTf for the oxidation of cycloalkenes. They prepared cycloalk-2-enyl benzoates in satisfactory or good yields. For instance, the transformation products of cyclopentene and cycloheptene were isolated with an enantiomeric excess of 74% at 23 °C and 84% at a low temperature; in the case of cyclohexene, the enantioselectivity is somewhat lower (*ee* 64%–77%). Feringa and co-workers[73] have reported allylic oxidation of cyclohexene with a number of chiral Cu(II) complexes with amino acids.

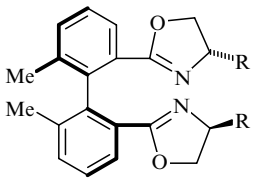
It was found[74] that the copper(II) triflate complex with the tridentate tris(oxazoline) ligand **225** is an efficient chiral catalyst for the asymmetric allylic oxidation of various cycloalkenes with *tert*-butyl peroxybenzoate (Kharash — Sosnovsky reaction).



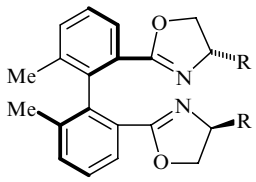
225

Cycloalkenyl benzoates are formed in this reaction in good yields and good enantioselectivities (*ee* > 81%). The reaction can be carried out in acetone, acetonitrile or 1,2-dichloroethane, the highest enantioselectivity being attained in the last-mentioned solvent.

The asymmetric allylic oxidation of cyclohexene and cyclopentene by treatment with *tert*-butyl 4-nitro-, 2-iodo- and 2,4,6-trichloro-substituted peroxybenzoates was also attempted for copper(I) hexafluorophosphate complexes with bis(*o*-tolyl)bisoxazolines **226a**–**d** and **227a**–**d**. This gave allyl benzoates with medium to high selectivities.[75]



(*S*,*S*,*S*)-**226a**–**d**

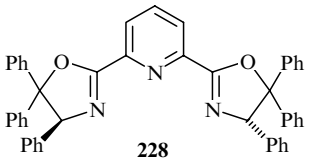


(*S*,*R*,*S*)-**227a**–**d**

R = Ph (**a**), Bu^t (**b**), Bn (**c**), Pr^i (**d**).

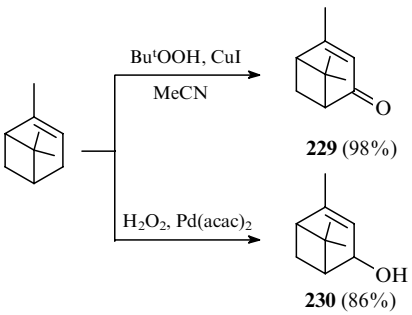
The highest selectivity was reached with 4-nitro-substituted *tert*-butyl peroxybenzoate and ligand **226a** (for cyclohexene, *ee* 73%) or **226c** (for cyclopentene, *ee* 72%).

Indian researchers[76] have used bisoxazoline ligand **228**. This allowed them to increase the enantioselectivity of allylic oxidation of cyclohexene to 86%.



228

Catalytic allylic oxidation of α-pinene with *tert*-butyl hydroperoxide and hydrogen peroxide in the presence of transition metal salts has been reported.[77] It was found that oxidation of α-pinene with the Bu^tOOH–CuI system gives verbenone (**229**) as the major product, while the oxidation with the H_2O_2–$Pd(acac)_2$ system gives predominantly verbenol (**230**).



229 (98%)

230 (86%)

Other terpene alkenes (limonene, 3-carene) have also been involved in this reaction.

Sartori and co-workers[78] reported the use of the Cu-Na-HSZ-320 zeolite as an efficient and reusable catalyst for allylic oxidation

of alkenes into allylic alcohols on treatment with *tert*-butyl peroxybenzoate.

Catalytic allylic oxidation of alkenes with the use of the asymmetric version of the Kharash – Sosnovsky reaction is the subject of a review.[79]

6. Miscellaneous reagents for alkene α-oxidation

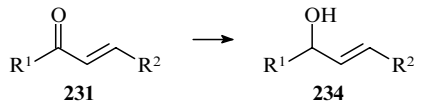
Oxidation of the methylene group in an allylic position with SeO_2 ‡ to give allylic alcohols has been reported.[79, 80]

The SeO_2-catalysed allylic oxidation with *tert*-butyl hydroperoxide as a stoichiometric reagent is more efficient.[28, 81] This reaction has been used for allylic hydroxylation of vinyl fluorides.[82] Photochemical synthesis of allylic alcohols from alkenes has also been described.[83] In this case, a benzene or pyridine solution of alkene or a conjugated diene is irradiated in the presence of oxygen and a sensitiser (methylene blue, some porphyrin derivatives); this gives a hydroperoxide, which is reduced to yield the allylic alcohol. By this method, one can convert alkenes into allylic alcohols with a shifted double bond.[84]

IV. Reagents for the reduction of α,β-unsaturated carbonyl compounds

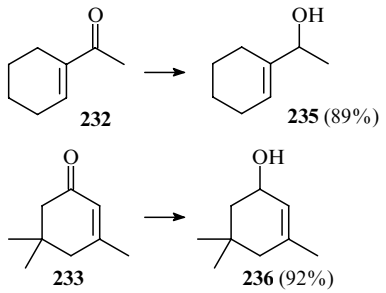
Reduction of α,β-unsaturated carbonyl compounds (aldehydes, ketones, and esters) is a key method for the synthesis of allylic alcohols. However, the use of the most readily available reducing agents such as $NaBH_4$ or $LiAlH_4$ results in the partial or even complete reduction of the double bond;[85] therefore, other hydride reducing agents have been proposed for this purpose.[86, 87]

For example, $Li[(CH_2)_4NBH_3]$ has been used for selective reduction of ketones **231** – **233** into allylic alcohols **234** – **236**.[88, 89]



231 **234**

R^1 = H, R^2 = Ph (99%); R^1 = Me: R^2 = Ph (99%), n-C_5H_{11} (96%).



232 **235** (89%)

233 **236** (92%)

The ratio of 1,2- to 1,4-reduction products was > 99 : 1 in all cases.

Lithium aminoborohydrides are not pyrophoric; therefore, they are used in large-scale reduction processes.

Later, it was shown[90] that α,β-unsaturated ketones **237** are reduced with the $Bu_2SnH_2 - Bu_2SnF_2$ system in combination with HMPA to give allylic alcohols **238**.

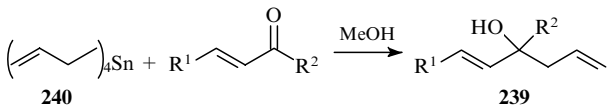


237 **238**

R = H (75%), Me (89%), Ph (56%).

If HMPA is replaced by LiI, the C = C bond is reduced, while the keto group remains intact.

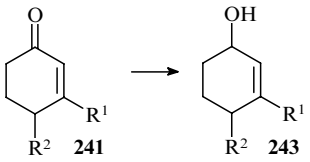
The synthesis of allyl vinyl alcohols **239** by treatment of α,β-unsaturated ketones with tetraallyltin (**240**) has been described.[91]



240 **239**

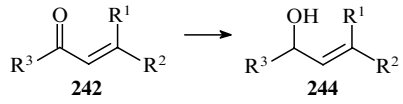
R^1 = H, R^2 = Et (73%); R^1 = Ph, R^2 = Me (91%),
$R^1 - R^2 = (CH_2)_3$ (65%).

Ranu and Das[92, 93] reported that the zinc borohydride – silica gel system is able to reduce conjugated ketones to allylic alcohols. For example, conjugated ketones **241**, **242** were converted into alcohols **243**, **244** in high yields.



241 **243**

R^1 = R^2 = H (15%); R^1 = Me: R^2 = H (80%), COOEt (82%), COOMe (85%).

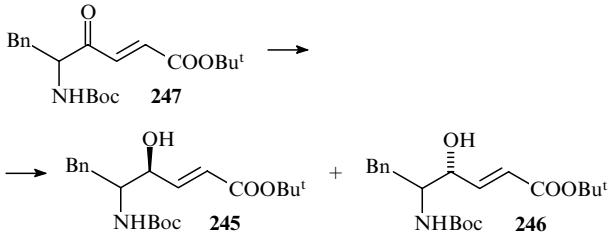


242 **244**

R^1 = H, R^2 = Me: R^3 = H (80%), Me (85%);
R^1 = H, R^2 = Ph: R^3 = H (82%), Me (85%);
R^1 = R^2 = R^3 = Me (79%).

The yield of the product of α-ionone reduction was 85%.

A recent publication[94] describes the formation of diastereomeric allylic alcohols **245** and **246** in 95 : 5 ratio (overall yield 80%) upon the diastereoselective reduction of *N*-Boc-protected δ-amino-α,β-unsaturated γ-ketoester **247** with $LiAlH(OBu^t)_3$ in EtOH at −78 °C under chelation control. The same reduction carried out with non-chelating NB-enantride in THF at −78 °C (so-called Felkin – Anh control) produces alcohols **245** and **246** in 5 : 95 ratio (overall yield 98%).



247

245 **246**

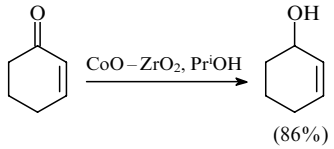
The reduction of ketoester **247** by standard reagents such as $NaBH_4 - CeCl_3$, $Zn(BH_4)_2$, Bu^i_2AlH (DIBAL-H) or a Bu^i_2AlH mixture with $ZnCl_2$ is non-selective.

Another study has also dealt with the reduction of enones to allylic alcohols.[95] It was shown that the reduction of amino-substituted enone obtained on the basis of L-serine with various reducing agents including L-selectride – THF, $LiAlH_4 - Et_2O$, $NaBH_4$ – MeOH, Red-Al – THF {Red-Al is $[(MeOCH_2.OCH_2)_2AlH_2]Na$} and so on results in a mixture of *syn*- and *anti*-isomers of aminoallylic alcohols in very high yields. The size of the hydride influences the diastereoselectivity of the reaction; the greater the hydride size, the higher the yield of the *syn*-isomer. The nature of the solvent also affects the isomer ratio.

Catalytic hydrogenation of the C = C – C = O fragment for the synthesis of allylic alcohols is normally difficult to arrange, especially under heterogeneous catalysis conditions. Nevertheless, a number of catalysts that increase the chemoselectivity and, in some cases, also the enantioselectivity of this reaction have been proposed in recent years.

‡ This reagent is also used in the synthesis of unsaturated carbonyl compounds.

The reduction of α,β-unsaturated ketones using isopropyl alcohol (as the source of hydrogen atoms) and a mixture of $CoO-ZrO_2$ oxides (as the catalyst) has been reported.[96]

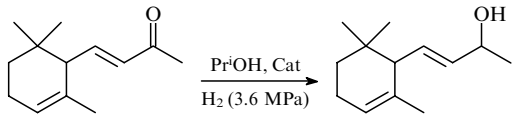


(86%)

$$R^1R^2C{=}CHCHO \xrightarrow{CoO-ZrO_2,\ Pr^iOH} R^1R^2C{=}CHCH_2OH$$

R^1 = H: R^2 = Pr^n (84%), Me (83%), Ph (80%);
R^1 = Me: R^2 = $(CH_2)_2CH{=}CMe_2$ (71%).

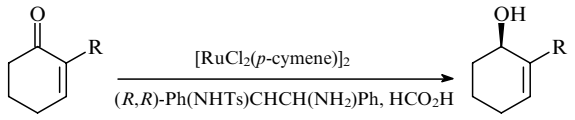
Iridium salts [for example, $Ir(acac)_3$] supported on various zeolites can be used as catalysts (Cat) instead of metal oxides. This method was used for chemoselective reduction of α- and β-ionones, testosterone, cholestenone, and so on.[97] For example,



(75%, *ee* 71%)

High catalytic efficiency in the Meerwein–Ponndorf–Verley reduction of unsaturated ketones to allylic alcohols was found for Zr and Hf catalysts supported on mesoporous materials of the MCM-41 and MCM-48 type.[98]

Wills and co-workers [99] reported the efficient use of asymmetric transfer hydrogenation for the reduction of enones. Numerous catalyst systems have been developed for this process. The system ruthenium(II) complex–chiral monotosylated diamine (or β-aminoalcohol)–formic acid is used most often.



R = Ph (47%, *ee* 72%), OBn (78%, *ee* 99%),
$NHCO_2Me$ (54%, *ee* > 99%).

Other examples of catalytic hydrogenation of enones can be found in the review by Noyori.[100]

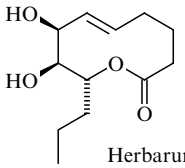
V. Miscellaneous methods

We have considered the most important reagents used to convert alkenes and their derivatives into allylic alcohols *via* cleavage of α-epoxides, allylic hydroxylation and reduction of α,β-unsaturated carbonyl compounds. This Section presents a brief discussion of other general methods for the synthesis of allylic alcohols.

1. Reactions of carbonyl compounds with alkenes and alkynes

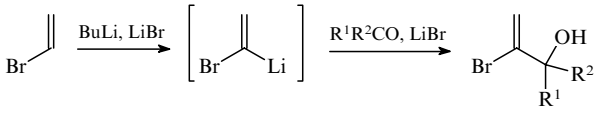
The reaction of alkenylmagnesium halides with aldehydes or ketones (Normann method) is a well-known method for the synthesis of allylic alcohols. The addition of divinylzinc to carbonyl compounds also deserves attention.[101] Subsequently, this strategy has been developed in the field of metal complex catalysis.

The use of nickel(II) chloride and palladium(II) acetate as catalysts of the cross-coupling of iodoalkenes with aldehydes, resulting in the formation of allylic alcohols, has been reported.[102] It is important that double bond configuration in the product is the same as that in iodoalkene. Diastereoselective synthesis of allylic alcohols from α-substituted aldehydes by the Nozaki–Hiyama–Kishi reaction has been reported.[103] This transformation was used in the synthesis of (+)-herbarumin I.



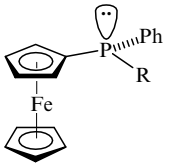
Herbarumin I

An efficient method for the synthesis of bromoallylic alcohols from 1-bromo-1-lithioethene and aldehydes or ketones has been reported.[104]



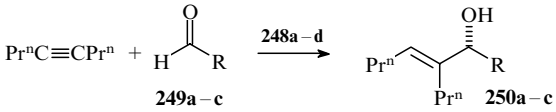
$R^1 = R^2$ = Me (77%); R^1 = Me, $R^2 = CH_2{=}CH$ (78%),
$CH_2{=}CH(CH_2)_2$ (84%), $CH_2{=}CHCMe_2CH_2CH_2$ (80%);
$R^1-R^2 = (CH_2)_5$ (85%); R^2 = H: R^1 = Et (46%), n-C_6H_{13} (50%),
Ph (81%), $CH_2{=}CH$ (74%).

Phosphines containing a ferrocene fragment proved to be efficient ligands for a number of catalytic reactions and a number of metal-catalysed asymmetric reactions.[105–107] It has been found [108] that P-chiral monodentate ferrocenylphosphines **248a–d** can be used as ligands in asymmetric catalytic reductive coupling of oct-4-yne with aldehydes **249a–c** to produce chiral allylic alcohols **250a–c** with high regio- and enantioselectivities.



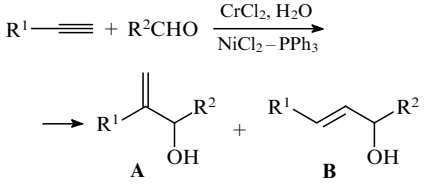
248a–d

R = Me (**a**), 4-$MeOC_6H_4$ (**b**), cyclo-C_6H_{11} (**c**), Bu^n (**d**);



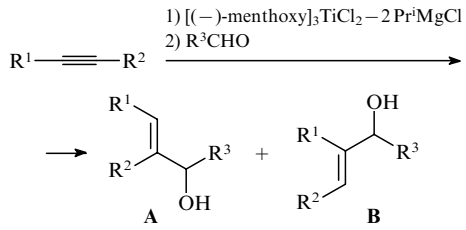
R = Ph (**a**), Pr^n (**b**), Pr^i (**c**).

Racemic allylic alcohols were also prepared *via* intramolecular [109, 110] and intermolecular [111] reductive coupling of alkynes and aldehydes. The reductive coupling of alkyne with aldehyde was also used to synthesise chiral allylic alcohols. Reductive coupling in the presence of stoichiometric amounts of transition metals has been studied by Takai and co-workers,[112] Negishi and co-workers,[113] Livinghouse and co-workers,[114] Takai and Utimoto and co-workers.[115, 116] For example,[112]



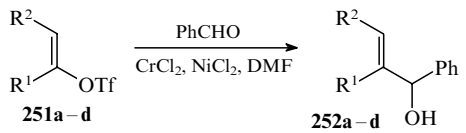
$R^1 = Ph(CH_2)_2$, R^2 = n-C_8H_{17} (82%, **A** : **B** = 95 : 5); R^1 = n-$C_{10}H_{21}$,
R^2 = Ph (99%, **A** : **B** = 94 : 6); R^1 = n-$C_{10}H_{21}$, R^2 = cyclo-C_6H_{11} (78%,
A : **B** = 90 : 10); $R^1 = HO(CH_2)_2$, $R^2 = Ph(CH_2)_2$ (83%, **A** : **B** = 99 : 1).

The use of a chiral titanium complex–alkyne system in the synthesis of chiral alcohols has been reported.[117]



$R^1 = R^2 = n\text{-}C_5H_{11}$: R^3 = Et, Pr^i, cyclo-C_6H_{11};
$R^1 = Me_3Si$, R^3 = cyclo-C_6H_{11}: $R^2 = n\text{-}C_6H_{13}$, Ph.

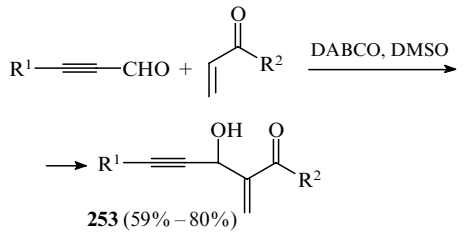
The reaction between alkenyl triflates and aldehydes[118] induced by $CrCl_2$ in the presence of catalytic amounts of $NiCl_2$ is similar in essence. For example, triflates **251a–c** react with benzaldehyde in the presence of $CrCl_2$ and catalytic amounts of $NiCl_2$ in DMF to give the corresponding allylic alcohols **252a–c** in high yields. In ether and THF, which sparingly dissolve $CrCl_2$, this reaction barely proceeds. Other aldehydes can also be introduced in this reaction, for example, $C_8H_{17}CHO$ or $Pr^iCH=CHCHO$. In the presence of other catalysts such as $MnCl_2$, $FeCl_3$, $CoCl_2$ and $PdCl_2$, the yield of the target product decreases. In addition, decomposition of triflates is possible. Steric factors associated with the presence of substituents at the double bond can have a pronounced influence on the reaction route.



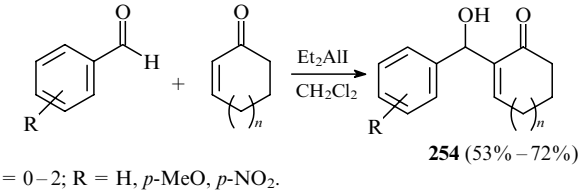
R^1 = Bu, R^2 = H (**a**); $R^1 = n\text{-}C_{10}H_{21}$, R^2 = H (**b**);
$R^1 - R^2 = (CH_2)_4$ (**c**); R^1 = Me, R^2 = Ph (**d**).

A mechanism including the reduction of nickel(II) chloride to nickel(0) with $CrCl_2$ has been proposed for this transformation. Nickel and triflates form organonickel compounds, which undergo transmetallation. The resulting organochromium compounds react with aldehydes.

For the synthesis of functionally substituted allylic alcohols, the Baylis–Hillman reaction is used. These alcohols are important intermediates in the synthesis of many natural compounds: alkaloids, pyrethroids, steroids, pheromones, and so on. In particular, allylpropargyl alcohols **253**[119] and 2-(α-hydroxybenzyl)cyclohex-2-enone (**254**)[120] have been synthesised in this way.



R^1 = Ph, $n\text{-}C_6H_{13}$; R^2 = Me, OEt; DABCO is diazabicyclooctane.

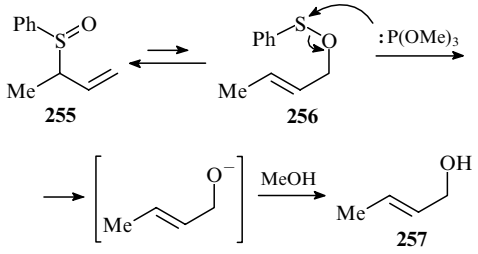


n = 0–2; R = H, *p*-MeO, *p*-NO_2.

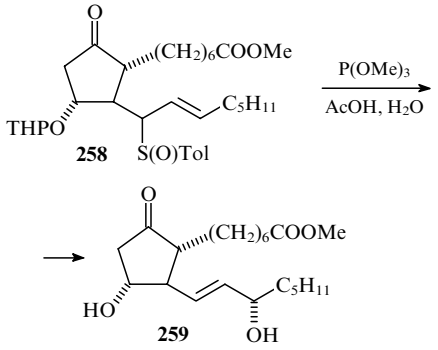
2. [2,3]-Sigmatropic rearrangements of chalcogen oxides

It has been noted above that oxidative elimination of a selenium group is a general method for the synthesis of alkenes.[28] However, during the oxidation of allyl selenides, the intermediate selenium oxide undergoes a [2,3]-sigmatropic rearrangement involving the double bond, resulting in the selenenic ester of the rearranged allylic alcohol and finally in the corresponding allylic alcohol.

In the case of analogous sulfur compounds, this reaction is less typical, although some examples are known (see the review[121]). Thus on heating in the presence of trimethyl phosphite, allyl sulfoxide **255** is partially rearranged into the allyl ester of sulfenic acid **256**.[121] As a rule, the equilibrium in this reaction is largely shifted toward the sulfoxide, but on treatment of the reaction mixture with a thiophilic reagent (for example, trimethyl phosphite and diethylamine), the sulfenate is irreversibly converted into allylic alcohol **257**.



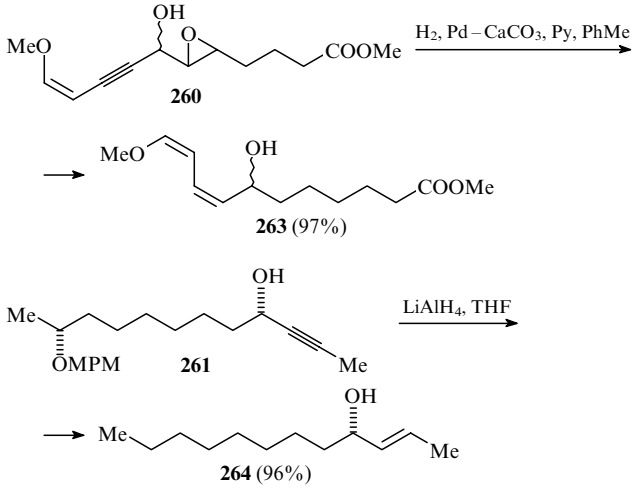
The transformation of sulfoxide **258** into allylic alcohol **259**, which is the racemic form of prostaglandin E (PGE_1), has been reported.[122]

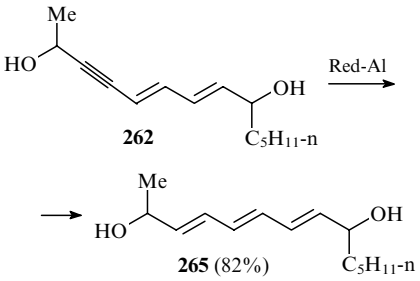


Other examples of rearrangement of sulfoxides and sulfones and the use of products of these rearrangements in total syntheses of natural compounds are given in the review by Prilezhaeva.[123]

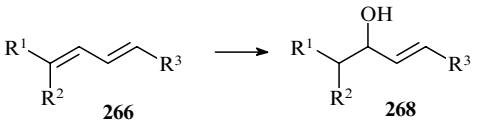
3. Other methods

In conclusion, we would like to note that allylic alcohols are formed upon partial hydrogenation of many acetylenic alcohols. The appropriate reducing agents include $LiAlH_4$, Red-Al, hydrogen with special catalysts, for example Pd–$CaCO_3$ (Lindlar catalyst) and so on. The reduction of acetylenes **260–262** has resulted in the preparation of allylic alcohols **263–265**.[124–126]

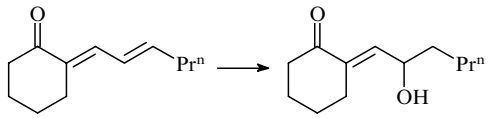




The reduction – oxygenation sequence induced by molecular oxygen and triethylsilane catalysed by cobalt(II) porphyrinate followed by treatment with trimethyl phosphite performs the transformation of compounds **266**, **267** into compounds **268**, **269**, containing an allyl alcohol fragment.[127]



$R^1 = R^2 = Me$, $R^3 = COOEt$ (81%); $R^1 = Bu^n$, $R^2 = H$, $R^3 = CHO$ (54%); $R^1 = n\text{-}C_6H_{13}$, $R^2 = H$, $R^3 = COOBu^t$ (73%); $R^1 = Pr^n$, $R^2 = H$, $R^3 = COOEt$ (82%).



References

1. J K Crandall, M Apparu *Org. React.* **29** 345 (1983)
2. J G Smith *Synthesis* 629 (1984)
3. A S Rao, S K Paknikar, J G Kirtane *Tetrahedron* **39** 2323 (1983)
4. P Mosset, S Manna, J Viala, J R Falck *Tetrahedron Lett.* **27** 299 (1986)
5. J K Crandall, L H Chang *J. Org. Chem.* **32** 532 (1967)
6. M Asami *Tetrahedron Lett.* **26** 5803 (1985)
7. M Asami *Bull. Chem. Soc. Jpn.* **63** 721 (1990)
8. M Asami, T Ishizaki, S Inone *Tetrahedron Lett.* **36** 1893 (1995)
9. D Bhuniya, V K Singh *Synth. Commun.* **24** 375 (1994)
10. B Colman, S E de Sousa, P O'Brien, T D Towers, W Watson *Tetrahedron: Asymmetry* **10** 4175 (1999)
11. M Asami, M Ogawa, S Inoue *Tetrahedron Lett.* **40** 1563 (1999)
12. P O'Brien, T D Towers, M Voith *Tetrahedron Lett.* **39** 8175 (1998)
13. P O'Brien *J. Chem. Soc., Perkin Trans. 1* 1439 (1998)
14. M J Sodergren, S K Bertilsson, P G Andersson *J. Am. Chem. Soc.* **122** 6610 (2000)
15. M J Sodergren, P G Andersson *J. Am. Chem. Soc.* **120** 10760 (1998)
16. S K Bertilsson, P G Andersson *Tetrahedron* **58** 4665 (2002)
17. A Gayet, S K Bertilsson, P G Andersson *Org. Lett.* **4** 3777 (2002)
18. S V Malhotra *Tetrahedron: Asymmetry* **14** 645 (2003)
19. A Johansson, P Abrahamsson, Ö Davidson *Tetrahedron: Asymmetry* **14** 1261 (2003)
20. A Yasuda, H Yamamoto, H Nozaki *Bull. Chem. Soc. Jpn.* **52** 1705 (1979)
21. S Murata, M Suzuki, R Noyori *J. Am. Chem. Soc.* **101** 2738 (1979)
22. G A Kraus, K Frazier *J. Org. Chem.* **45** 2579 (1980)
23. M E Jung, M A Lyster *J. Org. Chem.* **42** 3761 (1977)
24. M R Detty *J. Org. Chem.* **45** 924 (1980)
25. G A Olah, S C Narang, B G B Gupta, R Malhotra *J. Org. Chem.* **44** 1247 (1979)
26. M E Jung, T A Blumenkopf *Tetrahedron Lett.* 3657 (1978)
27. T L Ho, G A Olah *Synthesis* 417 (1977)
28. K C Nicolaou, N A Petasis *Selenium in Natural Products Synthesis* (Philadelphia: CIS INC, 1984)
29. X Huang, W Xu *Tetrahedron Lett.* **43** 5495 (2002)
30. C Baylon, M P Heck, C Mioskowski *J. Org. Chem.* **64** 3354 (1999)
31. R J Davoille, D T Rutherford, S D R Christie *Tetrahedron Lett.* **41** 1255 (2000)
32. L Alcaraz, A Cridland, E Kinchin *Org. Lett.* **3** 4051 (2001)
33. G A Molander, B E La Belle, G Hahn *J. Org. Chem.* **51** 5259 (1986)
34. J M Aurrecoechea, W H Okamura *Tetrahedron Lett.* **28** 4947 (1987)
35. K C Nicolaou, M E Duggan, T Ladduwahetty *Tetrahedron Lett.* **25** 2069 (1984)
36. T Katsuki, K B Sharpless *J. Am. Chem. Soc.* **102** 5974 (1980)
37. L A Sarandeses, A Mouriño, J-L Luche *J. Chem. Soc., Chem. Commun.* 818 (1991)
38. J S Yadav, T Shekharam, V R Gadgil *J. Chem. Soc., Chem. Commun.* 843 (1990)
39. J S Yadav, V R Gadgil *J. Chem. Soc., Chem. Commun.* 1824 (1989)
40. J S Yadav, T Shekharam, D Srinivas *Tetrahedron Lett.* **33** 7973 (1992)
41. E Vedejs, J M Dolphin, W T Stolle *J. Am. Chem. Soc.* **101** 249 (1979)
42. S Chandrasekhar, M Takhi, J S Yadav *Tetrahedron Lett.* **36** 307 (1995)
43. Y Gao, R M Hannon, J M Klunder, S Y Ko, H Masamune, K B Sharpless *J. Am. Chem. Soc.* **109** 5765 (1987)
44. L Dehoux, E Doris, C Mioskowski *Chem. Commun.* 549 (1996)
45. D M Hodgson, M A H Stent, F X Wilson *Org. Lett.* **3** 3401 (2001)
46. D M Hodgson, C R Maxwell, T J Miles, E Paruch, M A H Stent, I R Matthews, F X Wilson, J Witherington *Angew. Chem., Int. Ed.* **41** 4313 (2002)
47. J A Marshall *Chem. Rev.* **89** 1503 (1989)
48. J P Marino, N Hatanaka *J. Org. Chem.* **44** 4467 (1979)
49. J P Marino, R F Pradilla, E Labrode *J. Org. Chem.* **52** 4898 (1987)
50. Y Yamamoto *Angew. Chem., Int. Ed. Engl.* **25** 947 (1986)
51. B H Lipshutz *Synlett* 119 (1990)
52. E Nakamura *Synlett* 539 (1991)
53. S K Kang, D H Lee, H S Sim, J S Lim *Tetrahedron Lett.* **34** 91 (1993)
54. K Mori, T Suguro, M Uchida *Tetrahedron* **34** 3119 (1978)
55. F Badalassi, P Crotti, F Macchia, M Pineschi, A Arnold, B L Feringa *Tetrahedron Lett.* **39** 7795 (1998)
56. H B Kagan, J C Fiaud *Top. Stereochem.* **18** 249 (1988)
57. O Molt, T Schrader *Synthesis* 2633 (2002)
58. S Brandange, J E Backvall, H Leijonmarck *J. Chem. Soc., Perkin Trans. 1* 2051 (2001)
59. J R Gilmore, J M Mellor *J. Chem. Soc.* 2355 (1971)
60. W Kitching, Z Rappaport, S Winstein, W G Young *J. Am. Chem. Soc.* **88** 2054 (1966)
61. G H Whitham *J. Chem. Soc.* 2232 (1961)
62. A Heumann, M Reglier, B Waegell *Angew. Chem., Int. Ed. Engl.* **21** 366 (1982)
63. B M Trost *Tetrahedron* **33** 2615 (1977)
64. B M Trost, T R Verhoeven, J M Fortunak *Tetrahedron Lett.* 2301 (1979)
65. S Hansson, A Heumann, T Rein, B Aakermark *J. Org. Chem.* **55** 975 (1990)
66. S B Bystroem, E M Larsson, B Aakermark *J. Org. Chem.* **55** 5674 (1990)
67. E M Larsson, B Aakermark *Tetrahedron Lett.* **34** 2523 (1993)
68. M A Brimble, M K Edmonds, G M Williams *Tetrahedron Lett.* **31** 7509 (1990)
69. B Bernet, P M Bishop, M Caron, T Kawamata, B L Roy, L Ruest, G Sauve, P Soucy, P Deslongchamps *Can. J. Chem.* **63** 2810 (1985)
70. A Levina, J Mazart *Tetrahedron: Asymmetry* **6** 147 (1995)
71. M B Andrus, A B Argade, X Chen, M G Pamment *Tetrahedron Lett.* **36** 2945 (1995)
72. A S Gokhale, A B E Mindis, A Pfaltz *Tetrahedron Lett.* **36** 1831 (1995)
73. M T Rispens, C Zondervan, B L Feringa *Tetrahedron: Asymmetry* **6** 661 (1995)

74. Y Kohmura, T Katsuki *Tetrahedron Lett.* **41** 3941 (2000)
75. M B Andrus, D Asgari *Tetrahedron* **56** 5775 (2000)
76. R M Kamble, G Sekar, V K Singh *Proc. Indian Natl. Sci. Acad.* **68** 423 (2002)
77. B A Allal, L El Firdoussi, S Allaoud, A Karim, Y Castanet, A Mortreux *J. Mol. Catal. A: Chem.* **200** 177 (2003)
78. S Carloni, B Frullanti, R Maggi, A Mazzacani, F Bigi, G Sartori *Tetrahedron Lett.* **41** 8947 (2000)
79. J Eames, M Watkinson *Angew. Chem., Int. Ed.* **40** 3567 (2001)
80. G Aranda, M BertranneDelahaye, R Azerad, M Maurs, M Cortes, H Ramirez, G Vernal, T Prange *Synth. Commun.* **27** 45 (1997)
81. M A Umbreit, K B Sharpless *J. Am. Chem. Soc.* **99** 5526 (1977)
82. T Ernet, G Haufe *Synthesis* 953 (1997)
83. R W Denny, A Nickon *Org. React.* **20** 133 (1973)
84. A K Banerjee, A Martin, T Nakano, A Usubillaga *J. Org. Chem.* **38** 3807 (1973)
85. R S Varma, G W Kabalka *Synth. Commun.* **15** 985 (1985)
86. J M Fortunato, B Ganem *J. Org. Chem.* **41** 2194 (1976)
87. E J Corey, J O Link *Tetrahedron Lett.* **30** 6275 (1989)
88. Y Okude, S Hirano, T Hiyama, H Nozaki *J. Am. Chem. Soc.* **99** 3179 (1977)
89. J C Fuller, E L Stangeland, C T Goralski, B Singaram *Tetrahedron Lett.* **34** 257 (1993)
90. T Moriuchi-Kawakami, H Matsuda, I Shibata, M Miyatake, T Suwa, A Baba *Bull. Chem. Soc. Jpn.* **72** 465 (1999)
91. S K Leitch, A McCluskey *Synlett* 699 (2003)
92. B C Ranu *Synlett* 885 (1993)
93. B C Ranu, A R Das *J. Org. Chem.* **56** 4796 (1991)
94. J Vabena, M Brisander, T Lejan, K Luthman *J. Org. Chem.* **67** 9186 (2002)
95. A M P Koskinen, P M Koskinen *Tetrahedron Lett.* **34** 6765 (1993)
96. S U Sonavane, R V Jayaram *Synlett* 146 (2004)
97. M De Bruyn, S Coman, R Bota, V I Parvulescu, D E De Vos *Angew. Chem., Int. Ed.* **42** 5333 (2003)
98. M De Bruyn, M Limbourg, J Denayer, G V Baron, V I Parvulescu, P J Grobet, D E De Vos, P A Jacobs *Appl. Catal. A* **254** 189 (2003)
99. J Hannedouche, J A Kenny, T Walsgrove, M Wills *Synlett* 263 (2002)
100. R Noyori *Angew. Chem., Int. Ed.* **41** 2008 (2002)
101. W Oppolzer, R N Radinov *Tetrahedron Lett.* **29** 5645 (1988)
102. H Jin, J-i Uenishi, W J Christ, Y Kishi *J. Am. Chem. Soc.* **108** 5644 (1986)
103. A A Sabino, R A Pilli *Tetrahedron Lett.* **43** 2819 (2002)
104. Y Y Novikov, P Sampson *Org. Lett.* **5** 2263 (2003)
105. K Tanaka, S Quio, M Tobisu, M M Lo, G C Fu *J. Am. Chem. Soc.* **122** 9870 (2000)
106. C J Richards, A J Locke *Tetrahedron: Asymmetry* **9** 2377 (1998)
107. R Shintani, M M Lo, G C Fu *Org. Lett.* **2** 3695 (2000)
108. E A Colby, T F Jamison *J. Org. Chem.* **68** 156 (2003)
109. J Montgomery *Acc. Chem. Res.* **33** 467 (2000)
110. X-Q Tang, J Montgomery *J. Am. Chem. Soc.* **122** 6950 (2000)
111. W S Huang, J Chan, T F Jamison *Org. Lett.* **2** 4221 (2000)
112. K Takai, S Sakamoto, T Isshiki *Org. Lett.* **5** 653 (2003)
113. K Takagi, C J Rousset, E-i Negishi *J. Am. Chem. Soc.* **113** 1440 (1991)
114. B C van Wagenen, T Livinghouse *Tetrahedron Lett.* **30** 3495 (1989)
115. K Takai, Y Kataoka, K Utimoto *J. Org. Chem.* **55** 1707 (1990)
116. Y Kataoka, J Miyai, K Oshima, K Takai, K Utimoto *J. Org. Chem.* **57** 1973 (1992)
117. Y Takayanagi, K Yamashita, Y Yoshida, F Sato *Chem. Commun.* 1725 (1996)
118. K Takai, M Tagashira, T Kuroda, K Oshima, K Utimoto, H Nosaki *J. Am. Chem. Soc.* **108** 6048 (1986)
119. P R Krishna, E R Sekhar, V Kannan *Tetrahedron Lett.* **44** 4973 (2003)
120. W Pei, H-X Wei, G Li *Chem. Commun.* 2412 (2002)
121. D A Evans, G C Andrews *Acc. Chem. Res.* **7** 147 (1974)
122. Y Masaki, K Hashimoto, K Kaji *Chem. Pharm. Bull.* **32** 3959 (1984)
123. E N Prilezhaeva *Usp. Khim.* **70** 1013 (2001) [*Russ. Chem. Rev.* **70** 897 (2001)]
124. E J Corey, J O Albright *J. Org. Chem.* **48** 2114 (1983)
125. S Takano, T Murakami, K Samizu, K Ogasawara *Heterocycles* **39** 67 (1994)
126. M Mladenova, M Alami, G Linstrumelle *Synth. Commun.* **26** 2831 (1996)
127. Y Matsushita, K Sugamoto, T Nakama, T Sakamoto, T Matsui, M Nakayama *Tetrahedron Lett.* **36** 1879 (1995)